

Title: Artichoke (*Cynara scolymus* L.): a review of its health-promoting properties.

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Abstract

Cynara scolymus L., called artichoke or globe artichoke, is a perennial herbaceous plant cultivated worldwide. This plant is a common component of the Mediterranean diet and has been used as a remedy for health conditions since antiquity. The aim of this review is to find the health-promoting properties of artichoke, conducting a literature search in PubMed. The results show that 119 studies describe these effects and 17 health benefits of artichoke are reported in the scientific literature. Antioxidant activity and effects on the liver and lipid profile are the main health-promoting properties of this plant. We found that artichoke also improves cardiovascular and gastrointestinal health and exerts anticancer, antimetabolic and antiobesity, prebiotic and probiotic, renoprotective and antidiabetic activities. Only one or two research articles reported the positive effects of this plant on the immune system, arthritis, photoaging, the reproductive system, the nervous system, fungal infections and periodontal diseases. The health benefits are mainly exerted by phenolics. In conclusion, this review shows the health-promoting properties of artichoke. The main beneficial effects are antioxidant activity and effects on lipid profile and the liver, which are mainly mediated by phenolics. The results of the scientific articles described in this review and the molecular mechanisms related to the health benefits of artichoke should be confirmed by future experimental studies.

Keywords: Artichoke, *Cynara scolymus* L., Antioxidant, Hepatoprotective, Lipid profile

Impact statement: Artichoke (*Cynara scolymus* L.) has many health benefits and the main properties are antioxidant activity and effects on the liver and lipid profile.

1. Introduction

Cynara scolymus L. is a plant species which belongs to the family Asteraceae (IPNI, 2023). This perennial plant, commonly known as artichoke or globe artichoke, is grown worldwide. Artichoke is endemic to the Mediterranean region and has probably been tamed in southern Italy. The Arabs brought it to other parts of the Mediterranean in medieval times (Pignone and Sonnante, 2004). Ancient populations did know artichoke for its nutritional and health-promoting properties (Sonnante *et al.*, 2007). The scientific name comes from the Latin word "*cinis*" and the Greek word "*skolymos*", which mean "ash" and "cardoon", respectively (Verotta *et al.*, 2015).

Artichoke is a herbaceous plant that can reach about 1.80 metres in height. The flower head is globe-shaped with green and violet external bracts. The receptacle is located in the lower part of the artichoke head and the "choke" made up of bristles is found above it. Many blue-purple flowers are arranged in the centre of the head (Fig.1). Artichoke buds are cut before blooming and the edible part includes the receptacle and the inner bracts (Basay, 2022; Grieve, 1931). This plant is a common ingredient of the Mediterranean diet and is widely utilised for health purposes. Artichoke leaves are mainly used in infusions and extracts for their health-promoting properties (Mulinacci *et al.*, 2004; Pereira *et al.*, 2015).

[Insert Fig. 1 here]

This plant contains minerals, vitamins, dietary fibres and bioactive compounds, which are responsible for its beneficial effects. Phenolics include: hydroxycinnamic acids, such as chlorogenic acid (Fig.2), caffeic acid and cynarine (Fig.3); anthocyanidins, such as cyanidin; flavones, such as apigenin and luteolin (Fig.4). Triterpenes and sesquiterpene lactones (e.g., cynaropicrin) (Fig.5) are also found in artichoke. Finally, this plant contains inulin, which is a

fibre with health-promoting properties (Azzini *et al.*, 2007; Ceccarelli *et al.*, 2010; Lattanzio *et al.*, 2009; Panizzi and Scarpati, 1954; Rocchetti *et al.*, 2020).

[Insert Fig. 2, Fig. 3, Fig. 4 and Fig. 5 here]

In this review, we search the scientific literature to identify the health benefits of artichoke. This plant has been used for treating health conditions since ancient times and is still largely utilised by healthcare and herbal practitioners. Research has focused on its properties and there is increasing interest in the different beneficial effects and the molecular mechanisms involved in these activities. Our work has great significance, as it includes the latest research findings on this topic.

2. Methods

We investigated the beneficial effects of artichoke on human health, searching for scientific articles in the PubMed database (<https://pubmed.ncbi.nlm.nih.gov/>). The following keywords were used: "artichoke", "*Cynara scolymus*", "artichoke therapeutic effects", "*Cynara scolymus* therapeutic effects", "artichoke properties", "artichoke health benefits", "artichoke health-promoting properties", "artichoke phytotherapy", "*Cynara scolymus* phytotherapy", "artichoke disease treatment" and "*Cynara scolymus* disease treatment". The article types selected in PubMed were: clinical trials, randomized controlled trials, books and documents. We included only previous studies relating to the topic of this review and written in English. We excluded reviews, systematic reviews, meta-analyses and articles which show only negative results or adverse effects of artichoke. We chose the scientific studies through an initial screening by reading titles and abstracts. In a second moment, we read the whole texts to find the proper scientific articles.

3. Results and Discussion

The results of literature search indicate that 1374 articles are included in PubMed. We chose 119 studies after article screening and we identified 17 health-promoting properties of artichoke (Table 1).

[Insert Table 1 here]

3.1. Effects on the liver

Two previous studies showed the beneficial effect of artichoke leaf extract (ALE) alone (Panahi *et al.*, 2018) or in combination with metformin or vitamin E (Majnooni *et al.*, 2021) in individuals with non-alcoholic fatty liver disease (NAFLD). Other scientific articles reported that artichoke extracts improve NAFLD in rodents (Deng *et al.*, 2022; Lee *et al.*, 2021b). Rangboo and colleagues (2016) showed that ALE exerts hepatoprotective activity in a sample of 60 individuals with non-alcoholic steatohepatitis (NASH). A study by Tang *et al.* (2017) found that an artichoke extract has a beneficial effect on alcoholic liver disease (ALD) in mice. Previous studies demonstrated that ALE exerts hepatoprotective effects *in vivo* (Ahmadi *et al.*, 2019; Ben Salem *et al.*, 2017b; Ben Salem *et al.*, 2019; Celepli *et al.*, 2022a; Celepli *et al.*, 2022b; El-Boshy *et al.*, 2017; El Morsy and Kamel, 2015; Elsayed Elgarawany *et al.*, 2020; Heidarian and Rafieian-Kopaei, 2013; Küçükgergin *et al.*, 2010; Kurt *et al.*, 2014; Kwon *et al.*, 2018; Liao *et al.*, 2021; Mehmetçik *et al.*, 2008; Nasef *et al.*, 2022; Sharaf El-Deen *et al.*, 2017), *in vitro* (Menghini *et al.*, 2010) and *ex vivo* (Wauquier *et al.*, 2021). Sümer and colleagues (2020) demonstrated that stem and receptacle extracts have this effect in rats. A study by Speroni *et al.* (2003) showed that an extract with high phenolic content exerts hepatoprotective and choleric effects in rats and scientific articles reported that artichoke has hepatoprotective effects in these laboratory animals (Colak *et al.*, 2016; Metwally *et al.*, 2011; Wang *et al.*, 2021). Qiang and

colleagues (2012) found that ALE increases bile acid secretion in hamsters. Scientific articles showed that artichoke extracts exert choleric activity *in vivo* (Kirchhoff *et al.*, 1994; Saénz Rodríguez *et al.*, 2002) and *in vitro* (Frigerio *et al.*, 2021). Previous studies demonstrated that this plant extracts have hepatoprotective (Gebhardt, 1997; Gebhardt and Fausel, 1997; Miccadei *et al.*, 2008) and anticholestatic (Gebhardt, 2001; Gebhardt, 2002b) effects *in vitro*, which are mainly exerted by phenolics. Gebhardt (2002a) showed that liver cholesterol synthesis can be inhibited by ALE *in vitro* and flavones are the bioactive compounds mainly involved in this effect.

3.2. Effects on lipid profile

Previous studies found that ALE intake alone (Panahi *et al.*, 2018) or in association with metformin or vitamin E (Majnooni *et al.*, 2021) improves lipid profile in individuals with NAFLD. A study by Rangboo *et al.* (2016) showed that ALE consumption is effective in lowering triglycerides, total cholesterol and low-density lipoprotein cholesterol (LDL-C) in a cohort of 60 individuals with NASH. Shimoda and colleagues (2003) demonstrated that the beneficial effect of artichoke on lipid profile is exerted by sesquiterpenes. Another study by Bundy *et al.* (2008) showed that ALE can be effective in reducing total cholesterol in individuals with hypercholesterolemia. Englisch and colleagues (2000) demonstrated that ALE can lower LDL-C and total cholesterol in a cohort of 143 individuals with hyperlipoproteinemia. A previous study by Rondanelli *et al.* (2013) found that ALE intake reduces total cholesterol and LDL-C and raises high-density lipoprotein cholesterol (HDL-C) in a sample of 92 patients with hypercholesterolemia, while other scientific articles reported that artichoke extracts can decrease triglycerides, total cholesterol and LDL-C and improve HDL-C in rats (Ben Salem *et al.*, 2017b; Deng *et al.*, 2022). Rondanelli and colleagues (2019) demonstrated that ALE improves HDL-C and lowers total cholesterol/HDL-C ratio in a cohort of 20 individuals with mild

hypercholesterolemia. Another study found that consumption of an artichoke extract ameliorates lipid profile in a sample of 55 overweight individuals with impaired fasting glycaemia (Rondanelli *et al.*, 2014). Two articles reported the beneficial effect of ALE on cholesterol homeostasis, performing *in vitro* (Frigerio *et al.*, 2021) and *ex vivo* (Wauquier *et al.*, 2021) experiments. Previous studies found the beneficial effect of artichoke extracts on lipid profile in rodents (Ben Salem *et al.*, 2019; Ben Salem *et al.*, 2022a; Bogavac-Stanojevic *et al.*, 2018; Heidarian and Rafieian-Kopaei, 2013; Ibrahim *et al.*, 2022; Küçükgergin *et al.*, 2010; Kuskü-Kiraz *et al.*, 2010; Kwon *et al.*, 2018; Liao *et al.*, 2021; Qiang *et al.*, 2012; Qinna *et al.*, 2012; Tang *et al.*, 2017). A study by Gebhardt (1998) showed that ALE is effective in suppressing hepatic cholesterol synthesis in rats and luteolin is implicated in this activity.

3.3. Effects on the cardiovascular system

A previous study by Lupattelli *et al.* (2004) found that artichoke leaf juice has beneficial effects on endothelial function in a sample of 28 individuals with hyperlipidemia, while Roghani-Dehkordi and Kamkhah (2009) demonstrated that artichoke leaf juice is effective in reducing blood pressure in individuals with mild hypertension. Other studies showed the protective effects of artichoke extracts on the cardiovascular system *in vivo* (Ben Salem *et al.*, 2022a; Bogavac-Stanojevic *et al.*, 2018; Crevar-Sakac *et al.*, 2016; Küçükgergin *et al.*, 2010) and *in vitro* (Juzyszyn *et al.*, 2008; Zapolska-Downar *et al.*, 2002). A previous scientific article reported the health benefits of artichoke bud extract in a rat model of hypertension (Wang *et al.*, 2021). Li and colleagues (2004) found that ALE can improve expression and function of endothelial nitric oxide synthase (eNOS), performing *in vitro* and *ex vivo* experiments and flavones are involved in this activity. Another study showed that ALE can inhibit the expression of inducible nitric oxide synthase (iNOS) in vascular smooth muscle cells and the phytochemical compounds mainly implicated in this effect are cynarine and cyanidin (Xia *et al.*, 2014).

3.4. Effects on the gastrointestinal system

Previous studies demonstrated the beneficial effect of ALE on the gastrointestinal system in individuals with functional (Holtmann *et al.*, 2003) and mild (Marakis *et al.*, 2002) dyspepsia. Other studies showed that ALE is effective in alleviating irritable bowel syndrome (IBS) symptoms in individuals with this condition (Bundy *et al.*, 2004; Walker *et al.*, 2001). Nassar and colleagues (2013) found that an artichoke head extract can exert antiulcerogenic activity in rats. Other studies showed that cynaropicrin has antispasmodic effect on the gastrointestinal tract of guinea pigs (Emendörfer *et al.*, 2005) and antigastritis activity in rats (Ishida *et al.*, 2010). Verspohl and colleagues (2008) demonstrated the beneficial effect of ALE on IBS in an experiment performed on the ileum of rats and a previous study found the anti-colitis activity of artichoke pectin in mice (Sabater *et al.*, 2019).

3.5. Antimetabolic and antiobesity activity

Previous studies showed that ALE intake is effective in ameliorating metabolic syndrome biomarkers (Ebrahimi-Mameghani *et al.*, 2018; Rezazadeh *et al.*, 2018a; Rezazadeh *et al.*, 2018b). Ardalani and colleagues (2020) found that ALE can reduce body mass index (BMI) in overweight individuals, while Wauquier and colleagues (2021) demonstrated the protective effect of ALE on obesity and metabolic syndrome, performing an *ex vivo* study. A previous study showed the health benefits of an artichoke extract, studying a cohort of 55 overweight individuals with impaired fasting glycaemia (Rondanelli *et al.*, 2014). Other studies demonstrated the antiobesity and antimetabolic syndrome activities of ALE in rodents (Ben Salem *et al.*, 2019; Ben Salem *et al.*, 2022a; Kwon *et al.*, 2018).

3.6. Anticancer activity

A previous study showed the protective effect of an artichoke extract on pleural mesothelioma in a sample of 18 individuals with asbestos-related benign pleural disease (Muti *et al.*, 2022). A study by Pulito *et al.* (2015) found the antitumor effect of ALE against malignant pleural mesothelioma *in vivo* and *in vitro*. Liu and colleagues (2019) demonstrated the anticancer activity of cynaropicrin in HeLa cells. This bioactive compound found in artichoke may exert an inhibitory effect on thioredoxin reductase and promote oxidative stress, which lead to apoptosis. Previous studies showed the beneficial effects of this plant in a rat model of hepatocellular carcinoma (Metwally *et al.*, 2011) and the potential anticancer effects of artichoke extracts in human hepatocellular carcinoma (Menghini *et al.*, 2010; Miccadei *et al.*, 2008), uterine leiomyoma (Islam *et al.*, 2021), breast cancer (Mileo *et al.*, 2012; Mileo *et al.*, 2015; Mileo *et al.*, 2020) and colon cancer (Villarini *et al.*, 2021) cells. Scientific articles reported that cynaropicrin may exert anticancer activity in anaplastic thyroid cancer (Lepore *et al.*, 2019) and lung carcinoma (Ding *et al.*, 2021) cells. Yang and colleagues (2022) showed the antitumor effects of this bioactive compound against neuroblastoma *in vivo* and *in vitro*. A study by Abdel-Moneim *et al.* (2021) found the beneficial effect of artichoke extracts on lung cancer in rats, which is exerted mainly through antioxidant, proapoptotic and antiproliferative activities.

3.7. Probiotic and prebiotic activities

Previous studies showed that the intake of artichoke fortified with a probiotic (i.e., *Lactobacillus paracasei*) can improve constipation in individuals with this condition (Riezzo *et al.*, 2012; Valerio *et al.*, 2010). Other scientific articles reported the prebiotic activity of long-chain inulin from artichoke in a sample of 31 healthy individuals (Costabile *et al.*, 2010) and *in vitro* (López-Molina *et al.*, 2005; Zeaiter *et al.*, 2019). Fissore and colleagues (2015) demonstrated that artichoke fibres (i.e., inulin and pectin of low degree of methylation) have

prebiotic effects *in vitro*. A study by Van den Abbeele *et al.* (2020) showed that an artichoke extract exerts this activity *in vitro*.

3.8. Antioxidant activity

A previous study found that ALE intake exerts antioxidant activity in individuals with metabolic syndrome, lowering oxidized-LDL (ox-LDL) levels (Rezazadeh *et al.*, 2018a). Skarpanska-Stejnborn and colleagues (2008) showed the antioxidant effect of ALE in a sample of 22 rowers during the training. Other studies found the antioxidant activity of cynaropicrin from artichoke in HeLa cells (Liu *et al.*, 2019) and human keratinocytes (Takei *et al.*, 2015). Two scientific articles reported that sesquiterpene lactones (Matsumoto *et al.*, 2021) or cynarine and cyanidin (Xia *et al.*, 2014) from artichoke can inhibit the expression of iNOS *in vitro*. Previous studies showed that artichoke extracts exert this activity in rodent models of different health conditions (Abdel-Moneim *et al.*, 2021; Ahmadi *et al.*, 2019; Ben Salem *et al.*, 2017b; Ben Salem *et al.*, 2019; Ben Salem *et al.*, 2022a; Ben Salem *et al.*, 2022b; Bogavac-Stanojevic *et al.*, 2018; Celepli *et al.*, 2022a; Celepli *et al.*, 2022b; Cicek *et al.*, 2022; Colak *et al.*, 2016; Crevar-Sakac *et al.*, 2016; Deng *et al.*, 2022; El-Boshy *et al.*, 2017; El Morsy and Kamel, 2015; Elsayed Elgarawany *et al.*, 2020; Gurel *et al.*, 2007; Heidarian and Rafieian-Kopaei, 2013; Ibrahim *et al.*, 2022; Khattab *et al.*, 2016; Küçükgergin *et al.*, 2010; Küskü-Kiraz *et al.*, 2010; Liao *et al.*, 2021; Magielse *et al.*, 2014; Mehmetçik *et al.*, 2008; Metwally *et al.*, 2011; Mohammed *et al.*, 2020; Nasef *et al.*, 2022; Nassar *et al.*, 2013; Tang *et al.*, 2017; Wang *et al.*, 2021). Lee and colleagues (2021b) found the protective role of ALE against oxidative stress, performing experiments in NAFLD mice and HepG2 cells. Other studies showed the beneficial effect of artichoke extracts with high phenolic contents on oxidative stress (Biel *et al.*, 2020; Brown and Rice-Evans, 1998; D'Antuono *et al.*, 2018; Speroni *et al.*, 2003). Pérez-García and colleagues (2000) demonstrated the antioxidant effect of ALE *in vitro*. This artichoke extract is

effective in blocking reactive oxygen species (ROS) generation in human leukocytes and the phytochemicals mainly involved are luteolin, caffeic acid, cynarine and chlorogenic acid. Previous studies showed that artichoke extracts exert antioxidant activity *in vitro* (Carpentieri *et al.*, 2022; Gebhardt, 1997; Gebhardt and Fausel, 1997; Juzyszyn *et al.*, 2008; Menghini *et al.*, 2010; Miccadei *et al.*, 2008; Zapolska-Downar *et al.*, 2002). Sarawek and colleagues (2008) found that luteolin from artichoke is effective in inhibiting xanthine oxidase (XO) *in vitro*. Two previous studies showed the antioxidant effects of this plant extracts, performing *in vivo* and *in vitro* experiments (Ben Salem *et al.*, 2017a; Jiménez-Escrig *et al.*, 2003). Other studies demonstrated that artichoke seeds (Durazzo *et al.*, 2013), rhizome (Lee *et al.*, 2021a), buds (Lin *et al.*, 2022) and pollen (Kostić *et al.*, 2021) have antioxidant activity and phenolics are mainly involved in this beneficial effect.

3.9. Antidiabetic effects

Rondanelli and colleagues (2014) found the beneficial effect of an artichoke extract on glucose metabolism in a sample of 55 overweight individuals with impaired fasting glycaemia. Previous studies demonstrated that artichoke extracts are effective in improving insulin resistance in individuals with metabolic syndrome (Ebrahimi-Mameghani *et al.*, 2018) and rodents (Deng *et al.*, 2022; Kwon *et al.*, 2018; Ibrahim *et al.*, 2022). Ben Salem and colleagues (2017b) found the antihyperglycaemic activity of ALE in diabetic rats. Another study showed the hypoglycaemic activity of an artichoke flower head extract in obese and normal rats (Fantini *et al.*, 2011).

3.10. Antiarthritic effects

Two previous studies found the antiarthritic activity of artichoke. Wauquier and colleagues (2021) showed that ALE has a beneficial effect on osteoarthritis, performing an *ex*

in vivo experiment using human articular chondrocytes. Another study demonstrated the beneficial effect of cynaropicrin on the metabolism of cartilage *in vitro* (Masutani *et al.*, 2016). These two scientific articles represent a preliminary evidence that artichoke exerts antiarthritic activity and other studies are required to confirm these results.

3.11. Renoprotective activity

Previous studies showed the protective effect of artichoke bud (Wang *et al.*, 2021), leaf (Ben Salem *et al.*, 2022b; El-Boshy *et al.*, 2017), receptacle and stem (Sümer *et al.*, 2020) extracts on renal function in rats. Khattab and colleagues (2016) found that ALE exerts a beneficial effect on kidney function in a rat model of gentamicin nephrotoxicity.

3.12. Neuroprotective effects

Two previous studies found that ALE exerts a neuroprotective effect in rodent models and this effect may be mediated by the antioxidant activity of artichoke (Cicek *et al.*, 2022; Ibrahim *et al.*, 2022). Future studies are needed to confirm these results.

3.13. Effects on the reproductive system

Previous studies found that ALE may ameliorate gonadal health in rat models through antioxidant effects (Gurel *et al.*, 2007; Mohammed *et al.*, 2020). The results show the potential beneficial effects of ALE on the reproductive system, but other studies are required to confirm these results and describe in detail the molecular mechanisms underlying these effects.

3.14. Effects on the immune system

A previous study by El-Boshy *et al.* (2017) found that ALE is effective in improving the levels of immunostimulatory cytokines in a rat model of cadmium toxicity. Hueza and

colleagues (2019) showed that an artichoke extract exerts immunomodulatory activity in rats. These two studies provide evidence of the effects of artichoke on the immune system. Other studies are needed to confirm the results and explain the molecular mechanisms.

3.15. Antiphotaging effects

A previous study demonstrated that cynaropicrin has antiphotaging effect *in vivo* and *in vitro* by regulating the nuclear factor kappa B (NF- κ B) signalling pathway (Tanaka *et al.*, 2013). Takei and colleagues (2015) showed that this bioactive compound from artichoke may prevent ultraviolet B (UVB)-induced photaging in human keratinocytes through antioxidant effects. These results should be confirmed by future studies.

3.16. Antifungal effects

A previous study studied the antifungal activity of different artichoke extracts *in vitro* and found that ALE is the most effective. The authors analysed the effect against *Candida albicans*, *Candida lusitaniae*, *Saccharomyces cerevisiae*, *Saccharomyces carlsbergensis*, *Aspergillus niger*, *Penicillium oxalicum*, *Mucor mucedo* and *Cladosporium cucumerinum* (Zhu *et al.*, 2005). Further studies should corroborate these results.

3.17. Prevention of periodontal diseases

A previous study showed that cynaropicrin from artichoke exerts a preventive effect on periodontal diseases *in vitro* by modulating the NF- κ B signalling pathway (Hayata *et al.*, 2019). Only one study found this activity and these results should be confirmed.

This review has some limitations. We reported only scientific articles published in PubMed indexed journals, personal criteria were utilised for conducting the literature search and many studies are characterized by small sample sizes or require replication of results.

4. Conclusions

In this study, we show the health-promoting properties of artichoke after performing a literature search. The most common beneficial effects of this plant are those on the liver and lipid profile and antioxidant activity. Other health benefits include improved gastrointestinal and cardiovascular health and anticancer, antimetabolic and antiobesity, prebiotic and probiotic, antidiabetic and renoprotective effects. Only few studies found the beneficial effects of artichoke on the immune system, the reproductive system, the nervous system, arthritis, photoaging, periodontal diseases and fungal infections. Phenolics are the bioactive compounds mainly involved in these properties and ALE is the extract most commonly utilised for these purposes. The health benefits of artichoke are well documented in the scientific literature. Further studies should confirm the results of the articles reported in this review and the molecular mechanisms involved in the health-promoting properties of this plant.

Abbreviations

ALD: alcoholic liver disease

ALE: artichoke leaf extract

BMI: body mass index

eNOS: endothelial nitric oxide synthase

HDL-C: high-density lipoprotein cholesterol

IBS: irritable bowel syndrome

iNOS: inducible nitric oxide synthase

LDL-C: low-density lipoprotein cholesterol

NAFLD: non-alcoholic fatty liver disease

NASH: non-alcoholic steatohepatitis

NF- κ B: nuclear factor kappa B

ox-LDL: oxidized-LDL

ROS: reactive oxygen species

UVB: ultraviolet B

XO: xanthine oxidase

Declarations

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Conflict of interest

None.

Availability of data and material

Data and material available on request from the authors.

Code availability

Not applicable

Authors' contributions

All co-authors conceptualised and designed the study. ADN conducted the literature search and drafted the article. All co-authors revised it and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

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Reference list

- Abdel-Moneim A, Ahmed OM, Abd El-Twab SM, Zaky MY, Bakry LN. Prophylactic effects of *Cynara scolymus* L. leaf and flower hydroethanolic extracts against diethylnitrosamine/acetylaminoflourene-induced lung cancer in Wistar rats. *Environ Sci Pollut Res Int* 2021;28(32):43515-27.
- Ahmadi A, Heidarian E, Ghatreh-Samani K. Modulatory effects of artichoke (*Cynara scolymus* L.) leaf extract against oxidative stress and hepatic TNF- α gene expression in acute diazinon-induced liver injury in rats. *J Basic Clin Physiol Pharmacol* 2019;30(5).
- Ardalani H, Jandaghi P, Meraji A, Hassanpour Moghadam M. The effect of *Cynara scolymus* on blood pressure and BMI in hypertensive patients: a randomized, double-blind, placebo-controlled, clinical trial. *Complement Med Res* 2020;27(1):40-46.
- Azzini E, Bugianesi R, Romano F, Di Venere D, Miccadei S, Durazzo A, Foddai MS, Catasta G, Linsalata V, Maiani G. Absorption and metabolism of bioactive molecules after oral consumption of cooked edible heads of *Cynara scolymus* L. (cultivar Violetto di Provenza) in human subjects: a pilot study. *Br J Nutr* 2007;97(5):963-69.
- Basay S. Study of the structure of artichoke (*Cynara scolymus* L.) flowers. *JAST* 2022;24(4):913-24.
- Ben Salem M, Affes H, Athmouni K, Ksouda K, Dhouibi R, Sahnoun Z, Hammami S, Zeghal KM. Chemicals compositions, antioxidant and anti-inflammatory activity of *Cynara scolymus* leaves extracts, and analysis of major bioactive polyphenols by HPLC. *Evid Based Complement Alternat Med* 2017a;2017:4951937.

- Ben Salem M, Affes H, Dhouibi R, Charfi S, Turki M, Hammami S, Ayedi F, Sahnoun Z, Zeghal KM, Ksouda K. Effect of artichoke (*cynara scolymus*) on cardiac markers, lipid profile and antioxidants levels in tissue of HFD-induced obesity. Arch Physiol Biochem. 2022a;128(1):184-194.
- Ben Salem M, Affes H, Dhouibi R, Charfi S, Turki M, Hammami S, Ayedi F, Sahnoun Z, Zeghal KM, Ksouda K. Preventive effect of Artichoke (*Cynara scolymus* L.) in kidney dysfunction against high fat-diet induced obesity in rats. Arch Physiol Biochem 2022b;128(3):586-592.
- Ben Salem M, Ben Abdallah Kolsi R, Dhouibi R, Ksouda K, Charfi S, Yaich M, Hammami S, Sahnoun Z, Zeghal KM, Jamoussi K, Affes H. Protective effects of *Cynara scolymus* leaves extract on metabolic disorders and oxidative stress in alloxan-diabetic rats. BMC Complement Altern Med 2017b;17(1):328.
- Ben Salem M, Ksouda K, Dhouibi R, Charfi S, Turki M, Hammami S, Ayedi F, Sahnoun Z, Zeghal KM, Affes H. LC-MS/MS analysis and hepatoprotective activity of artichoke (*Cynara scolymus* L.) leaves extract against high fat diet-induced obesity in rats. Biomed Res Int 2019;2019:4851279
- Biel W, Witkowicz R, Piątkowska E, Podsiadło C. Proximate composition, minerals and antioxidant activity of artichoke leaf extracts. Biol Trace Elem Res 2020;194(2):589-95.
- Bogavac-Stanojevic N, Kotur Stevuljevic J, Cerne D, Zupan J, Marc J, Vujic Z, Crevar-Sakac M, Sopic M, Munjas J, Radenkovic M, Jelic-Ivanovic Z. The role of artichoke leaf tincture (*Cynara scolymus*) in the suppression of DNA damage and atherosclerosis in rats fed an atherogenic diet. Pharm Biol 2018;56(1):138-44.

- Brown JE, Rice-Evans CA. Luteolin-rich artichoke extract protects low density lipoprotein from oxidation *in vitro*. Free Radic Res 1998;29(3):247-55.
- Bundy R, Walker AF, Middleton RW, Marakis G, Booth JC. Artichoke leaf extract reduces symptoms of irritable bowel syndrome and improves quality of life in otherwise healthy volunteers suffering from concomitant dyspepsia: a subset analysis. J Altern Complement Med 2004;10(4):667-9.
- Bundy R, Walker AF, Middleton RW, Wallis C, Simpson HC. Artichoke leaf extract (*Cynara scolymus*) reduces plasma cholesterol in otherwise healthy hypercholesterolemic adults: a randomized, double blind placebo controlled trial. Phytomedicine 2008;15(9):668-75.
- Carpentieri S, Augimeri G, Ceramella J, Vivacqua A, Sinicropi MS, Pataro G, Bonofiglio D, Ferrari G. Antioxidant and anti-inflammatory effects of extracts from pulsed electric field-treated artichoke by-products in lipopolysaccharide-stimulated human THP-1 macrophages. Foods 2022;11(15):2250.
- Ceccarelli N, Curadi M, Picciarelli P, Martelloni L, Sbrana C, Giovannetti M. Globe artichoke as a functional food. Mediterr J Nutr Metab 2010;3:197-201.
- Celepli S, Çolak B, Celepli P, Bigat İ, Batur HG, Soysal F, Karakurt S, Hücümenoğlu S, Kısmet K, Şahin M. Artichoke for biochemistry, histology, and gene expression in obstructive jaundice. Rev Assoc Med Bras 2022a;68(5):647-52.
- Celepli S, Çolak B, Celepli P, Bigat İ, Batur HG, Soysal F, Karakurt S, Hücümenoğlu S, Kısmet K, Şahin M. Effects of artichoke leaf extract on hepatic ischemia-reperfusion injury. Rev Assoc Med Bras 2022b;68(1):87-93.

- Cicek B, Genc S, Yeni Y, Kuzucu M, Cetin A, Yildirim S, Bolat I, Kantarci M, Hacimuftuoglu A, Lazopoulos G, Tsatsakis A, Tsarouhas K, Taghizadehghalehjoughi A. Artichoke (*Cynara scolymus*) methanolic leaf extract alleviates diethylnitrosamine-induced toxicity in BALB/c mouse brain: involvement of oxidative stress and apoptotically related Klotho/PPAR γ signaling. *J Pers Med* 2022;12(12):2012.

- Colak E, Ustuner MC, Tekin N, Colak E, Burukoglu D, Degirmenci I, Gunes HV. The hepatocurative effects of *Cynara scolymus* L. leaf extract on carbon tetrachloride-induced oxidative stress and hepatic injury in rats. *Springerplus* 2016;5:216.

- Costabile A, Kolida S, Klinder A, Gietl E, Bäuerlein M, Frohberg C, Landschütze V, Gibson GR. A double-blind, placebo-controlled, cross-over study to establish the bifidogenic effect of a very-long-chain inulin extracted from globe artichoke (*Cynara scolymus*) in healthy human subjects. *Br J Nutr* 2010;104(7):1007-17.

- Crevar-Sakac M, Vujić Z, Kotur-Stevuljević J, Ivanisević J, Jelić-Ivanović Z, Milenković M, Markelić M, Vujčić Z. Effects of atorvastatin and artichoke leaf tincture on oxidative stress in hypercholesterolemic rats. *Vojnosanit Pregl* 2016;73(2):178-87.

- D'Antuono I, Carola A, Sena LM, Linsalata V, Cardinali A, Logrieco AF, Colucci MG, Apone F. Artichoke polyphenols produce skin anti-age effects by improving endothelial cell integrity and functionality. *Molecules* 2018;23(11):2729.

- Deng A, Liu F, Tang X, Wang Y, Xie P, Yang Q, Xiao B. Water extract from artichoke ameliorates high-fat diet-induced non-alcoholic fatty liver disease in rats. *BMC Complement Med Ther* 2022;22(1):308.

- Ding Z, Xi J, Zhong M, Chen F, Zhao H, Zhang B, Fang J. Cynaropicrin induces cell cycle arrest and apoptosis by inhibiting PKM2 to cause DNA damage and mitochondrial fission in A549 cells. *J Agric Food Chem* 2021;69(45):13557-67.
- Durazzo A, Foddai MS, Temperini A, Azzini E, Venneria E, Lucarini M, Finotti E, Maiani G, Crinò P, Saccardo F, Maiani G. Antioxidant properties of seeds from lines of artichoke, cultivated cardoon and wild cardoon. *Antioxidants (Basel)* 2013;2(2):52-61.
- Ebrahimi-Mameghani M, Asghari-Jafarabadi M, Rezazadeh K. TCF7L2-rs7903146 polymorphism modulates the effect of artichoke leaf extract supplementation on insulin resistance in metabolic syndrome: a randomized, double-blind, placebo-controlled trial. *J Integr Med* 2018;16(5):329-334.
- El-Boshy M, Ashshi A, Gaith M, Qusty N, Bokhary T, AlTaweel N, Abdelhady M. Studies on the protective effect of the artichoke (*Cynara scolymus*) leaf extract against cadmium toxicity-induced oxidative stress, hepatorenal damage, and immunosuppressive and hematological disorders in rats. *Environ Sci Pollut Res Int* 2017;24(13):12372-83
- El Morsy EM, Kamel R. Protective effect of artichoke leaf extract against paracetamol-induced hepatotoxicity in rats. *Pharm Biol* 2015;53(2):167-73.
- Elsayed Elgarawany G, Abdou AG, Maher Taie D, Motawea SM. Hepatoprotective effect of artichoke leaf extracts in comparison with silymarin on acetaminophen-induced hepatotoxicity in mice. *J Immunoassay Immunochem* 2020;41(1):84-96.
- Emendörfer F, Emendörfer F, Bellato F, Noldin VF, Cechinel-Filho V, Yunes RA, Delle Monache F, Cardozo AM. Antispasmodic activity of fractions and cynaropicrin from *Cynara scolymus* on guinea-pig ileum. *Biol Pharm Bull* 2005;28(5):902-04.

- Englisch W, Beckers C, Unkauf M, Ruepp M, Zinserling V. Efficacy of artichoke dry extract in patients with hyperlipoproteinemia. *Arzneimittelforschung* 2000;50(3):260-65.
- Fantini N, Colombo G, Giori A, Riva A, Morazzoni P, Bombardelli E, Carai MA. Evidence of glycemia-lowering effect by a *Cynara scolymus* L. extract in normal and obese rats. *Phytother Res* 2011;25(3):463-66.
- Fissore EN, Santo Domingo C, Gerschenson LN, Giannuzzi L. A study of the effect of dietary fiber fractions obtained from artichoke (*Cynara cardunculus* L. var. *scolymus*) on the growth of intestinal bacteria associated with health. *Food Funct* 2015;6(5):1667-74.
- Frigerio J, Tedesco E, Benetti F, Insolia V, Nicotra G, Mezzasalma V, Pagliari S, Labra M, Campone L. Anticholesterolemic activity of three vegetal extracts (artichoke, caigua, and fenugreek) and their unique blend. *Front Pharmacol* 2021;12:726199.
- Gebhardt R. Antioxidative and protective properties of extracts from leaves of the artichoke (*Cynara scolymus* L.) against hydroperoxide-induced oxidative stress in cultured rat hepatocytes. *Toxicol Appl Pharmacol* 1997;144(2):279-86.
- Gebhardt R. Inhibition of cholesterol biosynthesis in primary cultured rat hepatocytes by artichoke (*Cynara scolymus* L.) extracts. *J Pharmacol Exp Ther* 1998;286(3):1122-28.
- Gebhardt R. Anticholestatic activity of flavonoids from artichoke (*Cynara scolymus* L.) and of their metabolites. *Med Sci Monit* 2001;7 Suppl 1:316-20.
- Gebhardt R. Inhibition of cholesterol biosynthesis in HepG2 cells by artichoke extracts is reinforced by glucosidase pretreatment. *Phytother Res* 2002a;16(4):368-72.

- Gebhardt R. Prevention of tauroolithocholate-induced hepatic bile canalicular distortions by HPLC-characterized extracts of artichoke (*Cynara scolymus*) leaves. *Planta Med* 2002b;68(9):776-9.
- Gebhardt R, Fausel M. Antioxidant and hepatoprotective effects of artichoke extracts and constituents in cultured rat hepatocytes. *Toxicol In Vitro* 1997;11(5):669-72.
- Grieve MA. *Modern Herbal*. Dover Publications, New York, 1931.
- Gurel E, Caner M, Bayraktar L, Yilmazer N, Dogruman H, Demirci C. Effects of artichoke extract supplementation on gonads of cadmium-treated rats. *Biol Trace Elem Res* 2007;119(1):51-59.
- Hayata M, Watanabe N, Kamio N, Tamura M, Nodomi K, Tanaka K, Iddamalgoda A, Tsuda H, Ogata Y, Sato S, Ueda K, Imai K. Cynaropicrin from *Cynara scolymus* L. suppresses *Porphyromonas gingivalis* LPS-induced production of inflammatory cytokines in human gingival fibroblasts and RANKL-induced osteoclast differentiation in RAW264.7 cells. *J Nat Med* 2019;73(1):114-23.
- Heidarian E, Rafieian-Kopaei M. Protective effect of artichoke (*Cynara scolymus*) leaf extract against lead toxicity in rat. *Pharm Biol* 2013;51(9):1104-09.
- Holtmann G, Adam B, Haag S, Collet W, Grünewald E, Windeck T. Efficacy of artichoke leaf extract in the treatment of patients with functional dyspepsia: a six-week placebo-controlled, double-blind, multicentre trial. *Aliment Pharmacol Ther* 2003;18(11-12):1099-105.
- Hueza IM, Gotardo AT, da Silva Mattos MI, Górnaiak SL. Immunomodulatory effect of *Cynara scolymus* (artichoke) in rats. *Phytother Res* 2019;33(1):167-73.

- Ibrahim EA, Yousef MI, Ghareeb DA, Augustyniak M, Giesy JP, Aboul-Soud MAM, El Wakil A. Artichoke leaf extract-mediated neuroprotection against effects of aflatoxin in male rats. *Biomed Res Int* 2022;2022:4421828.
- IPNI. International Plant Names Index. Published on the Internet <http://www.ipni.org>, The Royal Botanic Gardens, Kew, Harvard University Herbaria & Libraries and Australian National Herbarium. Accessed April 15, 2023.
- Ishida K, Kojima R, Tsuboi M, Tsuda Y, Ito M. Effects of artichoke leaf extract on acute gastric mucosal injury in rats. *Biol Pharm Bull* 2010;33(2):223-29.
- Islam MS, Greco S, Delli Carpini G, Giannubilo SR, Segars J, Ciavattini A, Ciarmela P. Hop and artichoke extracts inhibit expression of extracellular matrix components in uterine leiomyoma cells. *F S Sci* 2021;2(4):407-18.
- Jiménez-Escrig A, Dragsted LO, Daneshvar B, Pulido R, Saura-Calixto F. In vitro antioxidant activities of edible artichoke (*Cynara scolymus* L.) and effect on biomarkers of antioxidants in rats. *J Agric Food Chem* 2003;51(18):5540-45.
- Juzyszyn Z, Czerny B, Pawlik A, Drożdżik M. The effect of artichoke (*Cynara scolymus* L.) extract on ROS generation in HUVEC cells. *Phytother Res* 2008;22(9):1159-61.
- Khattab HA, Wazzan MA, Al-Ahdab MA. Nephroprotective potential of artichoke leaves extract against gentamicin in rats: antioxidant mechanisms. *Pak J Pharm Sci* 2016;29(5 Suppl):1775-82.
- Kirchhoff R, Beckers C, Kirchhoff GM, Trinczek-Gärtner H, Petrowicz O, Reimann HJ. Increase in choleresis by means of artichoke extract. *Phytomedicine* 1994;1(2):107-15.

- Kostić AŽ, Milinčić DD, Nedić N, Gašić UM, Špirović Trifunović B, Vojt D, Tešić ŽL, Pešić MB. Phytochemical profile and antioxidant properties of bee-collected artichoke (*Cynara scolymus*) pollen. *Antioxidants (Basel)* 2021;10(7):1091.
- Küçükgergin C, Aydın AF, Ozdemirler-Erata G, Mehmetçik G, Koçak-Toker N, Uysal M. Effect of artichoke leaf extract on hepatic and cardiac oxidative stress in rats fed on high cholesterol diet. *Biol Trace Elem Res* 2010;135(1-3):264-74.
- Kurt H, Toprak O, Bülbül E. The possible efficacy of artichoke in fluconazole related hepatotoxicity. *Case Reports Hepatol* 2014;2014:697359.
- Küskü-Kiraz Z, Mehmetçik G, Dogru-Abbasoglu S, Uysal M. Artichoke leaf extract reduces oxidative stress and lipoprotein dyshomeostasis in rats fed on high cholesterol diet. *Phytother Res* 2010;24(4):565-70.
- Kwon EY, Kim SY, Choi MS. Luteolin-enriched artichoke leaf extract alleviates the metabolic syndrome in mice with high-fat diet-induced obesity. *Nutrients* 2018;10(8):979.
- Lattanzio V, Kroon PA, Linsalata V, Cardinali A. Globe artichoke: A functional food and source of nutraceutical ingredients. *Journal of Functional Foods* 2009;1(2):131-44.
- Lee CL, Liao KC, Chen CC, Lin YA, Wu TY, Jhan YL, Chen CJ, Yang JC, Wu YC. Characterization of secondary metabolites from the rhizome of *Cynara scolymus* and their antioxidant properties. *Nat Prod Res* 2021a;35(12):2051-55.
- Lee M, Kim D, Park SJ, Kim KS, Park GD, Kim OK, Lee J. Artichoke extract directly suppresses inflammation and apoptosis in hepatocytes during the development of non-alcoholic fatty liver disease. *J Med Food* 2021b;24(10):1058-67.

- Lepore SM, Maggisano V, Lombardo GE, Maiuolo J, Mollace V, Bulotta S, Russo D, Celano M. Antiproliferative effects of cynaropicrin on anaplastic thyroid cancer cells. *Endocr Metab Immune Disord Drug Targets* 2019;19(1):59-66.
- Li H, Xia N, Brausch I, Yao Y, Förstermann U. Flavonoids from artichoke (*Cynara scolymus* L.) up-regulate endothelial-type nitric-oxide synthase gene expression in human endothelial cells. *J Pharmacol Exp Ther* 2004;310(3):926-32.
- Liao GC , Jhuang JH , Yao HT . Artichoke leaf extract supplementation lowers hepatic oxidative stress and inflammation and increases multidrug resistance-associated protein 2 in mice fed a high-fat and high-cholesterol diet. *Food Funct* 2021;12(16):7239-49.
- Lin X, Lu XK, Zhu KH, Jiang XY, Chen JC, Yan PZ, Zhao DS. Synchronous extraction, antioxidant activity evaluation, and composition analysis of carbohydrates and polyphenols present in artichoke bud. *Molecules* 2022;27(24):8962.
- Liu T, Zhang J, Han X, Xu J, Wu Y, Fang J. Promotion of HeLa cells apoptosis by cynaropicrin involving inhibition of thioredoxin reductase and induction of oxidative stress. *Free Radic Biol Med* 2019;135:216-26.
- López-Molina D, Navarro-Martínez MD, Rojas Melgarejo F, Hiner AN, Chazarra S, Rodríguez-López JN. Molecular properties and prebiotic effect of inulin obtained from artichoke (*Cynara scolymus* L.). *Phytochemistry* 2005;66(12):1476-84.
- Lupattelli G, Marchesi S, Lombardini R, Roscini AR, Trinca F, Gemelli F, Vaudo G, Mannarino E. Artichoke juice improves endothelial function in hyperlipemia. *Life Sci* 2004;76(7):775-82.

- Magielse J, Verlaet A, Breynaert A, Keenoy BM, Apers S, Pieters L, Hermans N. Investigation of the in vivo antioxidative activity of *Cynara scolymus* (artichoke) leaf extract in the streptozotocin-induced diabetic rat. *Mol Nutr Food Res* 2014;58(1):211-15.

- Majnooni MB, Ataee M, Bahrami G, Heydarpour F, Aneva IY, Farzaei MH, Ahmadi-Juoibari T. The effects of co-administration of artichoke leaf extract supplementation with metformin and vitamin E in patients with nonalcoholic fatty liver disease: A randomized clinical trial. *Phytother Res* 2021;35(11):6324-34.

- Marakis G, Walker AF, Middleton RW, Booth JC, Wright J, Pike DJ. Artichoke leaf extract reduces mild dyspepsia in an open study. *Phytomedicine* 2002;9(8):694-99.

- Masutani T, Tanaka YT, Kojima H, Tsuboi M, Hara A, Niwa M. Cynaropicrin is dual regulator for both degradation factors and synthesis factors in the cartilage metabolism. *Life Sci* 2016;158:70-77.

- Matsumoto T, Nakashima S, Nakamura S, Hattori Y, Ando T, Matsuda H. Inhibitory effects of cynaropicrin and related sesquiterpene lactones from leaves of artichoke (*Cynara scolymus* L.) on induction of iNOS in RAW264.7 cells and its high-affinity proteins. *J Nat Med* 2021;75(2):381-92.

- Mehmetçik G, Ozdemirler G, Koçak-Toker N, Cevikbaş U, Uysal M. Effect of pretreatment with artichoke extract on carbon tetrachloride-induced liver injury and oxidative stress. *Exp Toxicol Pathol* 2008;60(6):475-80.

- Menghini L, Genovese S, Epifano F, Tirillini B, Ferrante C, Leporini L. Antiproliferative, protective and antioxidant effects of artichoke, dandelion, turmeric and rosemary extracts and their formulation. *Int J Immunopathol Pharmacol* 2010;23(2):601-10.

- Metwally NS, Kholeif TE, Ghanem KZ, Farrag AR, Ammar NM, Abdel-Hamid AH. The protective effects of fish oil and artichoke on hepatocellular carcinoma in rats. *Eur Rev Med Pharmacol Sci* 2011;15(12):1429-44.
- Miccadei S, Di Venere D, Cardinali A, Romano F, Durazzo A, Foddai MS, Fraioli R, Mobarhan S, Maiani G. Antioxidative and apoptotic properties of polyphenolic extracts from edible part of artichoke (*Cynara scolymus* L.) on cultured rat hepatocytes and on human hepatoma cells. *Nutr Cancer* 2008;60(2):276-83.
- Mileo AM, Di Venere D, Abbruzzese C, Miccadei S. Long term exposure to polyphenols of artichoke (*Cynara scolymus* L.) exerts induction of senescence driven growth arrest in the MDA-MB231 human breast cancer cell line. *Oxid Med Cell Longev* 2015;2015:363827.
- Mileo AM, Di Venere D, Linsalata V, Fraioli R, Miccadei S. Artichoke polyphenols induce apoptosis and decrease the invasive potential of the human breast cancer cell line MDA-MB231. *J Cell Physiol* 2012;227(9):3301-09.
- Mileo AM, Di Venere D, Mardente S, Miccadei S. Artichoke polyphenols sensitize human breast cancer cells to chemotherapeutic drugs via a ROS-mediated downregulation of flap endonuclease 1. *Oxid Med Cell Longev* 2020;2020:7965435.
- Mohammed ET, Radi AM, Aleya L, Abdel-Daim MM. *Cynara scolymus* leaves extract alleviates nandrolone decanoate-induced alterations in testicular function and sperm quality in albino rats. *Environ Sci Pollut Res Int* 2020;27(5):5009-17.
- Mulinacci N, Prucher D, Peruzzi M, Romani A, Pinelli P, Giaccherini C, Vincieri FF. Commercial and laboratory extracts from artichoke leaves: estimation of caffeoyl esters and flavonoidic compounds content. *J Pharm Biomed Anal* 2004;34(2):349-57.

- Muti P, Sacconi A, Pulito C, Orlandi G, Donzelli S, Morrone A, Jiulian J, Cox GP, Kolb M, Pond G, Kavsak P, Levine MN, Blandino G, Strano S. Artichoke phytochemicals modulates serum microRNAs in patients exposed to asbestos: a first step of a phase II clinical trial. *J Exp Clin Cancer Res* 2022;41(1):255.
- Nasef MA, Yousef MI, Ghareeb DA, Augustyniak M, Aboul-Soud MAM, El Wakil A. Hepatoprotective effects of a chemically-characterized extract from artichoke (*Cynara scolymus* L.) against AFB₁-induced toxicity in rats. *Drug Chem Toxicol* 2022 Oct 4:1-13.
- Nassar MI, Mohamed TK, Elshamy AI, El-Toumy SA, Abdel Lateef AM, Farrag AR. Chemical constituents and anti-ulcerogenic potential of the scales of *Cynara scolymus* (artichoke) heads. *J Sci Food Agric* 2013;93(10):2494-501.
- Panahi Y, Kianpour P, Mohtashami R, Atkin SL, Butler AE, Jafari R, Badeli R, Sahebkar A. Efficacy of artichoke leaf extract in non-alcoholic fatty liver disease: A pilot double-blind randomized controlled trial. *Phytother Res* 2018;32(7):1382-87.
- Panizzi L and Scarpati ML. Constitution of cynarine, the active principle of the artichoke. *Nature* 1954;174:1062-63.
- Pereira C, Barros L, Carvalho AM, Santos-Buelga C, Ferreira IC. Infusions of artichoke and milk thistle represent a good source of phenolic acids and flavonoids. *Food Funct* 2015;6(1):56-62.
- Pérez-García F, Adzet T, Cañigueral S. Activity of artichoke leaf extract on reactive oxygen species in human leukocytes. *Free Radic Res* 2000;33(5):661-65.
- Pignone D and Sonnante G. Wild artichokes of south Italy: did the story begin here? *Genetic Resources and Crop Evolution* 2004;51(6):577-80.

- Pulito C, Mori F, Sacconi A, Casadei L, Ferraiuolo M, Valerio MC, Santoro R, Goeman F, Maidecchi A, Mattoli L, Manetti C, Di Agostino S, Muti P, Blandino G, Strano S. *Cynara scolymus* affects malignant pleural mesothelioma by promoting apoptosis and restraining invasion. *Oncotarget* 2015;6(20):18134-50.
- Qiang Z, Lee SO, Ye Z, Wu X, Hendrich S. Artichoke extract lowered plasma cholesterol and increased fecal bile acids in Golden Syrian hamsters. *Phytother Res* 2012;26(7):1048-52.
- Qinna NA, Kamona BS, Alhussainy TM, Taha H, Badwan AA, Matalka KZ. Effects of prickly pear dried leaves, artichoke leaves, turmeric and garlic extracts, and their combinations on preventing dyslipidemia in rats. *ISRN Pharmacol* 2012;2012:167979.
- Rangboo V, Noroozi M, Zavoshy R, Rezaadoost SA, Mohammadpoorasl A. The effect of artichoke leaf extract on alanine aminotransferase and aspartate aminotransferase in the patients with nonalcoholic steatohepatitis. *Int J Hepatol* 2016;2016:4030476.
- Rezazadeh K, Aliashrafi S, Asghari-Jafarabadi M, Ebrahimi-Mameghani M. Antioxidant response to artichoke leaf extract supplementation in metabolic syndrome: a double-blind placebo-controlled randomized clinical trial. *Clin Nutr* 2018a;37(3):790-96.
- Rezazadeh K, Rahmati-Yamchi M, Mohammadnejad L, Ebrahimi-Mameghani M, Delazar A. Effects of artichoke leaf extract supplementation on metabolic parameters in women with metabolic syndrome: influence of TCF7L2-rs7903146 and FTO-rs9939609 polymorphisms. *Phytother Res* 2018b;32(1):84-93.
- Riezzo G, Orlando A, D'Attoma B, Guerra V, Valerio F, Lavermicocca P, De Candia S, Russo F. Randomised clinical trial: efficacy of *Lactobacillus paracasei*-enriched artichokes in

the treatment of patients with functional constipation--a double-blind, controlled, crossover study. *Aliment Pharmacol Ther* 2012;35(4):441-50.

- Rocchetti G, Lucini L, Corrado G, Colla G, Cardarelli M, Pascale S, Roupheal Y. Phytochemical profile, mineral content, and bioactive compounds in leaves of seed-propagated artichoke hybrid cultivars. *Molecules* 2020;25(17):3795.
- Roghani-Dehkordi F, Kamkhah AF. Artichoke leaf juice contains antihypertensive effect in patients with mild hypertension. *J Diet Suppl* 2009;6(4):328-41.
- Rondanelli M, Castellazzi AM, Riva A, Allegrini P, Faliva MA, Peroni G, Naso M, Nichetti M, Tagliacarne C, Valsecchi C, Fazio T, Perna S, Graziano F, Grassi M, Bernardinelli L. Natural killer response and lipo-metabolic profile in adults with low HDL-cholesterol and mild hypercholesterolemia: beneficial effects of artichoke leaf extract supplementation. *Evid Based Complement Alternat Med* 2019;2019:2069701.
- Rondanelli M, Giacosa A, Opizzi A, Faliva MA, Sala P, Perna S, Riva A, Morazzoni P, Bombardelli E. Beneficial effects of artichoke leaf extract supplementation on increasing HDL-cholesterol in subjects with primary mild hypercholesterolaemia: a double-blind, randomized, placebo-controlled trial. *Int J Food Sci Nutr* 2013;64(1):7-15.
- Rondanelli M, Opizzi A, Faliva M, Sala P, Perna S, Riva A, Morazzoni P, Bombardelli E, Giacosa A. Metabolic management in overweight subjects with naive impaired fasting glycaemia by means of a highly standardized extract from *Cynara scolymus*: a double-blind, placebo-controlled, randomized clinical trial. *Phytother Res* 2014;28(1):33-41.
- Sabater C, Molina-Tijeras JA, Vezza T, Corzo N, Montilla A, Utrilla P. Intestinal anti-inflammatory effects of artichoke pectin and modified pectin fractions in the dextran sulfate

sodium model of mice colitis. Artificial neural network modelling of inflammatory markers. *Food Funct* 2019;10(12):7793-805.

- Saénz Rodríguez T, García Giménez D, de la Puerta Vázquez R. Choleric activity and biliary elimination of lipids and bile acids induced by an artichoke leaf extract in rats. *Phytomedicine* 2002;9(8):687-93.
- Sarawek S, Feistel B, Pischel I, Butterweck V. Flavonoids of *Cynara scolymus* possess potent xanthinoxidase inhibitory activity *in vitro* but are devoid of hypouricemic effects in rats after oral application. *Planta Med* 2008;74(3):221-27.
- Sharaf El-Deen SA, Brakat RM, Mohamed ASED. Artichoke leaf extract protects liver of *Schistosoma mansoni* infected mice through modulation of hepatic stellate cells recruitment. *Exp Parasitol* 2017;178:51-59.
- Shimoda H, Ninomiya K, Nishida N, Yoshino T, Morikawa T, Matsuda H, Yoshikawa M. Anti-hyperlipidemic sesquiterpenes and new sesquiterpene glycosides from the leaves of artichoke (*Cynara scolymus* L.): structure requirement and mode of action. *Bioorg Med Chem Lett* 2003;13(2):223-28.
- Skarpanska-Stejnborn A, Pilaczynska-Szczesniak L, Basta P, Deskur-Smielcka E, Horoszkiewicz-Hassan M. The influence of supplementation with artichoke (*Cynara scolymus* L.) extract on selected redox parameters in rowers. *Int J Sport Nutr Exerc Metab* 2008;18(3):313-27.
- Sonnante G, Pignone D, Hammer K. The domestication of artichoke and cardoon: from Roman times to the genomic age. *Ann Bot* 2007;100(5):1095-100.

- Speroni E, Cervellati R, Govoni P, Guizzardi S, Renzulli C, Guerra MC. Efficacy of different *Cynara scolymus* preparations on liver complaints. J Ethnopharmacol 2003;86(2-3):203-11.
- Sümer E, Senturk GE, Demirel ÖU, Yesilada E. Comparative biochemical and histopathological evaluations proved that receptacle is the most effective part of *Cynara scolymus* against liver and kidney damages. J Ethnopharmacol 2020;249:112458.
- Takei K, Hashimoto-Hachiya A, Takahara M, Tsuji G, Nakahara T, Furue M. Cynaropicrin attenuates UVB-induced oxidative stress via the AhR-Nrf2-Nqo1 pathway. Toxicol Lett 2015;234(2):74-80.
- Tanaka YT, Tanaka K, Kojima H, Hamada T, Masutani T, Tsuboi M, Akao Y. Cynaropicrin from *Cynara scolymus* L. suppresses photoaging of skin by inhibiting the transcription activity of nuclear factor-kappa B. Bioorg Med Chem Lett 2013;23(2):518-23.
- Tang X, Wei R, Deng A, Lei T. Protective effects of ethanolic extracts from artichoke, an edible herbal medicine, against acute alcohol-induced liver injury in mice. Nutrients 2017;9(9):1000.
- Valerio F, Russo F, de Candia S, Riezzo G, Orlando A, Lonigro SL, Lavermicocca P. Effects of probiotic *Lactobacillus paracasei*-enriched artichokes on constipated patients: a pilot study. J Clin Gastroenterol 2010;44 Suppl 1:S49-53.
- Van den Abbeele P, Ghyselincx J, Marzorati M, Villar A, Zangara A, Smidt CR, Risco E. In vitro evaluation of prebiotic properties of a commercial artichoke inflorescence extract revealed bifidogenic effects. Nutrients 2020;12(6):1552.

- Verotta L, Macchi MP, Venkatasubramanian P. Connecting Indian wisdom and western science: plant usage for nutrition and health. CRC Press, 2015;pp:316-20.
- Verspohl EJ, Ploch M, Windeck T, Klaes M, Schmidt T, Bauer K. Effect of two artichoke extracts (36_U and 36_EB) on rat ileum (with respect to bowel syndrome) and the peristaltic threshold. *Phytomedicine* 2008;15(11):1002-09.
- Villarini M, Acito M, di Vito R, Vannini S, Dominici L, Fatigoni C, Pagiotti R, Moretti M. Pro-apoptotic activity of artichoke leaf extracts in human HT-29 and RKO colon cancer cells. *Int J Environ Res Public Health* 2021;18(8):4166.
- Walker AF, Middleton RW, Petrowicz O. Artichoke leaf extract reduces symptoms of irritable bowel syndrome in a post-marketing surveillance study. *Phytother Res* 2001;15(1):58-61.
- Wang ZB, Jiang SL, Liu SB, Peng JB, Hu S, Wang X, Zhuo W, Liu T, Guo JW, Zhou HH, Yang ZQ, Mao XY, Liu ZQ. Metabolomics of artichoke bud extract in spontaneously hypertensive rats. *ACS Omega* 2021;6(29):18610-22.
- Wauquier F, Boutin-Wittrant L, Viret A, Guilhaudis L, Oulyadi H, Bourafai-Aziez A, Charpentier G, Rousselot G, Cassin E, Descamps S, Roux V, Macian N, Pickering G, Wittrant Y. Metabolic and anti-inflammatory protective properties of human enriched serum following artichoke leaf extract absorption: results from an innovative ex vivo clinical trial. *Nutrients* 2021;13(8):2653.
- Xia N, Pautz A, Wollscheid U, Reifenberg G, Förstermann U, Li H. Artichoke, cynarin and cyanidin downregulate the expression of inducible nitric oxide synthase in human coronary smooth muscle cells. *Molecules* 2014;19(3):3654-68.

- Yang R, Ma S, Zhuo R, Xu L, Jia S, Yang P, Yao Y, Cao H, Ma L, Pan J, Wang J. Suppression of endoplasmic reticulum stress-dependent autophagy enhances cynaropicrin-induced apoptosis via attenuation of the P62/Keap1/Nrf2 pathways in neuroblastoma. *Front Pharmacol* 2022;13:977622.
- Zapolska-Downar D, Zapolski-Downar A, Naruszewicz M, Siennicka A, Krasnodebska B, Kołodziej B. Protective properties of artichoke (*Cynara scolymus*) against oxidative stress induced in cultured endothelial cells and monocytes. *Life Sci* 2002;71(24):2897-08.
- Zeaiter Z, Regonesi ME, Cavini S, Labra M, Sello G, Di Gennaro P. Extraction and characterization of inulin-type fructans from artichoke wastes and their effect on the growth of intestinal bacteria associated with health. *Biomed Res Int* 2019;2019:1083952.
- Zhu XF, Zhang HX, Lo R. Antifungal activity of *Cynara scolymus* L. extracts. *Fitoterapia* 2005;76(1):108-11.

FIGURE LEGENDS

Figure 1. Artichoke. A botanical illustration of artichoke. ("*Cynara scolymus*" by Adriana Morgante Giornetti).

Figure 2. Chlorogenic acid. A chemical structure image of chlorogenic acid (Retrieved from: <https://pubchem.ncbi.nlm.nih.gov/compound/1794427#section=2D-Structure>).

Figure 3. Cynarine. A chemical structure image of cynarine (Retrieved from: <https://pubchem.ncbi.nlm.nih.gov/compound/5281769#section=2D-Structure>).

Figure 4. Luteolin. A chemical structure image of luteolin (Retrieved from: <https://pubchem.ncbi.nlm.nih.gov/compound/5280445#section=2D-Structure>).

Figure 5. Cynaropicrin. A chemical structure image of cynaropicrin (Retrieved from: <https://pubchem.ncbi.nlm.nih.gov/compound/119093#section=2D-Structure>).

Health-promoting effects	References
Effects on the liver	Ahmadi <i>et al.</i> , 2019; Ben Salem <i>et al.</i> , 2017b; Ben Salem <i>et al.</i> , 2019; Celepli <i>et al.</i> , 2022a; Celepli <i>et al.</i> , 2022b; Colak <i>et al.</i> , 2016; Deng <i>et al.</i> , 2022; El-Boshy <i>et al.</i> , 2017; El Morsy and Kamel, 2015; Elsayed Elgarawany <i>et al.</i> , 2020; Frigerio <i>et al.</i> , 2021; Gebhardt, 1997; Gebhardt, 2001; Gebhardt, 2002a; Gebhardt, 2002b; Gebhardt and Fausel, 1997; Heidarian and Rafieian-Kopaei, 2013; Kirchhoff <i>et al.</i> , 1994; Küçükgergin <i>et al.</i> , 2010; Kurt <i>et al.</i> , 2014; Kwon <i>et al.</i> , 2018; Lee <i>et al.</i> , 2021b ; Liao <i>et al.</i> , 2021; Majnooni <i>et al.</i> , 2021; Mehmetçik <i>et al.</i> , 2008; Menghini <i>et al.</i> , 2010; Metwally <i>et al.</i> , 2011; Miccadei <i>et al.</i> , 2008; Nasef <i>et al.</i> , 2022; Panahi <i>et al.</i> , 2018; Qiang <i>et al.</i> , 2012; Rangboo <i>et al.</i> , 2016; Saénz Rodriguez <i>et al.</i> , 2002; Sharaf El-Deen <i>et al.</i> , 2017; Speroni <i>et al.</i> , 2003; Sümer <i>et al.</i> , 2020; Tang <i>et al.</i> , 2017; Wang <i>et al.</i> , 2021; Wauquier <i>et al.</i> , 2021
Effects on lipid profile	Ben Salem <i>et al.</i> , 2017b; Ben Salem <i>et al.</i> , 2019; Ben Salem <i>et al.</i> , 2022a; Bogavac-Stanojevic <i>et al.</i> , 2018; Bundy <i>et al.</i> , 2008; Deng <i>et al.</i> , 2022; Englisch <i>et al.</i> , 2000; Frigerio <i>et al.</i> , 2021; Gebhardt, 1998; Heidarian and Rafieian-Kopaei, 2013; Ibrahim <i>et al.</i> , 2022; Küçükgergin <i>et al.</i> , 2010; Küskü-Kiraz <i>et al.</i> , 2010; Kwon <i>et al.</i> , 2018; Liao <i>et al.</i> , 2021; Majnooni <i>et al.</i> , 2021; Panahi <i>et al.</i> , 2018; Qiang <i>et al.</i> , 2012; Qinna <i>et al.</i> , 2012; Rangboo <i>et al.</i> , 2016; Rondanelli <i>et al.</i> , 2013; Rondanelli <i>et al.</i> , 2014; Rondanelli <i>et al.</i> , 2019; Shimoda <i>et al.</i> , 2003; Tang <i>et al.</i> , 2017; Wauquier <i>et al.</i> , 2021
Effects on the cardiovascular system	Ben Salem <i>et al.</i> , 2022a; Bogavac-Stanojevic <i>et al.</i> , 2018; Crevar-Sakac <i>et al.</i> , 2016; Juzyszyn <i>et al.</i> , 2008; Küçükgergin <i>et al.</i> , 2010; Li <i>et al.</i> , 2004; Lupattelli <i>et al.</i> , 2004; Roghani-Dehkordi and Kamkhah, 2009; Wang <i>et al.</i> , 2021; Xia <i>et al.</i> , 2014; Zapolska-Downar <i>et al.</i> , 2002
Effects on the gastrointestinal system	Bundy <i>et al.</i> , 2004; Emendörfer <i>et al.</i> , 2005; Holtmann <i>et al.</i> , 2003; Ishida <i>et al.</i> , 2010; Marakis <i>et al.</i> , 2002; Nassar <i>et al.</i> , 2013; Sabater <i>et al.</i> , 2019; Verspohl <i>et al.</i> , 2008; Walker <i>et al.</i> , 2001
Antimetabolic and antiobesity activity	Ardalani <i>et al.</i> , 2020; Ben Salem <i>et al.</i> , 2019; Ben Salem <i>et al.</i> , 2022a; Ebrahimi-Mameghani <i>et al.</i> , 2018; Kwon <i>et al.</i> , 2018; Rezazadeh <i>et al.</i> , 2018a; Rezazadeh <i>et al.</i> , 2018b; Rondanelli <i>et al.</i> , 2014; Wauquier <i>et al.</i> , 2021
Anticancer activity	Abdel-Moneim <i>et al.</i> , 2021; Ding <i>et al.</i> , 2021; Islam <i>et al.</i> , 2021; Lepore <i>et al.</i> , 2019; Liu <i>et al.</i> , 2019; Menghini <i>et al.</i> , 2010; Metwally <i>et al.</i> , 2011; Miccadei <i>et al.</i> , 2008; Mileo <i>et al.</i> , 2012; Mileo <i>et al.</i> , 2015; Mileo <i>et al.</i> , 2020; Muti <i>et al.</i> , 2022; Pulito <i>et al.</i> , 2015; Villarini <i>et al.</i> , 2021; Yang <i>et al.</i> , 2022
Probiotic and prebiotic activities	Costabile <i>et al.</i> , 2010; Fissore <i>et al.</i> , 2015; López-Molina <i>et al.</i> , 2005; Riezzo <i>et al.</i> , 2012; Valerio <i>et al.</i> , 2010; Van den Abbeele <i>et al.</i> , 2020; Zeaiter <i>et al.</i> , 2019

Antioxidant activity	Abdel-Moneim <i>et al.</i> , 2021; Ahmadi <i>et al.</i> , 2019; Ben Salem <i>et al.</i> , 2017a; Ben Salem <i>et al.</i> , 2017b; Ben Salem <i>et al.</i> , 2019; Ben Salem <i>et al.</i> , 2022a; Ben Salem <i>et al.</i> , 2022b; Biel <i>et al.</i> , 2020; Bogavac-Stanojevic <i>et al.</i> , 2018; Brown and Rice-Evans, 1998; Carpentieri <i>et al.</i> , 2022; Celepli <i>et al.</i> , 2022a; Celepli <i>et al.</i> , 2022b; Cicek <i>et al.</i> , 2022; Colak <i>et al.</i> , 2016; Crevar-Sakac <i>et al.</i> , 2016; D'Antuono <i>et al.</i> , 2018; Deng <i>et al.</i> , 2022; Durazzo <i>et al.</i> , 2013; El-Boshy <i>et al.</i> , 2017; El Morsy and Kamel, 2015; Elsayed Elgarawany <i>et al.</i> , 2020; Gebhardt, 1997; Gebhardt and Fausel, 1997; Gurel <i>et al.</i> , 2007; Heidarian and Rafieian-Kopaei, 2013; Ibrahim <i>et al.</i> , 2022; Jiménez-Escrig <i>et al.</i> , 2003; Juzyszyn <i>et al.</i> , 2008; Khattab <i>et al.</i> , 2016; Kostić <i>et al.</i> , 2021; Küçükgergin <i>et al.</i> , 2010; Küskü-Kiraz <i>et al.</i> , 2010; Lee <i>et al.</i> , 2021a; Lee <i>et al.</i> , 2021b; Liao <i>et al.</i> , 2021; Lin <i>et al.</i> , 2022; Liu <i>et al.</i> , 2019; Magielse <i>et al.</i> , 2014; Matsumoto <i>et al.</i> , 2021; Mehmetçik <i>et al.</i> , 2008; Menghini <i>et al.</i> , 2010; Metwally <i>et al.</i> , 2011; Miccadei <i>et al.</i> , 2008; Mohammed <i>et al.</i> , 2020; Nasef <i>et al.</i> , 2022; Nassar <i>et al.</i> , 2013; Pérez-García <i>et al.</i> , 2000; Rezazadeh <i>et al.</i> , 2018a; Sarawek <i>et al.</i> , 2008; Skarpanska-Stejnborn <i>et al.</i> , 2008; Speroni <i>et al.</i> , 2003; Takei <i>et al.</i> , 2015; Tang <i>et al.</i> , 2017; Wang <i>et al.</i> , 2021; Xia <i>et al.</i> , 2014; Zapolska-Downar <i>et al.</i> , 2002
Antidiabetic effects	Ben Salem <i>et al.</i> , 2017b; Deng <i>et al.</i> , 2022; Ebrahimi-Mameghani <i>et al.</i> , 2018; Fantini <i>et al.</i> , 2011; Ibrahim <i>et al.</i> , 2022; Kwon <i>et al.</i> , 2018; Rondanelli <i>et al.</i> , 2014
Antiarthritic effects	Masutani <i>et al.</i> , 2016; Wauquier <i>et al.</i> , 2021
Renoprotective activity	Ben Salem <i>et al.</i> , 2022b; El-Boshy <i>et al.</i> , 2017; Khattab <i>et al.</i> , 2016; Sümer <i>et al.</i> , 2020; Wang <i>et al.</i> , 2021
Neuroprotective effects	Cicek <i>et al.</i> , 2022; Ibrahim <i>et al.</i> , 2022
Effects on the reproductive system	Gurel <i>et al.</i> , 2007; Mohammed <i>et al.</i> , 2020
Effects on the immune system	El-Boshy <i>et al.</i> , 2017; Hueza <i>et al.</i> , 2019
Antiphotaging effects	Takei <i>et al.</i> , 2015; Tanaka <i>et al.</i> , 2013
Antifungal effects	Zhu <i>et al.</i> , 2005
Prevention of periodontal diseases	Hayata <i>et al.</i> , 2019

Table 1. Health-promoting properties of artichoke. The table shows the beneficial properties of artichoke and the scientific articles which report these effects.



Figure 1. Artichoke. A botanical illustration of artichoke. ("*Cynara scolymus*" by Adriana Morgante Giornetti).

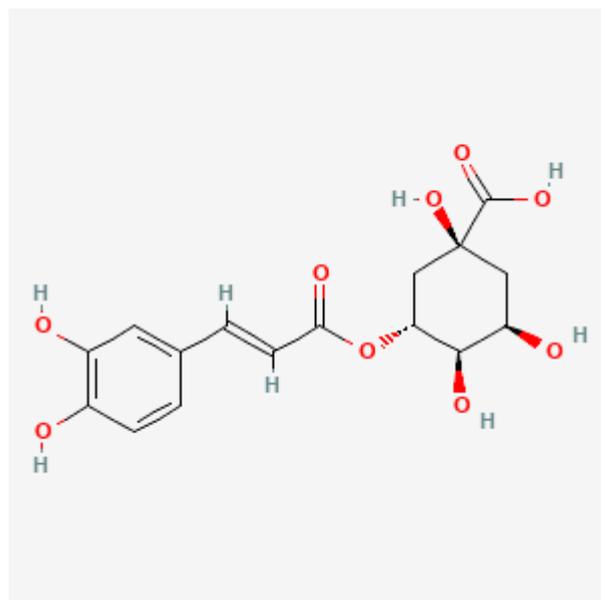


Figure 2. Chlorogenic acid. A chemical structure image of chlorogenic acid (Retrieved from: <https://pubchem.ncbi.nlm.nih.gov/compound/1794427#section=2D-Structure>).

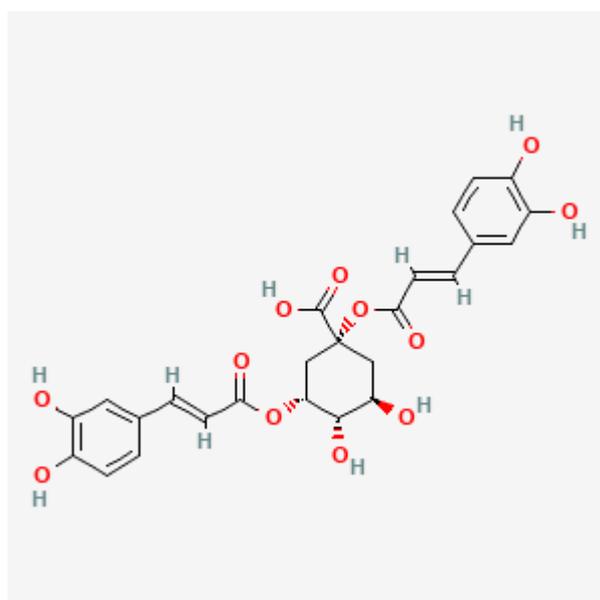


Figure 3. Cynarine. A chemical structure image of cynarine (Retrieved from: <https://pubchem.ncbi.nlm.nih.gov/compound/5281769#section=2D-Structure>).

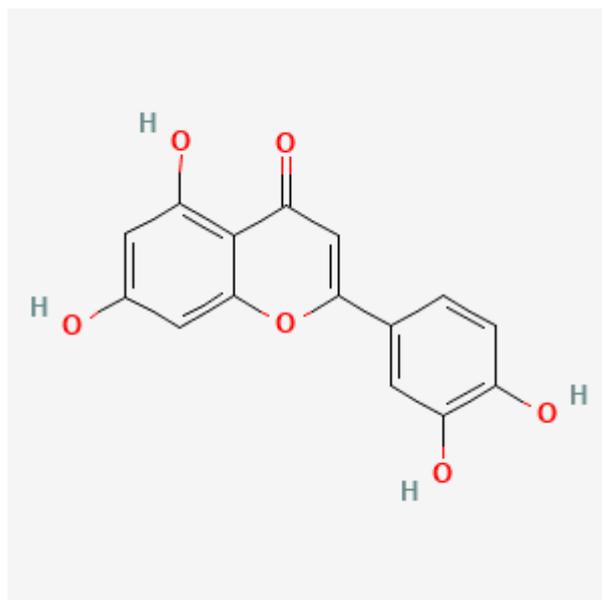


Figure 4. Luteolin. A chemical structure image of luteolin (Retrieved from: <https://pubchem.ncbi.nlm.nih.gov/compound/5280445#section=2D-Structure>).

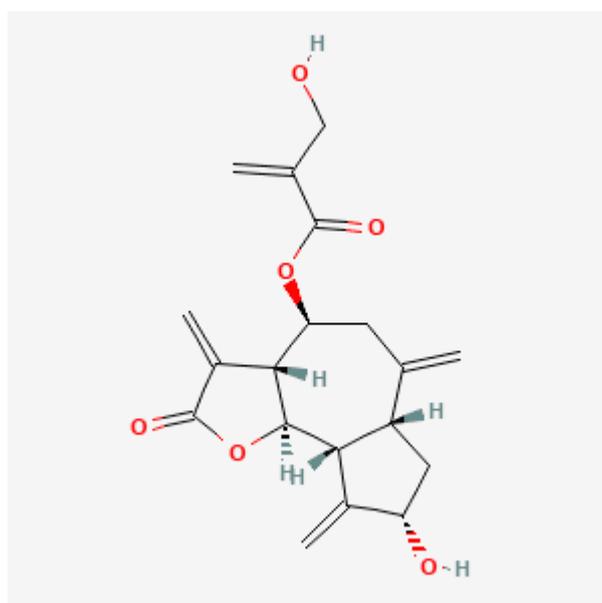


Figure 5. Cynaropicrin. A chemical structure image of cynaropicrin (Retrieved from: <https://pubchem.ncbi.nlm.nih.gov/compound/119093#section=2D-Structure>).