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Der Pharmacia Lettre, 2016, 8 (9):168-173
(http://scholarsresearchlibrary.com/archive.html)

Scholars Research Library
ISSN 0975-5071
USA CODEN: DPLEB4

Study of therapeutic effects of *Cynara scolymus L.*: A review

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ABSTRACT

Cynara scolymus L. is is a perennial plant native to the Mediterranean region a variety of a species of thistle cultivated as a food.This review article was carried out by searching studies in PubMed, Medline, Web of Science, and Iran Medex databases. The initial search strategy identified about 102 references. In this study, 42 studies was accepted for further screening and met all our inclusion criteria [in English, full text, therapeutic effects of Cynara scolymus L. and dated mainly from the year 2008 to 2016.The search terms were "Cynara scolymus L.", "therapeutic properties", "pharmacological effects". It is commonly used for milk clotting effect, Antioxidant effect, Anti-cancer effect, Prebiotic activity, Anti-metabolic syndrome, Functional properties, Anti-fungal effect, Anti-ulcerogenic effect, Anti-obesity, Genotoxicity effect, Antiphotoaging activity, Synergetic effect, Hypoglycemic effect, Bifid genic effect, Prebiotic effect, Mitochondrial respiratory chain system activity, Antihypercholesterolemic effect, Xanthinoxidase inhibitory activity. Cynara scolymus L. l. is widely used for therapeutic and non-therapeutic purposes that trigger its significant value. However, more studies about the other useful and unknown properties of this multipurpose plant is essential.

Keywords: *Cynara scolymus L.*, Phytochemicals, Therapeutic effects, Pharmacognosy, Alternative and complementary medicine.

INTRODUCTION

Cynara scolymus L or artichokes is a perennial plant[1] native to the Mediterranean region a variety of a species of thistle cultivated as a food[2]. Both wild forms and cultivated varieties (cultivars) exist[3].This vegetable grows to 1.4–2 m tall, with arching, deeply lobed, silvery, glaucous-green leaves 50–82 cm long. This plant was traditionally used as a food among the ancient Greeks and Romans [4]. In North Africa, where it is still found in the wild state, the seeds of artichokes, probably cultivated, were found during the excavation of Roman-period Mons Claudianus in Egypt [5]. *Cynara scolymus* is a pharmacologically important medicinal plant containing phenolic acids and flavonoids. Experimental studies indicate antioxidant and hepatoprotective effects of C. scolymus but there have been no studies about therapeutic effects of liver diseases [6, 7]. *Cynara scolymus L.* (Asteraseae) (artichoke) is commonly eaten as a vegetable; its leaves are frequently used in folk medicine in the treatment of hepatitis, hyperlipidemia, obesity and dyspeptic disorders.

Chemical constituents

Artichoke contains the bioactive agent's apigenin and luteolin. The total antioxidant capacity of artichoke flower heads is one of the highest reported for vegetables [8]. Cynarine is a chemical constituent in Cynara [9]. The

majority of the cynarine found in artichoke is located in the pulp of the leaves, though dried leaves and stems of artichoke also contain it. It inhibits taste receptors, making water (and other foods and drinks) seem sweet.

Hepatocurative effects

Hepatocurative effects of C. scolymus leaf extract on carbon tetrachloride (CCl4)-induced oxidative stress and hepatic injury in rats were investigated .results indicated that C. scolymus leaf extract has hepatocurative effects of on CCl4-induced oxidative stress and hepatic injury by reducing lipid peroxidation, providing affected antioxidant systems towards the normal range. It also had positive effects on the pathway of the regulatory mechanism allowing repair of DNA damage on CCl4-induced hepatotoxicity [10].

Milkclotting effect

Two different milk clotting enzymes, belonging to the aspartic protease family, were extracted from both artichoke leaves and alpine thistle flowers, and the latter was covalently immobilized by using a polyacrylic support containing polar epoxy groups. Our findings showed that the alpine thistle aspartic protease was successfully immobilized at pH 7.0 on Immobeads IB-150P beads and that, under these experimental conditions, an immobilization yield of about 68% and a recovery of about 54% were obtained. Since the enzyme showed an optimal pH of 5.0, a value very similar to the one generally used for milk clotting during cheese making, and exhibited a satisfactory stability over time, the use of such immobilized vegetable rennet for the production of novel dairy products is suggested[11].

Antioxidant effect

The protective effects of coenzyme Q10 (CoQ10) and *Cynara scolymus L* (CS) on doxorubicin (dox)-induced toxicity was Evaluated. It is concluded that pretreatment with CoQ10 and CS is associated with up-regulation of favorable protective enzymes and down-regulation of oxidative stress. That can be advised as a supplement to dox-treated patients [12].

The potential for bioavailability of the artichoke polyphenols was estimated by using both in vitro digestion and Caco-2 human intestinal cell models. It was shown that the utilized in vitro models, although not fully responding to the morphological and physiological features of human in vivo conditions, could be a useful tool for investigating mechanistic effects of polyphenols released from the food matrix [13].

In an in vivo study, antioxidant activity of a quantified leaf extract of *Cynara scolymus* (artichoke) was examined and it was suggested that 0.2 g/kg BW/day of ALE decreased oxidative stress: malondialdehyde and 8-hydroxydeoxyguanosine levels significantly diminished, whereas erythrocyte glutathione levels significantly increased. A 1.0 g/kg BW/day ALE did not show higher antioxidant activity [14].

The phenolic compounds of this plant was evaluated by using HPLC. It was indicated that the artichoke extract could be regarded as a bioactive functional food and also as a promising source of antioxidant phenolic compounds [15].

The ability of C. scolymus L. LE to modulate the mutagenicity of EMS was examined using the cytokinesis block micronucleus (CBMN) cytome assay in three antigenotoxic protocols, pre- post- and simultaneous treatments and it was suggested that the protective activity of C. scolymus L. could be associated to its constitutive antioxidants compounds [16].

The protective effect of the hydroethanolic extract of artichoke against altered biochemical parameters in rats fed with lead-containing diet was evaluated.These results clearly show that the artichoke extract in lead-poisoned rats has suitable chelating properties for the reduction of blood lead levels [17].

The catecholase and cresolase activities of PPO from three different Sicilian artichokes cultivar were evaluated with regard to substrate specificity and enzyme kinetics, optimum pH and temperature, temperature and pH stability, and inhibitor test; the results were used for technological purposes, particularly to optimize minimally processed productions (ready-to-eat and cook-chilled artichokes)[18].

The effect of an artichoke extract on induced reactive oxygen species (ROS) generation in cultured human umbilical endothelial cells (HUVECs) and its reductive properties were evaluated. The results was confirmed application of artichoke extracts as endothelium protecting agents [19].

The influence of supplementation with artichoke-leaf extract on parameters describing balance between oxidants and antioxidants in competitive rowers was investigated and it was demonstrated that consuming artichoke-leaf extract, a natural vegetable preparation of high antioxidant potential, resulted in higher plasma TAC than placebo but did not limit oxidative damage to erythrocytes in competitive rowers subjected to strenuous training [20].

The hepatoprotective properties of polyphenolic extracts from the edible part of artichoke (AE) was evaluated and it was illustrated that AE reduced cell viability and had an apoptotic activity on a human liver cancer cell line [21].

The effect of the artichoke extract (AE) on oxidation of palmitic-1-14C acid administered intravenously to rats at a dose 25 and 50 mg/kg bwwas investigated.The results demonstrate that the AE possess stimulatory properties with respect to oxidation of palmitic acid administered to rats, and provide new information on the mechanism of antilipemic activity of the extract associated with activation of lipid oxidation in the organism [22].

Anti-cancer effect
Chronic and low doses of AEs treatment at sublethal concentrations was demonstrated .Findings demonstrate that chronic AEs treatment inhibits breast cancer cell growth via the induction of premature senescence through epigenetic and ROS-mediated mechanisms.[23].

Antitumoral effects of the leaf extract of Cynara scolymus both *in vitro* and *in vivo* on mesothelioma cell lines was investigated. It was found that Cynara scolymus treatment affects strongly cell growth, migration and tumor engraftment of mesothelioma cell lines. [24].

Prebiotic activity
The positive prebiotic activity scores observed with respect to Escherichia coli 25922 indicated that fibers assayed are metabolized as well as glucose by Lactobacillus plantarum 8114 and Bifidobacterium bifidum ATCC 11863 and that they are selectively metabolized by these microorganisms. The potential capacity to selectively stimulate the growth of intestinal bacteria associated with health shown by fraction A can be ascribed to its high inulin and low methylation degree pectin contents [25].

Anti-metabolic syndrome
Cynara scolymus showed moderate ACE inhibitory activity. The results indicate some moderate potential of the dietary supplement Boldocynara and its single ingredients for the prevention of metabolic disorders [26].

Functional properties
The basic chemical composition and functional properties of six by-product fractions collected from different steps of artichoke industrial processing were evaluated and it showed that Fractions differed in thermal treatment, the bract position in the artichoke head and the cutting size. The more interesting fractions for use as functional ingredients were those situated closer to the artichoke heart and thermally treated [27].

Anti-fungal effect
The possible endophytic behavior of B. bassiana and B. ochroleuca on artichoke, Cynara scolymus, after foliar spraying technique was investigated. The results reveals significant new data on the interaction of inoculated fungi with artichoke plant as ecological roles that can be exploited for the protection of plants [28].

Anti-ulcerogenic effect
The role of the methanol extract as an anti-ulcer agent against ethanol-induced gastric ulcer in rats was evaluated. The result showed the high anti-ulcerogenic potential of scales of C. scolymus heads was established here for the first time [29].

Anti-obesity
The efficacy of a dietary supplementation with an extract from Cynara scolymus (Cs) on the glucose pattern in a group of patients with naïve impaired fasting glycaemia (IFG) was evaluated. The findings demonstrate the efficacy of Cs extract on the reduction of glycometabolic parameters in overweight subjects with IFG [30].

The effect of this extract combination and of each single extract in an experimental model of food craving, made up of rats was investigated and the results suggest that the extract combination can reduce the self-administration of the chocolate-flavoured beverage entirely relied on the Phaseolus vulgaris extract and combinations of Phaseolus vulgaris and Cynara scolymus extracts may possess anti-overweight, anti-obesity, and possibly anti-food-related addictive disorders [31].

The efficacy of a dietary supplementation with an extract from Phaseolus vulgaris and Cynara scolymus, on satiation, the glucose and lipid pattern was investigated. It found that in the supplemented group, the homeostasis model assessment, the body mass index and the susceptibility-to-hunger score of the TFEQ, decreased significantly after intervention; these parameters did not change in the controls. This treatment appears potentially useful in the management of overweight and dysglycaemia[32].

In an animal study, non-selected Wistar and genetically obese Zucker rats were treated acutely with a purified extract of Cynara scolymus flowering heads (500-1500 mg/kg by gavage) immediately prior to 1 h access to a fixed amount of food. The results obtained constitute the first evidence of a hypoglycemic effect of an artichoke preparation in laboratory rodents and confirm previous observations made in humans [33].

Genotoxicity effect
Genotoxic and mutagenic activities of artichoke leaf aqueous extract in mice using the comet assay and the micronucleus test was evaluated. The genotoxic results showed that leaf extracts did not increase micronuclei in peripheral blood cells. Compared to the control group, a significant increase in comet assay values was observed only in bone marrow of group treated with 2000 mg/kg, the highest dose tested, indicating that artichoke tea should be consumed with moderation [34].

Antiphotoaging activity
Extracts of this plant for its possible inhibitory effect on the transcriptional activity of NF-κB was screened. *Cynara scolymus L*., showed a greatest effect on the suppression of NF-κB transactivation. So,it was found that cynaropicrin, which is a sesquiterpene lactone, inhibited the NF-κB-mediated transactivation of bFGF and MMP-1. The findings indicate that cynaropicrin is an effective antiphotoaging agent that acts by inhibiting NF-κB-mediated transactivation [35].

Synergetic effect
The effect of artichoke (*Cynara scolymus L*.) and zeolite nano-materials on urinary excretion of nicotine and consequently elimination of systematically absorbed nicotine was investigated. Artichoke leaf extract can cause increase in urinary excretion of nicotine in longer post administration times. It was observed that co-administration of nanozeolites and the leaf extract has the synergetic effect on increasing the urinary excretion of nicotine [36].

Hypoglycemic effect
The effect of standardized extracts of P. vulgaris and C. scolymus and their combination on food intake and glycemia in rats was investigated. The results suggest that a mixture of P. vulgaris and C. scolymus extracts is preferable over each single extract, as it combines the anorectic effect of the P. vulgaris extract with the hypoglycemic effect of both extracts. [37].

Bifid genic effect
The impact of a very-long-chain inulin on the human intestinal microbiota compared with maltodextrin was determined. Theresults were also confirmed that daily consumption of VLCI extracted from globe artichoke exerted a pronounced prebiotic effect on the human faecalmicrobiota composition and was well tolerated by all volunteers [38].

Prebiotic effect
The changes in carbohydrate composition occurring in artichoke heads during storage under different conditions were evaluated. The results showed Higher-temperature storage and storage without packing induce strong carbohydrate changes. Thereby, eating stored artichoke leads to consumption of an inulin quantity that does not provoke unwanted symptoms related to gas production but sufficient to have a prebiotic effect [39].

Mitochondrial respiratory chain system activity
The effect of artichoke extract on mitochondrial respiratory chain (MRC) activity in isolated rat liver mitochondria was studied. The results suggest a complex inhibitory mechanism of the extract. Inhibition of the succinate oxidase system was competitive whereas isolated cytochrome oxidase was inhibited noncompetitively [40].

Antihypercholesterolemic effect
The effect of ALE on plasma lipid levels and general well-being in otherwise healthy adults with mild to moderate hypercholesterolemia. 131 adults were screened .it is suggested that the apparent positive health status of the study population may have contributed to the modesty of the observed response [41].

Xanthinoxidase inhibitory activity
The xanthine oxidase (XO) inhibitory activity of an artichoke leaf extract (ALE) and some of its main compounds in vitro was examined.an aqueous ALE, caffeic acid derivatives and flavones exerted XO inhibitory effects in vitro but a hypouricemic activity could not be confirmed after oral administration [42].

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