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Globe artichoke: A functional food and source of nutraceutical ingredients

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ARTICLE INFO

Article history:
Received 13 October 2008
Accepted 23 December 2008
Available online 28 February 2009

Keywords:
Cynara
Caffeoylquinic acids
Cynarin
Flavonoids
Anthocyanin pigments
Inulin
By-products

ABSTRACT

Globe artichoke (Cynara cardunculus L. subsp. scolymus (L.) Hayek, (formerly Cynara scolymus L.) represents an important component of the Mediterranean diet, and is a rich source of bioactive phenolic compounds, and also inulin, fibre and minerals. In addition, artichoke leaf extracts have long been used in folk medicine, particularly for liver complaints. These therapeutic properties have often been ascribed to the cynarin (1,3-O-dicaffeoylquinic acid) content of these extracts. In various pharmacological test systems, artichoke leaf extracts have exhibited hepatoprotective, anticarcinogenic, antioxidative, antibacterial, anti-HIV, bile-expelling, and urinative activities as well as the ability to inhibit cholesterol biosynthesis and LDL oxidation. These broad therapeutic indications cannot be ascribed to a single, but to several active compounds that together generate additive or synergistic pharmacologic effects; these include mono- and dicaffeoylquinic acids, and flavonoids such as luteolin and its 7-O-glucoside. Artichoke by-products such as leaves, external bracts and stems that are produced by the artichoke processing industry, represent a huge amount of discarded material (about 80–85% of the total biomass of the plant), which could be used as a source of inulin but also of phenolics, and should be considered as a raw material for the production of food additives and nutraceuticals.

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1. Introduction

Over the last few years a renewed and growing interest in the artichoke, an old plant with new uses in functional foods, has been observed. Artichoke, Cynara cardunculus L. subsp. scolymus (L.) Hayek, (formerly Cynara scolymus L.) is an ancient herbaceous perennial plant, originating from the Mediterranean area, which today is widely cultivated all over the world. The botanical name is derived in part from the tradition of fertilizing the plant with ashes (Latin: cinis, cineris), and partly from the Greek skolymos, meaning “thistle” from the spines found on the bracts (they are not leaves) that enclose the flower heads forming the edible portion of the plant (Oliaro, 1969). Artichoke is widely cultivated for its large immature inflorescences, called capitula or heads, with edible fleshy leaves (bracts) and receptacle, which represent an important component of the Mediterranean diet and is a rich source of bioactive phenolic compounds, and also inulin, fibres and minerals (Lattanzio, 1982; Orlovskaya et al., 2007). In addition, the leaves, also rich in phenolic compounds (Lattanzio & Morone, 1979; Lattanzio & Van Sumere, 1987; Lattanzio et al., 1989, 1994; Fratianni et al., 2007), are used as a herbal medi-
cient and have been recognised since ancient times for their beneficial and therapeutic effects: extracts from artichoke have been used for hepatoprotection (Adzet et al., 1987) as a choleretic (Preziosi et al., 1959; Preziosi, 1962), diuretic (Preziosi, 1969), liver-protective, and lipid-lowering agents (Gebhardt, 1997).

Artichoke is a species belonging to the Asteraeace family, which has been known since the 4th century B.C. as a food and remedy. This plant has been appreciated by the ancient Egyptians, Greeks, and Romans, who used it both as a food and as a medicine (for their beneficial effects against hepatobiliary diseases and as a digestive aid) (Marzi et al., 1975; Sonnante et al., 2002). Globe artichoke still plays an important role in human nutrition, especially in the Mediterranean region. Globe artichoke contributes significantly to the Mediterranean agricultural economy, with an annual production of about 770,000 tonnes (t) (>60% of total global production) from over 80 kha of cultivated land. Italy is the leading world producer (about 474,000 t), followed by Spain (215,000 t), France (55,000 t) and Greece (25,000 t). Globe artichoke is also cultivated in the Near East (Turkey and Iran), North Africa (Egypt, Morocco, Algeria, Tunisia), South America (Argentina, Chile and Peru), and the United States (mainly in California), and its cultivation is spreading in China, India, Argentina, Chile and Peru), and the United States (mainly in California), and its cultivation is spreading in China. Globe artichoke contributes significantly to the Mediterranean agricultural economy, with an annual production of about 770,000 tonnes (t) (>60% of total global production) from over 80 kha of cultivated land. Italy is the leading world producer (about 474,000 t), followed by Spain (215,000 t), France (55,000 t) and Greece (25,000 t). Globe artichoke is also cultivated in the Near East (Turkey and Iran), North Africa (Egypt, Morocco, Algeria, Tunisia), South America (Argentina, Chile and Peru), and the United States (mainly in California), and its cultivation is spreading in China, India, Argentina, Chile and Peru), and the United States (mainly in California), and its cultivation is spreading in China.

The chemical components of artichoke have been studied extensively and this plant has been found to be a rich source of polyphenolic compounds, with mono- and dicaffeoylquinic acids as the major chemical components (Lattanzio, 1981). Artichoke accumulates various caffeic acid (3,4-dihydroxyxycinic acid) depsides, positional isomers of caffeic acid esters of quinic acid. Two mechanisms for the formation of such esters have been described; one involving the hydroxycinnamoyl-CoA thioester and the other one the 1-O-(hydroxycinnamic acid)-acyl glucoside (Barz et al., 1985; Strack et al., 1987). The former mechanism was first shown to operate in the formation of chlorogenic acid in Nicotiana cell-suspension cultures (Stockigt & Zenk, 1974). However, it is now known that both pathways can lead to the same product, depending on the source of enzyme used, since recently it was shown that Ipomoea root tissue catalyzes the formation of chlorogenic acid from 1-O-caffeoylglucose (Villegas & Kojima, 1985; Villegas & Kojima, 1986). Moreover, alternative esterification (transacylations) may also be possible. For example, chlorogenic acid, which is common in Asteraceae, may act as an acyl donor molecule for caffeoyltransfascerase (Kojima & Kondo, 1985; Villegas et al., 1987; Strack & Gross, 1990).

As far as the sub-cellular localization of caffeoylquinic derivatives is concerned, biochemical and ultrastructural evidence suggests a strict compartmentalization in the synthesis and transport of phenolic compounds in the cell. Such compartmentalization may be considered as pathways consisting of complexes composed of consecutively assembled, membrane-associated enzymes, where end products of synthesis are accumulated in a membrane enclosure. These vesicles could then be transported to the central vacuole for internal sequestration or to the plasma membrane for secretion. According to this mechanism, chloroplasts are involved in some steps of phenolic biosynthesis leading to the formation of cinnamic acid derivatives. It is likely that cinnamic units, formed at the level of phenylalanine-ammonia lyase (PAL, EC 4.1.3.5) (associated with the endoplasmic reticulum), are converted to quinic esters in the chloroplasts since the enzymes that catalyze the final steps in their biosynthesis are described as chloroplastic: the association with chloroplasts suggests that caffeoylquinic acids have a role in protecting against light damage (Alibert et al., 1977; Alibert & Boudet, 1982; Boudet et al., 1985; Hrazdina & Wagner, 1985; Mondolot et al., 2006).

Caffeic acid esters of quinic acid in artichoke extracts have been well characterized, especially by the Panizzi group starting from the 1950s (Panizzi & Scarpati, 1954, 1965; Panizzi et al., 1954, 1955; Scarpati et al., 1957, 1964; Scarpati et al., 1980).
The most well-known caffeoylquinic acid derivative identified in artichoke extracts (heads and leaves), even though it is not the most abundant, is cynarin. This compound was isolated from artichoke leaf extracts and characterized for the first time by Panizzi and Scarpati (1954). Within the framework of a multidisciplinary research effort to identify artichoke components that stimulate biliary secretion and cholesterinic metabolism, they isolated a crystalline substance showing these physiological activities. The substance exhibited left-handed rotatory power and a weak acid reaction; i.e. a deep yellow and slightly stable in air alkaline solution, and a green colour in the presence of ferric chloride.

In order to prevent confusion here, it must be pointed out that in the 1950s and 1960s a pre-IUPAC nomenclature for cyclitols (where the positional number of carbon atoms in the quinic acid ring were assigned in an anticlockwise manner; see Table 1) was utilized. The effect of this was that cynarin structure, initially described as 1,4-O-dicaffeoylquinic acid (Panizzi et al., 1954), was identified as 1,5-O-dicaffeoylquinic acid (Panizzi & Scarpati, 1965).

Other caffeoylquinic derivatives identified in artichoke extracts are: 1-O-cafeoylquinic acid; 3-O-cafeoylquinic acid (chlorogenic acid), 4-O-cafeoylquinic acid (cryptochlorogenic acid), 5-O-cafeoylquinic acid (neochlorogenic acid), 1,3-O-dicaffeoylquinic acid, 1,4-O-dicaffeoylquinic acid, and 3,5-O-dicaffeoylquinic acid. All these compounds can be found in both leaves and heads of artichoke; their relative abundance is dependent on the solvent, the pH, and the temperature used for their extraction (Panizzi et al., 1954, 1955; Scarpati et al., 1957, 1964; Dranik et al., 1964; Panizzi & Scarpati, 1965; Michaud, 1967; Niciforescu, 1970). In the 1970s and 1980s, following the advent of HPLC (high performance liquid chromatography) techniques for the separation and identification of plant phenolics, further caffeoylquinic derivatives, namely 3,4-O-dicaffeoylquinic acid and 4,5-O-dicaffeoylquinic acid, were identified (Fig. 1) (Lattanzio et al., 1989, 1994).

At this point, it is paramount that the reader understands that there were changes to the way caffeoylquinic acids were classified in 1973, and according to the new IUPAC nomenclature of cyclitols (positional number assigned to the carbon atoms of the quinic acid ring in clockwise sense) (IUPAC, 1976), the structures of both mono- and dicaffeoylquinic acids were renamed (Table 1). As a result, chlorogenic acid (formerly 3-O-cafeoylquinic acid), the most abundant phenolic compound in artichoke tissues, is now called 5-O-cafeoylquinic acid, while cynarin (formerly 1,5-O-dicaffeoylquinic acid) became 1,3-O-dicaffeoylquinic acid. For the purposes of this review, all subsequent references to caffeoylquinic acid structures will use the post-IUPAC nomenclature system.

Within the caffeoylquinic derivatives, chlorogenic acid (5-O-cafeoylquinic acid) is the most abundant single component (39%), followed by 1,5-O-dicaffeoylquinic acid (21%) and 3,4-O-dicaffeoylquinic acid (11%), based on total caffeoylquinic acid contents (see Table 2). Cynarin (1,3-O-dicaffeoylquinic acid) content in methanolic extracts of artichoke are very low (about 1.5%). It should be remembered that the caffeoylquinic derivative content of artichoke tissues is highly dependent on the physiological stage of the tissues: the total caffeoylquinic acid content ranges from about 8% on dry matter basis in young tissues to less than 1% in senescent tissues (Lattanzio & Morone, 1979; Lattanzio & Van Sumere, 1987; Lattanzio, 1981; Lattanzio et al., 1978, 2005; Adzet & Puigmacia, 1985).

Artichoke dry extracts are currently commercialized as drugs mainly for treatment of liver diseases: these include Cynara (200 mg of artichoke extract; Vesta Pharmaceuticals, Inc.), Artichoke 500 mg (artichoke leaf extract; Jarrow Formula, Inc.), Artichoke (artichoke leaf extract containing 0.3% flavonoids expressed as luteolin-7-O-glucoside and 2.5% caffeoylquinic acid expressed as chlorogenic acid, Indena S.p.A.), CINARAN® (artichoke flowering head extracts containing 13–18% of caffeoylquinic acids, Indena S.p.A.) among others (Llorach et al., 2002). This growing commercial utilization of artichoke active principle as choleric, hypcholesterolemic, and antidyspeptic compounds, and the need to describe the active principals, requires that there is great care in use of the nomenclature of caffeoylquinic derivatives. As previously stated, 1,5-O-dicaffeoylquinic acid is one of the most abundant phenolic compounds in artichoke tissues, while the content of 1,3-O-dicaffeoylquinic acid in methanolic extracts of artichoke is very low. Therefore, to establish the right nomenclature of cynarin (1,3-O-dicaffeoylquinic acid or 1,5-O-dicaffeoylquinic acid, depending on the IUPAC rules utilized), is of fundamental importance not only from a systematic viewpoint but also from an economic point of view.

<table>
<thead>
<tr>
<th>IUPAC recommendations, 1973^</th>
<th>Pre-IUPAC numbering</th>
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<tbody>
<tr>
<td>1-O-Caffeoylquinic acid</td>
<td>1-O-Caffeoylquinic acid</td>
</tr>
<tr>
<td>3-O-Caffeoylquinic acid (Neochlorogenic acid)</td>
<td>5-O-Caffeoylquinic acid</td>
</tr>
<tr>
<td>4-O-Caffeoylquinic acid (Cryptochlorogenic acid)</td>
<td>4-O-Caffeoylquinic acid</td>
</tr>
<tr>
<td>5-O-Caffeoylquinic acid (Chlorogenic acid)</td>
<td>3-O-Caffeoylquinic acid</td>
</tr>
<tr>
<td>1,3-O-Dicaffeoylquinic acid (Cynarin)</td>
<td>1,5-O-Dicaffeoylquinic acid</td>
</tr>
<tr>
<td>1,4-O-Dicaffeoylquinic acid</td>
<td>1,4-O-Dicaffeoylquinic acid</td>
</tr>
<tr>
<td>4,5-O-Dicaffeoylquinic acid</td>
<td>3,4-O-Dicaffeoylquinic acid</td>
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<td>3,5-O-Dicaffeoylquinic acid</td>
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<td>1,5-O-Dicaffeoylquinic acid</td>
<td>1,3-O-Dicaffeoylquinic acid</td>
</tr>
<tr>
<td>3,4-O-Dicaffeoylquinic acid</td>
<td>4,5-O-Dicaffeoylquinic acid</td>
</tr>
</tbody>
</table>

^ IUPAC (1976).
Quinic acid: \( R_1 = H; R_3 = H; R_4 = H; R_5 = H \)
1-O-Caffeoylquinic acid: \( R_1 = X; R_3 = H; R_4 = H; R_5 = H \)
3-O-Caffeoylquinic acid or Neocholesterolic acid: \( R_1 = H; R_3 = X; R_4 = H; R_5 = H \)
4-O-Caffeoylquinic acid or Cryptochlorogenic acid: \( R_1 = H; R_3 = H; R_4 = X; R_5 = H \)
5-O-Caffeoylquinic acid or Chlorogenic acid: \( R_1 = H; R_3 = H; R_4 = H; R_5 = X \)
1,3-O-Dicaffeoylquinic acid or Cynarin: \( R_1 = X; R_3 = X; R_4 = H; R_5 = H \)
1,4-O-Dicaffeoylquinic acid: \( R_1 = X; R_3 = H; R_4 = X; R_5 = H \)
1,5-O-Dicaffeoylquinic acid: \( R_1 = X; R_3 = H; R_4 = H; R_5 = X \)
3,4-O-Dicaffeoylquinic acid: \( R_1 = H; R_3 = X; R_4 = X; R_5 = H \)
3,5-O-Dicaffeoylquinic acid: \( R_1 = H; R_3 = X; R_4 = H; R_5 = X \)
4,5-O-Dicaffeoylquinic acid: \( R_1 = H; R_3 = H; R_4 = X; R_5 = X \)

Table 2 – Mono- and dicaffeoylquinic acids in artichoke heads of marketable quality (adapted from Lattanzio et al., 1994).

<table>
<thead>
<tr>
<th>Caffeoylquinic acid derivative</th>
<th>mg/100 g dry weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-O-Caffeoylquinic acid</td>
<td>38.14</td>
</tr>
<tr>
<td>3-O-Caffeoylquinic acid</td>
<td>57.22</td>
</tr>
<tr>
<td>4-O-Caffeoylquinic acid</td>
<td>267.02</td>
</tr>
<tr>
<td>5-O-Caffeoylquinic acid</td>
<td>1544.91</td>
</tr>
<tr>
<td>1,3-O-Dicaffeoylquinic acid</td>
<td>61.24</td>
</tr>
<tr>
<td>1,4-O-Dicaffeoylquinic acid</td>
<td>142.91</td>
</tr>
<tr>
<td>4,5-O-Dicaffeoylquinic acid</td>
<td>224.56</td>
</tr>
<tr>
<td>3,5-O-Dicaffeoylquinic acid</td>
<td>347.05</td>
</tr>
<tr>
<td>1,5-O-Dicaffeoylquinic acid</td>
<td>837.01</td>
</tr>
<tr>
<td>3,4-O-Dicaffeoylquinic acid</td>
<td>428.71</td>
</tr>
</tbody>
</table>
The presence of caffeoylquinic esters in artichoke tissues is responsible for the appearance of browning phenomena which occur through enzymatic oxidation of orthodihydroxyphenolic substrates by polyphenol oxidase (PPO, EC 1.14.18.1) or to formation of iron-chlorogenic acid complexes (Lattanzio, 2003). Browning of raw fruit and vegetables during handling and storage is a significant problem for the food industry and is believed to be one of the main causes of quality loss during storage of plant commodities. While enzymatic oxidations of phenolics generally promote brown discoloration in plant tissues, mechanically damaged iron-phenol complexes are relevant during processing of some fruits and vegetables such as potatoes, cauliflowers, asparagus and olives. This latter mechanism of darkening has been observed in stored plant commodities, in good agreement with the fact that in healthy, non-mechanically damaged plant tissues, the ripening process induces changes in cell membrane permeability, in phenolic metabolism, and in PPO properties: as the fruit ages more enzyme becomes soluble. Non-enzymatic browning reactions, caused by iron-polyphenol complexing, may occur in cold-stored non-mechanically damaged artichoke heads. During storage of artichoke heads at 4 °C low-temperature induction of PAL activity causes a biosynthetic increase of phenolics, especially chlorogenic acid. On the other hand, PPO activity does not change significantly during the storage period. Therefore, the increased content of phenolics is sufficient to provide an adequate substrate for the browning phenomenon. These reactions start from the chloroplasts, the site of chlorogenic acid biosynthesis where the iron is stored as ferritin. The release of ferritin iron, as Fe²⁺, is induced by chlorogenic acid, producing a colourless complex with an excess of chlorogenic acid. Subsequently, oxidizing conditions occurring during the senescence process and/or low temperature-induced formation of toxic oxygen products forms lead to the formation of a grey-blue chlorogenic acid/Fe³⁺ complex and subsequently the browning phenomena (Lattanzio et al., 1994).

3. Flavonoids

Besides caffeoylquinic acid derivatives, other phenolics belonging to the flavonoid class such as the flavones apigenin and luteolin, and the anthocyanidinscyanidin, peonidin, and delphinidin have been identified in artichoke tissues. Apigenin and luteolin glycosides have been detected in both leaves and artichoke heads, while anthocyanin pigments are present only in capitula. From a quantitative viewpoint these compounds are considered minor constituents of the total phenolics content (about 10% or less) of artichoke tissues. Nevertheless, luteolin is a strong antioxidant that protects low density lipoproteins from oxidation while anthocyanin pigments, besides their health-promoting properties, play an important role in the appearance of food plants and therefore in food acceptance by consumers (Aubert & Foury, 1981; Lattanzio, 1981; Lattanzio & Van Sumere, 1987; Lattanzio et al., 1994; Brown & Rice-Evans, 1998).

Fig. 2 shows the most representatives flavone glycosides identified in artichoke tissues: luteolin-7-O-β-D-glucopyranoside (luteolin-7-O-glucoside = cynaroside) (I), luteolin-7-O-α-L-rhamnosyl(1→6)-β-D-glucopyranoside (luteolin-7-O-rutinoside = scolymoside) (II), apigenin-7-O-β-D-glucopyranoside (apigenin-7-O-glucoside) (III), apigenin-7-O-α-L-rhamnosyl(1→6)-β-D-glucopyranoside (apigenin-7-O-rutinoside) (IV) (Lattanzio, 1981; Lattanzio & Van Sumere, 1987; Lattanzio et al., 1994; Frietsche et al., 2002; Schütz et al., 2004; Zhu et al., 2004). More recently, two flavanone glycosides (naringenin-7-O-glucoside and naringenin-7-O-rutinoside) have been identified as minor phenolic compounds in artichoke (Sanchez-Rabaneda et al., 2003; Schütz et al., 2004). However, these observations require verification.

Anthocyanin pigments are responsible for most of the blue, purple, red and intermediate hues of plant tissues: generally an increase in anthocyanin pigmentation is considered a positive attribute of plant foods. The anthocyanin pattern of artichoke heads, whose colour ranges from green to violet, has been investigated initially by Foury and Aubert (1977), Rif-feri and Vaccari (1978), and by Aubert and Foury (1981), who tentatively identified some cyanidin glycosides: cyanidin 3-O-β-glucoside (V), cyanidin 3-0-β-sophoroside (VI), cyanidin 3-cafeoeyglucoside, cyanidin 3-cafeoylsohposoroside, cyanidin 3-dicaffeoylsohposoroside, and cyanidin 3,5-diglucoside (VII). More recently Schütz et al. (2006a) found that the main antho-
cyanins in artichoke heads were cyanidin 3,5-diglucoside, cyanidin 3-O-β-glucoside, cyanidin 3,5-malonyldiglucoside, cyanidin 3-(3’-malonyl)glucoside (VIII), and cyanidin 3-(6’- malonyl)glucoside (IX). Besides the main anthocyanins, sev-
eral minor compounds, consisting of aglycones other than those of cyanidin, have been found. Among these, two peoni-
din derivatives and one delphinidin derivative have been characterized by high performance liquid chromatography-electrospray ionization mass spectrometry: the two peonidin derivatives were identified as peonidin 3-O-β-glucoside (X) and peonidin 3-(6’-malonyl)glucoside (XI) (Fig. 3).

4. Inulin

Fructans are a diverse group of linear or branched fructose (oligo)polymers that contain one or more β-linked fructose units. In the most prominent structural types, inulin and le-
van, the fructose chain emerges from the fructose part of a sucorose molecule, proceeding via β-2,1- and β-2,6-linkages, respectively. Besides inulin and levan, the so-called neo-kos-
tose series has been described where chain elongation occurs at the glucose portion of sucrose or in both directions (Rober-
fröid & Delzenne, 1998; Heyer et al., 1999). Fructans are of growing interest as functional food ingredients because of their potential benefits for human health. As human enzymes cannot digest fructans, they reach the colon and serve as a substrate for enterobacterial growth. Fructan containing diets selectively stimulate bifidobacteria and make them the pre-
dominant species (Roberfroid et al., 1998). Consequently, an increased fecal content of short-chain fatty acids and a decreased concentration of tumour-promoting substances, such as ammonia, is observed (Gallaher et al., 1996; Heyer et al., 1999).

Inulin is a highly water-soluble carbohydrate, which serves as an alternative storage carbohydrate in the vacuole of approximately 15% of all flowering plant species. Inulin-type
fructans are mainly found in dicot species belonging to the Asteraceae, including well-investigated species such as chicory (*Cichorium intybus* L.), Jerusalem artichoke (*Helianthus tuberosus* L.), artichoke (*C. scolymus*), dandelion (*Taraxacum officinale*), dahlia (*Dahlia variabilis*) and yacon (*Polymnia sonchifolia*) (Hellwege et al., 1998, 2000). Unlike dietary carbohydrates that are absorbed as hexose sugars (glucose, fructose) and which have a caloric value of 3.9 kcal/g (16.3 kJ/g), and whose cellular metabolism produces about 38 mol ATP/mol, inulin and oligofructose resist digestion and they are not absorbed in the upper part of the gastrointestinal tract [=non-digestible oligosaccharides (NDO)]. After oral ingestion, they reach the colon intact where they are hydrolyzed and extensively fermented by saccharolytic bacteria. Depending on both the degree of their colonic fermentation and the assumptions of the model used, the caloric value of such non-digested but fermented carbohydrates varies between 0 and 2.5 kcal/g (Roberfroid, 1999a). As far as the functional food properties of NDO is concerned: (i) there is strong evidence for a prebiotic effect of NDO in human subjects (a prebiotic effect was defined as a food-induced increase in numbers and/or activity predominantly of bifidobacteria and lactic acid bacteria in the human large intestine); (ii) there is strong evidence for a positive effect of NDO on bowel habit; (iii) there is emerging evidence that consumption of inulin-type fructans may result in increased Ca absorption in man; (iv) there are preliminary indications that inulin-type fructans interact with the functioning of lipid metabolism (Van Loo et al., 1999). Research in experimental animal models has revealed that inulin-type fructans have anticarcinogenic properties. A number of studies report the effects of inulin-type fructans on chemically induced pre-neoplastic lesions or tumours in the colon.
of rats and mice. The effects have been reported to be associated with gut flora-mediated fermentation and production of butyrate. In human cells, inulin-derived fermentation products inhibited cell growth, modulated differentiation and reduced metastasis activities. Evidence that shows that inulin-type fructans and corresponding fermentation products reduced the risks for colon cancer has been accumulating. The proposed mechanisms include reducing the exposure to mutagens and carcinogens, and suppression of tumour cell survival (Pool-Zobel, 2005).

As previously stated, globe artichoke synthesizes inulin molecules with a chain length of up to 200 (Hellwege et al., 2000). A high molecular weight inulin has also been extracted from artichoke agro-industrial wastes where the source was the external bracts and the average degree of polymerization was 46, higher than found in Jerusalem artichoke, chicory, and dahlia inulins. The differences in the average degree of polymerization (DPn) between different inulins account for their distinctly different functional attributes. Long chain length inulins are less soluble, and they have the ability to form inulin microcrystals when sheared in water or milk. These crystals are not discretely perceptible in the mouth, but they interact to form a smooth creamy texture and provide a fat-like mouth sensation. Inulin has been used successfully to replace fat in table spreads, baked goods, fillings, dairy products, frozen desserts and dressings. Artichoke inulin is

Fig. 3 – Anthocyanins identified in artichoke heads.
moderately soluble in water (maximum 5% at room temperature), it has a bland neutral taste, without any off-flavour or aftertaste, and is not sweet. Therefore, it combines easily with other ingredients without modifying delicate flavours (López-Molina et al., 2005).

The edible part of artichoke heads is characterized by a high reducing sugar content and a high percentage of water-soluble polysaccharides (inulin) (Table 3), mainly located in the receptacle: the inulin content may represent still 75% of the total glucidic content. In addition, the inulin content of the edible portion is relatively higher (about 30%) in artichoke heads of marketable quality compared to those at earlier stages of development (Lattanzio et al., 2002).

Fig. 4 shows the variability of inulin content in the edible portion of different cultivars of globe artichoke. Inulin contents range between 18.9% and 36.2% on a dry matter basis: the highest content of inulin has been found in cv. Romanesco and the lowest inulin content in cv. Violet Margot. The observed variability in inulin content could be due to the samples use for analysis being at different physiological stages, since it virtually impossible to establish in an accurate way the morphological age of different artichoke heads. Similarly, morphological differences are the main factor determining the inulin content in different cultivars: e.g. cv. Romanesco, whose receptacle contributes more to the total weight of the capitula than cv. Violet of Provenza, has an inulin content of 36.2% of dry weight (d.w.) compared to only 21.5% of d.w. for that of Violet of Provence (Lattanzio et al., 2002). Although the inulin content in by-products originating from artichoke processing (leaves, external bracts of heads) is very high, from 20 to 21%, the inulin content in the edible portion varies between 18.9% and 36.2% on a dry matter basis (Table 3).

Long known as an herbal medicine, the dried leaves of artichoke have long been used in folk medicine for their choleretic and hepatoprotective activities, that are often related to the cyanarin content (Cairella & Vecchi, 1969; Preziosi, 1969). In various pharmacological test systems, artichoke leaf extracts have shown hepatoprotective (Eberhardt, 1973; Adzet et al., 1987), anticarcinogenic (Clifford, 2000), antioxidative (Gebhardt, 1997; Gebhardt & Fausel 1997; Brown & Rice-Evans, 1998; Jiménez-Escrig et al., 2003), antibacterial, anti-HIV, bile-expelling, and urinative activities (Cairella & Vecchi, 1969; Preziosi, 1969) as well as the ability to inhibit cholesterol biosynthesis and LDL oxidation (Clifford & Walker, 1987; English et al., 2000). These broad therapeutic indications cannot be ascribed to a single compound, but to several active compounds providing additive or synergistic pharmacological effects, including mono-caffeoylquinic and dicaffeoylquinic acids, and flavonoids such as luteolin and its 7-O-glucoside (Brown & Rice-Evans, 1998; Speroni et al., 2003; Wang et al., 2003; Šchütz et al., 2004, 2006b).

The hepatoprotective activity against CCl4 toxicity in isolated rat hepatocytes (an experimental model widely used to mimic several aspects related to liver pathology characterized by increased lipid peroxidation and cytotoxicity due to oxidative stress) of some polyphenolic compounds, such as cyanarin, isochromanolic acid, chlorogenic acid, luteolin-7-O-glucoside, and two organic acids (caffeic and quinic) from C. scolymus has been reported (Preziosi, 1969; Adzet et al., 1987). The toxic manifestations of CCl4 in isolated rat hepatocytes is typically detected by glutamate oxaloacetate transaminase and glutamate pyruvate transaminase leakage. In these experiments only cyanarin and, to a lesser extent, caffeic acid showed cytoprotective action, and this demonstrates that the activity of cyanarin is attributable only to the caffeoyl moiety. The observed effects of cyanarin and caffeic acid have been assigned to the antioxidant activity of these compounds, which prevents the CCl4-induced oxidation of the phospholipids that are constituents of the hepatocyte membranes. Gebhardt and Fausel (1997) show that aqueous artichoke extracts reduce lipid peroxidation (measured as production of malondialdehyde) and cytotoxicity (measured as lactate dehydrogenase leakage) in cultures of rat primary hepatocytes exposed to tert-butyl hydroperoxide (t-BHP). Furthermore, artichoke extracts prevented the corresponding loss of intracellular glutathione caused by t-BHP, which in turn induces lipid peroxidation. In contrast to the findings of Adzet et al. (1987), the t-BHP assay shows that a variety of artichoke specific compounds, like cyanarin and luteolin 7-O-glucoside, as well as other phenolic compounds such as caffeic and chlorogenic acids, all of which are present in artichoke, may contribute to the hepatoprotective potential of these extracts. In addition, it has been observed that extracts are resistant to tryptic digestion, boiling, acidification, and other treatments, but are slightly sensitive to alkalisation (Gebhardt, 1997).

A traditional use of artichoke leaf extract in gastroenterology is mainly based upon its strong antidiureptotic actions which are mediated through its choleretic activity. Saénz Rodriguez et al. (2002) investigated the effects of artichoke leaf extracts on bile flow and the formation of bile compounds in anaesthetised Wistar rats after acute and repeated oral administration. A significant increase in bile flow was observed after acute treatment with artichoke extract as well as after repeated administration. The choleric effects of artichoke extract were similar to those of the reference compound dehydrocholic acid. A strong artichoke extract-

<table>
<thead>
<tr>
<th>Glucidic content in the edible portion of artichoke heads cv. Romanesco (adapted from Lattanzio et al., 2002).</th>
<th>% Fresh weight</th>
<th>% Dry weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>0.44</td>
<td>3.18</td>
</tr>
<tr>
<td>Fructose</td>
<td>0.18</td>
<td>1.27</td>
</tr>
<tr>
<td>Sucrose</td>
<td>0.98</td>
<td>6.98</td>
</tr>
<tr>
<td>Inulin</td>
<td>5.18</td>
<td>37.00</td>
</tr>
</tbody>
</table>
induced increase in total bile acid concentration over the entire experiment was observed. With the highest dose (400 mg/kg), a significant increase was obtained after single and repeated administration. The bile acids-induced effects of artichoke leaf extracts were much more pronounced than those of the reference compound (dehydrocholic acid). Preziosi et al. (1959) observed a dose/activity relationship for cynarin on choleresis: 15–30 mg/kg of cynarin caused an increased secretion of bile similar to that of equimolecular doses of Na-dehydrocholate. Higher doses of cynarin (75–100 mg/kg), caused a bile secretion 130% higher compared to basal values, and this in turn caused an increased elimination of biliary cholesterol. This increased biliary flux coincided with an increase in urine secretion. The same authors reported that this diuretic activity was induced by both cynarin and artichoke extracts. Gebhardt (2001, 2002a), when studying the effect of water-soluble extracts of artichoke leaves on choleresis using primary cultured rat hepatocytes and cholephilic fluorescent compounds, noticed that the artichoke leaf extracts not only stimulated biliary secretion, but also re-established it when secretion was inhibited by addition of tauroliothicololate to the culture medium. Furthermore, tauroliothicololate-induced bizarre bile canalicular membrane distortions, detectable by electron microscopy, could be prevented by artichoke leaf extracts in a dose-dependent manner when added simultaneously with the bile acid. These effects were exerted by the flavone luteolin and, to a lesser extent, by luteolin-7-O-glucoside. These results demonstrate that artichoke leaf extracts exert a potent anticholestatic action at least in the case of tauroliothicololate-induced cholestasis and that luteolin may contribute significantly to this effect.

Artichoke extract retarded low density lipoprotein (LDL) oxidation in a dose-dependent manner as measured by a prolongation of the lag phase of conjugated diene formation, a decrease in the rate of propagation, and a sparing effect on the α-tocopherol within the LDL. The isolated flavone aglycone luteolin (1 μM) demonstrated an efficacy similar to that of 20 μg/ml artichoke extract in inhibiting lipid peroxidation. Luteolin-7-O-glucoside also demonstrated a dose-dependent inhibition of LDL oxidation but was less effective than luteolin. In addition, studies of the copper-chelating properties of luteolin-7-O-glucoside and its aglycon luteolin suggest a potential role for chelation in the antioxidant effects of artichoke extracts. It is therefore considered that the antioxidant activity of artichoke extracts relates in part to its flavonoids, which act as hydrogen donors and metal ion chelators, and in part to the increased effectiveness imparted by their partitioning between the aqueous and lipophilic phases (Brown & Rice-Evans, 1998).

Artichoke leaf extracts have been used for treating hypercholesterolemia, a metabolic derangement directly associated with an increased risk for coronary heart disease and other sequelae of atherosclerosis. In this connection, it has been shown by Gebhardt (1998) that aqueous extracts from artichoke leaves applied at high-doses were able to inhibit cholesterol biosynthesis from 14C-acetate in primary cultured rat hepatocytes in a concentration-dependent biphasic manner with moderate inhibition (approximately 20%) between 0.007 and 0.1 mg/ml and strong inhibition at 1 mg/ml. Cytotoxic effects (evidenced by lactate dehydrogenase leakage and the 3-[4,5-dimethylthiazol-2-yl]-2,5-dephenyl tetrazolium bromide assay) were restricted to higher concentrations. Inhibition was observed to occur in a time-dependent manner, to last for several hours even after washing out the extracts with fresh medium, and to be fully reversible within 20 h of removing the extracts. In addition, the stimulation of hydroxymethylglutaryl-CoA-reductase (EC 1.1.1.34) activity by insulin was efficiently blocked by the extracts, although other insulin-dependent phenomena, such as increased lactate production, were not influenced. These results suggest an indirect modulation of hydroxymethylglutaryl-CoA-reductase activity as the most likely inhibitory mechanism of the artichoke extracts. Screening of individual phenolic constituents of artichoke extracts revealed that...
Considering together the findings within the existing literature concerning artichokes, it is evident that the by-products originating from artichoke processing could be considered a promising source of inulin and also of phenolics that can be considered a raw material for food ingredient production. Artichoke by-products such as leaves, external bracts and stems produced by the artichoke processing industry represent a huge amount of discarded material (about 80–85% of the total biomass produced by the plant), which has the potential to be used as a source of health-promoting inulin and phenolics (Llorach et al., 2002; Lattanzio et al., 2005).

The current thinking in the field of diet and health research is that non-nutrient components of diets, although not essential for life, can modulate various functions at the cell, tissue and whole body levels in such ways that good health is maintained and age-related diseases are delayed or prevented. Related to this concept is that of “functional foods”. Following regulatory changes in Europe, it will be necessary for ‘functional foods’ to have any claims relating to health benefits authorised and it is envisaged that functional foods may become thought of as foods for which a claim has been authorised. A food can be regarded as functional if it is satisfactorily demonstrated to affect beneficially one or more target functions in the body, beyond adequate nutritional effects, in a way which is relevant to either the state of well-being and health or the reduction of the risk of a disease. In this connection, the functional food components of artichoke are inulin-type fructans and various secondary metabolites, especially polyphenolic compounds. Inulin-type fructans are non-digestible oligosaccharides that are classified as dietary fibre. The targets for their functional effects are the colonic microflora that use them as selective ‘fertilizers’; the gastrointestinal physiology; the immune functions; the bioavailability of minerals; and the metabolism of lipids. Potential health benefits may also concern reductions in the risk of some diseases like intestinal infections, constipation, non-insulin-dependent diabetes, obesity, osteoporosis or colon cancer (Roberfroid, 1999b; Roberfroid, 2002). As far as artichoke phenolic components are concerned, much of the research has focused on the antioxidant activity of artichoke leaf extracts. Leaf extracts have been reported to show antioxidative and protective properties against hydroperoxide-induced oxidative stress in cultured rat hepatocytes (Gebhardt, 1997), to protect lipoprotein from oxidation in vitro (Brown & Rice-Evans, 1998), to inhibit hemoysis induced by hydrogen peroxide, and to inhibit oxidative stress when human cells are stimulated with agents that generate reactive oxygen species such as hydrogen peroxide (Perez-Garcia et al., 2000). Nowadays there is a growing interest towards dietary supplements together with natural non-toxic food additives. Foods are among the most rapidly growing sectors in the food and personal care product industry. This development is due to the loss of consumer confidence in the modern diet, the aging population, and finally an overall enhancement in health awareness and disease prevention among customers (Schütz et al., 2006).

López-Molina et al. (2005) have prepared a high molecular weight inulin from artichoke agro-industrial wastes using environmentally benign aqueous extraction procedures. Physico-chemical analysis of the properties of artichoke inulin was reported. The average degree of polymerization was 46, which is higher than for Jerusalem artichoke, chicory, and dahlia inulins. GC–MS confirmed that the main constituent monosaccharide in artichoke inulin was fructose and its degradation by inulinase indicated that it contained the expected β-2,1-fructan bonds. The FT-IR spectrum was identical to that of chicory inulin. These data indicate that artichoke inulin is likely to be suitable for use in a wide range of food applications. In this connection, fat and carbohydrate replacement with artichoke inulin could offer the advantage of not compromising taste and texture, while delivering nutritionally enhanced products.

6. **Nutraceutical production**

Considering together the findings within the existing literature concerning artichokes, it is evident that the by-products originating from artichoke processing could be considered a promising source of inulin and also of phenolics that can be considered a raw material for food ingredient production. Artichoke by-products such as leaves, external bracts and stems produced by the artichoke processing industry represent a huge amount of discarded material (about 80–85% of the total biomass produced by the plant), which has the potential to be used as a source of health-promoting inulin and phenolics (Llorach et al., 2002; Lattanzio et al., 2005).
Artichoke by-products are also a potential good source of antioxidant activity because it contains large amounts of polyphenols that possess high antioxidant activity. Llorach et al. (2002) have used fast and commercially feasible protocols to extract antioxidant phenolics from artichoke by-products: raw artichoke (RA), blanched (thermally treated) artichoke (BA), and artichoke blanching waters (ABW). Two protocols, with possible industrial applicability, based on both methanol and water extractions have been described. Phenolic contents (expressed as caffeic acid derivatives) grams per 100 g of dry extract were 15.4 and 9.9 for RA when extracted with methanol and water, respectively; 24.3 and 10.3 for BA when extracted with methanol and water, respectively; and finally, 11.3 g of phenolics/100 mL of ABW. The higher amount of phenolics in BA could be due to the inactivation of polyphenol oxidase (PPO) at the industrial scale (due to blanching process), avoiding PPO-catalyzed oxidation of these phenolics, a phenomenon that could occur in RA by-products. The authors suggest that the “functionalization” of foodstuffs by adding artichoke by-product extracts should be considered. To this purpose, sensory modification of foodstuffs, as well as the stability and activity of artichoke extracts within food matrices, should be investigated. In addition, toxicological studies should be carried out to ascertain the boundary between health-beneficial effects and risk of harm.

Lattanzio et al. (2005) have evaluated methanolic extracts of artichoke by-products (offshoots, leaves and external bracts of artichoke heads) for their phenolic antioxidants. The artichoke extracts were assessed for their protective role in the control of oxidative damage to biological molecules (proteins, lipids and DNA), caused by free radicals such as \( \text{RCOO}^- \) and/or \( \text{OH}^- \), using the \( \beta \)-carotene/linoleate assay, the deoxyribose assay and the metmyoglobin assay. Artichoke by-products are rich in phenolic compounds, especially chlorogenic acid and 1,5-0-dicaffeoylquinic, 3,5,0-dicaffeoylquinic and 3,4,0-dicaffeoylquinic acids. When the biological activity of artichoke extracts is considered, the presence of lutelolin-7-glucoside and hydrolysable tannins, besides caffeoylquinic derivatives, in the phenolic fraction of these extracts must be taken into account: all these phenolics possess a good antioxidant activity against peroxy and hydroxyl radicals when assessed using the \( \beta \)-carotene/linoleate assay and the metmyoglobin assay.

Ready-to-eat foods such as soups are in great demand by consumers. In this context, the addition of new health-promoting active ingredients such as polyphenols could represent an important way to increase the dietary intake of these compounds. Llorach et al. (2005) analysed an artichoke by-products aqueous extract and reported that it contained a high level of polyphenols (100 mg of polyphenols/g of dry extract), comprising mainly of caffeic acid derivatives. A sensory panel with four trained judges evaluated soups to which different amounts of the extracts had been added and discovered that up to 10 mg of extract/mL of soup could be added without compromising the acceptability of the soup, which was compared to an unadulterated soup. Further, the antioxidant capacity, evaluated as free radical scavenging activity (ABTS assay) and ability to reduce the 2,4,6-tripyridyl-S-triazine (TPTZ)-Fe(III) complex to TPTZ-Fe(II) (FRAP assay), was substantially increased with addition of the extracts.

### 7. Conclusions

Globe artichoke is a large immature flower rich in medicinal substances. It is considered one of the most important vegetable crops in the countries bordering the Mediterranean basin. Globe artichoke is also cultivated, although to a lesser extent, in the Near East, North Africa, South America, and the United States. Globe artichoke has important nutritional values due to its particularly high content of bioactive phenolic compounds, such as caffeoylquinic derivatives and flavonoids, but also due to substantial amounts of inulin, fibres and minerals. The economic use of the crop is currently mainly focussed on the consumption of the edible immature flower heads (capitula), commonly referred to as ‘heads’, eaten as a fresh, canned or frozen vegetable, and more recently, demand has been increased because of its reputation as a health food. Furthermore leaves, stems, and roots are used to feed livestock. These raw material may be exploited for either the extraction of inulin, a water-soluble and low caloric carbohydrate, whose beneficial effects have been reported to be associated with gut flora-mediated fermentation and production of butyrate, or phenolic compounds, especially caffeoylquinic derivatives, bioactive substances which are reported to exert beneficial effects in the treatment of hepato-biliary diseases, hyperlipidaemia, dropsy, rheumatism and cholesterol metabolism. Clinical and pre-clinical trials have confirmed the therapeutic potential of this plant: among all the plants used in folk medicine against liver complaints artichoke can be considered the most effective.

As a consequence, due to the considerable interest in preventive medicine and in the food industry in the development of natural antioxidants from botanical sources, research has focussed on elucidating the composition of the artichoke phenolic fraction from a qualitative (four mono-caffeoylquinic isomers, six dicaffeoylquinic isomers, six flavonoid glycosides, and at least seven anthocyanins have been identified) and quantitative viewpoint, as well as the mechanisms underlying the therapeutic activity of artichoke extracts. These studies confirm the popular use of artichoke for the treatment of several ailments and reveal that this therapeutic activity is probably primarily due to the phenolic structure of these substances, which may function to inhibit free radical-mediated processes.

Besides the external bracts, the fleshy and developed artichoke root system could be used as a source of inulin. Currently, commercially available inulins are obtained mainly from chicory, Jerusalem artichoke, and dahlia. Artichoke inulin presents similar physico-chemical properties to high performance chicory inulin but an even higher degree of polymerization, which makes artichoke inulin desirable for applications in the food industry. Fat and carbohydrate replacement with artichoke inulin could offer the advantage of not compromising taste and texture, while delivering nutritionally enhanced products.

As far as the “functionalization” of foodstuffs through use of artichoke by-products is concerned, sensory modification of foodstuffs, as well as the stability and activity of artichoke extracts within food matrices, should be investigated. In addition, toxicological studies should be also carried out to...
ascertain the boundary between health-beneficial effects and the risk of toxicity.

REFERENCES


