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Review

A systematic review on *Cynara cardunculus* L.: chemical composition, bioactive properties of a sustainable food

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Abstract

The cardoon (*Cynara cardunculus* L.), is a perennial plant belonging to the Asteraceae family, and its cultivated species are widely used in the Mediterranean diet. This review provides an overview of the chemical composition, bioactive properties and multiple industrial and food applications of cardoon. Thanks to its nutritional composition, in recent years the use of cardoon has increased in food, cosmetic and industrial sectors, such as the energy sector or in the production of paper pulp or bio-packaging. An application in the food industry has involved the use of cardoon as a vegetable coagulant for gourmet cheeses-making, as the flowers are rich in aspartic proteases. Cardoon by-products are also rich in bioactive compounds with important health benefits. Most of these nutritional activities are due to the high presence of phenolic

compounds, minerals, inulin, fibre and sesquiterpene lactones with interesting antioxidant and antimicrobial, anti-inflammatory, anti-tumor, lipid-lowering, cytotoxic and anti-diabetic activities.

Keywords: cardoon cultivars; sustainable crops; biomass; biological activity; by-products; biowaste reduction; plant-based food; bio-refinery.

1. Introduction

In recent years, consumer demand for healthy, nutritious and organic foods has increased significantly. This has caused an intensification of production and consumption of fruits and vegetables.

Among foods that are considered healthy are herbs, thanks to the presence of bioactive and antioxidant molecules such as vitamins, minerals, fibre, inulin and polyphenols, with nutraceutical, nutritional and therapeutic action which can also improve the taste and quality of the food. Therefore, the use of plants and herbs also as a source of food fortification should be one of the main objectives of the industry (Frutos et al., 2019). Furthermore, another problem is the use of chemical preservatives to reduce microbial deterioration of foods. This problem could be solved by using antioxidants of natural origin from plants, which in addition to increasing the shelf-life of a food, have been used in the treatment of diseases thanks to their many therapeutic, antimicrobial and antiviral effects (Nasirpour et al., 2014).

In recent decades, plants of the Asteraceae family have gained popularity in the scientific community due to their broad pharmaceutical and therapeutic characteristics. They are among the most common herbs used in the medicinal and food industries thanks to the presence of numerous bioactive molecules (Azizi et al., 2010).

These plants possess many antimicrobial and therapeutic effects, contain important bioactive compounds, and for this reason, can be exploited in the food and pharmaceutical industries. In addition to improving the health role of foods, thanks to their antioxidant and antimicrobial capacity, these plants can also be used as safe preservatives and food additives (Mir et al., 2021).

The Asteraceae family includes the species *Achillea millefolium* L., *Chamaemelum nobile* L., *Arctium lappa* L., *Bellis perennis* L., *Artemisia annua* L., *Calendula officinalis* L., *Arnica montana* L., *Artemisia aucheri* L., *Artemisia persica* L., *Eupatorium cannabinum* L., *Matricaria chamomilla* L., *Cichorium intybus* L., *Taraxacum officinale* L., *Polygonum bistorta* L., *Helichrysum stoechas* L., and *Cynara cardunculus* L. in different parts of the world (Kazeminia et al., 2022) (Fig.1.). All species have the same characteristics, such as their prevalence and ability to survive in arid areas with little rainfall, mainly in the countries of the Mediterranean basin (Falce et al., 2016).

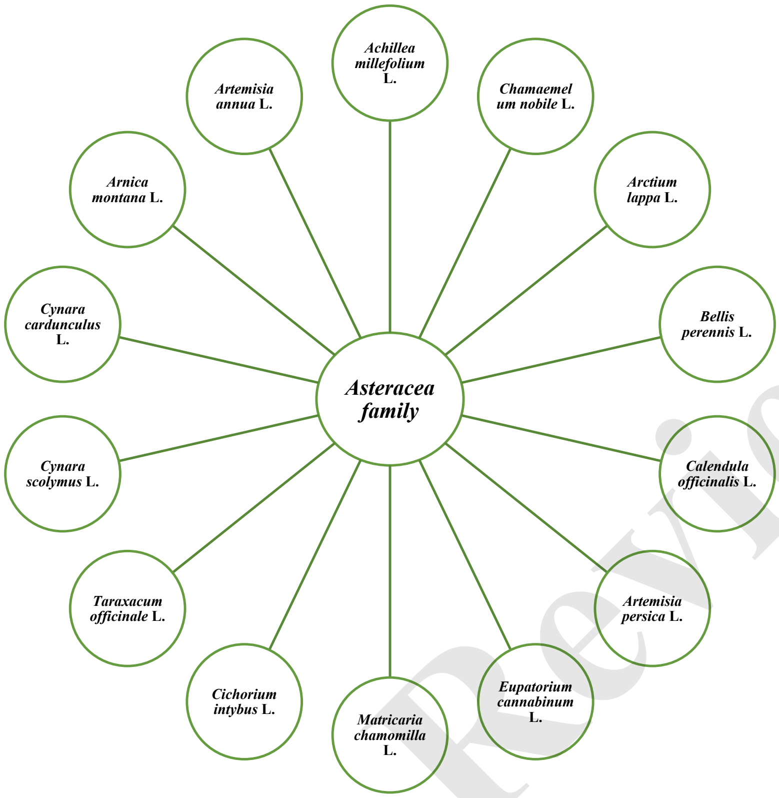

Fig. 1. Species included in the Asteraceae family.

Cardoon (*Cynara cardunculus* L.), also known as thistle or Spanish thistle, is a plant that grows in the Mediterranean area belonging to the Asteraceae family, and that has been used as food since ancient times in some countries, such as Spain, Italy and Greece (Ferioli et al., 2022), (Raccuia and Melilli, 2007). Cardoon is a food widely used in the Mediterranean diet and has been identified as a promising plant at an industrial level (Raccuia and Melilli, 2007), (Raccuia et al., 2011), (Mandim et al., 2020), (Zayed et al., 2020). Mediterranean plant-based foods have been used since ancient times also in traditional medicine (Alirezalu et al., 2020). Cardoon is also considered a functional food, with an important nutritional value, being an interesting source of bioactive compounds, such as phenols, vitamins, minerals, inulin, fibres and sesquiterpene lactones (Conceição et al., 2018). These bioactive compounds exhibit many beneficial effects and therapeutic properties, such as antimutagenic, anticancer, antimicrobial, antibacterial, antifungal, anti-inflammatory, antitumor, antioxidant, lipid-lowering, cytotoxic, antidiabetic, antihemorrhoidal, cardiotonic, choleretic and neuroprotective activity (Ozarowski et al., 2021), (Newman et al., 2020), (Gostin et al., 2019).

In this review, the importance of the *Cynara cardunculus*, cultivated and wild species, will be discussed and an overview of the therapeutic potential, chemical-nutritional composition of the cardoon and its applications in the food industry will be provided.

2. *Cynara cardunculus*

Cynara cardunculus L. belongs to the Asteraceae family, native to the Mediterranean basin (Conceição et al., 2018). *Cynara cardunculus* includes three taxa: the globe artichoke *(Cynara cardunculus* L. var. *scolymus* L.*);* the wild or uncultivated cardoon *(Cynara cardunculus* L. var. *sylvestris* Lam.*),* and the cultivated cardoon *(Cynara cardunculus* L. var. *altilis* DC) (Christaki et al., 2012) (Fig.2.).

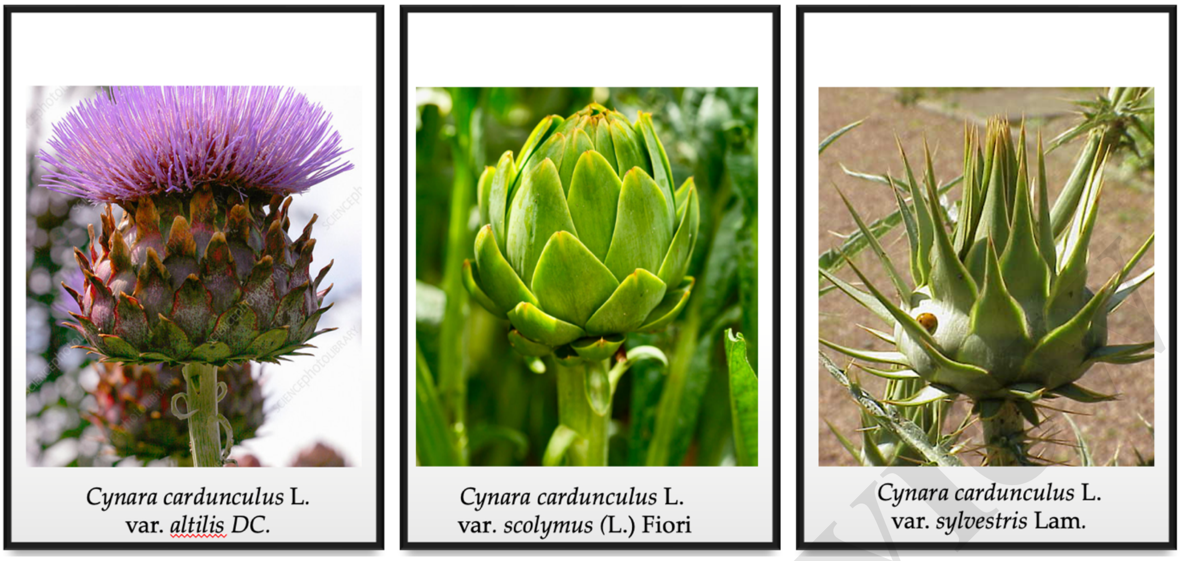

Fig. 2. Three taxa that include *Cynara cardunculus*: the wild or uncultivated cardoon (*Cynara cardunculus* L. var. *sylvestris*), the artichoke (*Cynara cardunculus* var. *scolymus* L.) and the cultivated cardoon (*Cynara carduncul*us var. *altilis* DC).

Several genetic studies have highlighted that both cultivated species, the domestic cardoon and the globe artichoke, evolved from the wild cardoon considered to be the wild ancestor (Raccuia et al., 2004). As for the cultivated cardoon, its production is more limited to southern Europe (France, Greece, Italy, Portugal and Spain). Furthermore, *C. cardunculus* L. is distributed in the Mediterranean basin, North Africa, Cyprus, Macaronesia and Turkey, and also colonised Peru, Australia, Mexico, Chile, China, California, Argentina and West Africa (Conceição et al., 2018). In these areas, where the climate is semi-arid and with low humidity, the cardoon has adapted perfectly, allowing its cultivation as a perennial crop (Fig.3.).

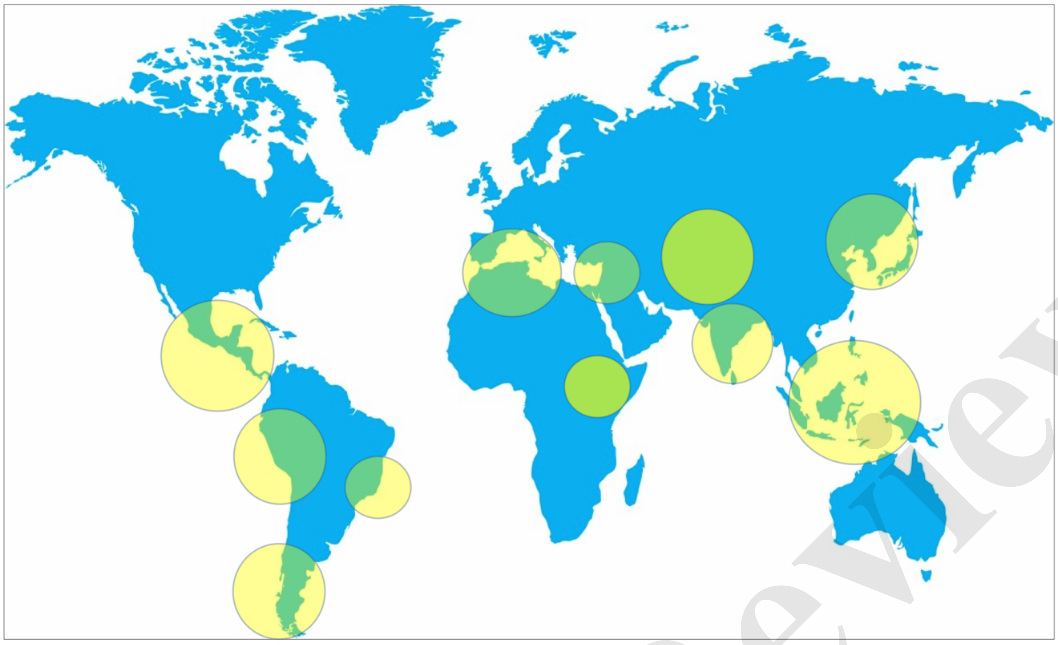

Fig. 3. Main worldwide distribution of cardoon.

The cardoon is a perennial plant, which has a thick and rigid stem of about 1.5 m in diameter and which can reach more than 2 m in height, with the upper parts branched and covered in cotton. The plant begins germinating seeds in spring or autumn and is completed in summer; therefore, it presents an annual cycle of development. The upper part of the plant regenerates annually, while the roots can grow up to 1 m deep. (Pesce et al., 2019).

An outline of the main features of the cardoon cultivation system follows. The establishment of a plantation is carried out from seed in the first year. Every year the aerial biomass is harvested at the end of the growth cycle, during which, the plant canopy dries and the fruits ripen. Later (when the climate conditions are favourable) some buds of the plant stock sprout and gradually a leaf rosette is formed. This is the beginning of a new growth cycle. The main plant growth stages and their approximate dates in the Mediterranean area follows: plant sprouting in September–October; winter leaf rosette in November; stem elongation in April–May; full blossom in June; ripe fruits in July; fully dry aerial biomass in August. As a result of this cycle, *C. cardunculus* helps to conserve the fragile agro-systems of the Mediterranean area, because of its effect of soil erosion control. The cardoon leaves reach 120 x 30 cm and form a robust basal rosette; the upper ones are smaller, about 10–50 cm. Leaves have a colour ranging from green to grey and are covered with down underneath. At the tips of the leaves, there are yellow/orange spines, 5–20 mm long. The seeds have an average size of 6–8 mm and are square and smooth. Their colour is variable, it has streaks ranging from light grey to black. The seeds are surrounded in the upper part by a circle of feathery hairs, 25–40 mm long (Pesce et al., 2019).

The flowers are single and are located at the end of the branch of a thick stem, 1–6 cm long. The flower heads have a rounded shape and reach a diameter of 4-5 cm. The flowers have a characteristic blue, pink or purple colour and are arranged on a fleshy receptacle, enclosed by large purplish bracts, which taper at the end becoming a thorn (Pesce et al., 2019).

3. Nutritional and Chemical Composition: Macro and Micronutrients

The edible part of the cardoon is represented by the swollen stems which require a previous blanching process (Barbosa et al., 2020). The cardoon is a plant with high nutritional properties. It is, in fact, a source of carbohydrates (sugars, fibres and polysaccharides such as inulin), fatty acids, proteins, organic acids, vitamins and minerals. The cardoon also contains high quantities of bioactive molecules with an antioxidant and pharmaceutical function, such as phenolic compounds, phytosterols and volatile substances (Petropoulos et al., 2018), (Pari et al., 2021), (Zayed et al., 2020), (Gostin et al., 2019), (Raccuia & Melilli, 2010).

The high nutritional value is attributed to the low lipid content and the high content of minerals, vitamins and bioactive compounds (Gostin et al., 2019). Another important substance contained in the roots and rhizomes is inulin (Raccuia & Melilli, 2010), (Pari et al., 2021), (Raccuia & Melilli, 2004), (Melilli, et al., 2020), (Melilli et al., 2024) a polysaccharide that strengthens the human intestinal bacterial microflora; the leaves mainly provide dicaffeoylquinic acids and luteolin, substances with an antioxidant action (Gostin et al., 2019). The leaves are known in popular medicine for their antidiabetic, choleretic, diuretic, hepatoprotective and cholagogue effects (Paris & Moyse, 1971).

Various works in the literature dealed with the chemical composition of the different parts of the cardoon: leaves (Francaviglia et al., 2016), (Ramos et al., 2013); flowers (Ben Amira et al., 2018), roots (Pari et al., 2021), (Raccuia & Melilli, 2004 2010); stems (Cavalaglio et al., 2021); flower heads (receptacle, bracts, hairs and pappus) (Mandim et al., 2020); seeds (Mandim et al., 2022), (Petropoulos et al., 2019), (Mandim et al., 2020), (Silva et al., 2022) (Fig.4.).

Fig. 4. Cultivated and wild cardoons vegetable organs.

According to what was reported by the USDA (USDA, 2021), the cardoon leaves mainly contain water (which can reach 94% in raw cardoon) and has a low caloric content, equal to 17 kcal/100 g. Furthermore, raw cardoon contains approximately 4.07% of sugars, 0.1% of total lipids, 1.6% of dietary fibre, 0.7% of total proteins and 1.13% of ashes.

As reported by the World Health Organization (WHO), it is essential, for the prevention of chronic diseases, to follow a diet that includes carbohydrates (50–75%), fats (15–30%) and proteins (10–15%) (WHO, Technical Report, 2003). The cardoon, being rich in carbohydrates, proteins and fatty acids, therefore represents a balanced vegetable food.

3.1 Carbohydrates

Carbohydrates represent macromolecules contained in abundance in the various fractions of the cardoon. These play an essential role in the growth, metabolism and defensive actions of plants (Stein & Granot, 2019). In several studies by Mandim et al., it is reported that sucrose is the sugar contained mostly, up to concentrations of 8.77 g/100 g d.w. (Mandim et al., 2020), (Mandim et al., 2022).

Numerous recent studies have also reported the presence of inulin, another important complex sugar, present above all in the roots of the cardoon. This is included in a range from 22.4 to 49.6 g/100 g d.p. (Raccuia & Melilli, 2010), (Pari et al., 2021), and is considered the main reserve sugar for roots (Raccuia & Melilli, 2010). Inulin is a linear fructan, that is, a polymer with fructose units, and is classified as soluble dietary fibre. Inulin has β-(2,1) bonds between fructo-furanosyl units and branches at the β-(2,6) position (Melilli et al., 2024). It is considered a reserve carbohydrate that accumulates mainly in the roots and tubers of some plants of the Asteraceae family, such as the cardoon (Niness, 1999).

This polymer has been used in nutraceutical, food, pharmaceutical and other biorefining applications (Raccuia & Melilli, 2004), (Pari et al., 2021). Inulin, being a low-calorie soluble dietary fibre, has also been identified as a prebiotic, a sugar-mediated lipid metabolism agent in diabetics (López-Molina et al., 2005), and as a diagnostic agent for determining renal function (Mensink et al., 2015).

A recent review summarized the main physiological functions of inulin, including the prebiotic effect, metabolism regulator, antioxidant, prevention of diseases (such as diabetes and obesity, constipation, celiac disease, Crohn's disease, inflammatory bowel disease, ulcerative colitis and colon cancer) and anti-inflammatory effect, and the biological and technological properties (flexibility, availability, biodegradability, biocompatibility and low toxicity) were also evaluated (Fig.5.). In particular, the positive effect of inulin on the glycemic index and the inhibition of α-amylase of pasta enriched with inulin at two degrees of polymerization and the rheological and sensorial properties of fortified baked products added with inulin were evaluated. The molecular weight of inulin played a key role in the acceptability of the paste. In general, the addition of inulin to bread has improved its technological properties. In conclusion, inulin has rheological and technological characteristics that can be exploited in different food sectors (baked products, meat and dairy products) to obtain healthy and functional foods with a lower glycemic index and a higher total dietary fibre content (Melilli et al., 2024).

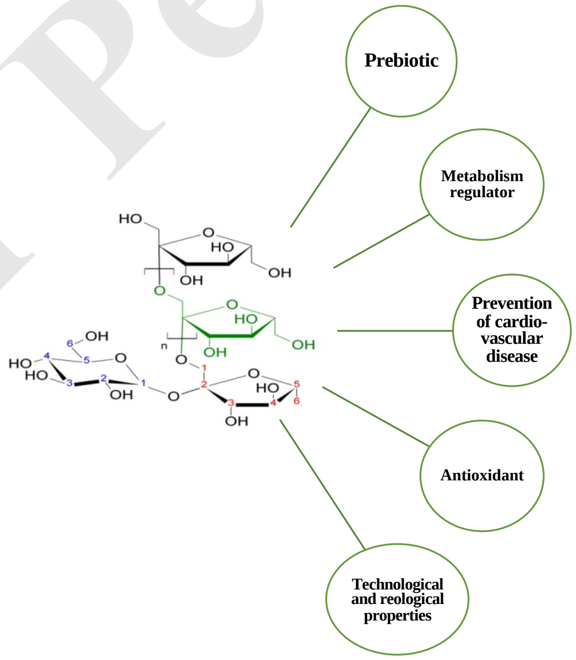

Fig. 5. Main physiological and technological functions of inulin.

In the roots of Cynara plants, inulin serves as a storage carbohydrate. It accumulates in the roots during the growing season, providing energy for the plant to grow and survive during periods of dormancy or stress. Due to the importance of this polymer, different studies have been focused on inulin content in the buds and roots of *Cynara* spp. At the beginning of 2000, the first trials were conducted in the Mediterranean environment on 15 genotypes, 5 globe artichokes, 5 cultivated cardoons, and 5 wild cardoons. At the end of the crop cycle (summer) the mean yield in biomass, roots and inulin were 20 t/ha, 9,8 t/ha and about 4 t/ha. Because of the good yields a study focused on seasonal dynamics of biomass, inulin, and water-soluble sugars in roots of three genotypes of *C. cardunculus* L., namely globe artichoke cv. Romanesco clone 15/4 (Rom), cultivated cardoon cv. Cardo di Nizza (CDN), and wild cardoon population Paterno` (P), were assessed. The growth of aerial organs and the subsequent sprouting of buds from underground reserve organs are processes that demand high amounts of energy. As though in anticipation, *C. cardunculus* plants first developed a large photosynthetic apparatus to optimize light capture and maximize carbon assimilation. Root development was slow at this stage because most of the photoassimilates were diverted to leaf growth. In the next stage, root growth predominated, and inulin content increased with the increase in fresh weight of roots. The marked increases in glucose, fructose, and sucrose concentration were induced for a very short period immediately following the cold month of January and during dormancy. Hence, the increase in biomass of the underground tissues could be correlated with inulin accumulation and occurred between February to May, suggesting that in this species, during the vegetative phase of aerial growth, sucrose is synthesized in excess and translocated to the underground organs where it is metabolized into inulin. Seasonal variations in the content of inulin during sprouting and flowering demonstrate mobilization from the storage organs to support rapid growth of aerial shoots and flower development. The patterns of biomass partitioning were different in the three genotypes: wild cardoon recorded the highest share of roots in total biomass, cultivated cardoon was characterized by a large share of leaves, and globe artichoke favoured accumulating biomass in heads. These patterns correspond to the choice of cultivated cardoon for leaves and of globe artichoke for heads, suggesting that the wild form of C. cardunculus develops a large root apparatus to cope better with the unfavourable Mediterranean climate. Concerning the ecophysiological role of fructans, it is important to consider that the Mediterranean environment is a stressful environment for herbaceous plants because of the prolonged drought. The storage of fructans in underground organs by the Mediterranean species has been interpreted as an adaptive strategy to overcome these unfavourable conditions. The data were confirmed by further studies on inulin metabolized enzymes (Melilli & Raccuia, 2012), (Melilli & Raccuia, 2013), (Branca et al., 2022).

A recent study evaluated the germplasm of eight ecotypes from six different regions of northern Tunisia of cardoon (*Cynara cardunculus* L. var. *sylvestris*) to evaluate the inulin content in leaves and roots collected in the vegetative and flowering phases. Mean inulin content varied among ecotypes from 1.57 to 27.46 mg/100 g. The results showed that the roots of the cardoon were richer in inulin than the leaves and that the inulin content increased during flowering (Sbai et al., 2023).

The lignocellulosic residues of the cardoon (cellulose, hemicellulose and lignin) (Fig.6.) represent approximately 70–80% of the plant (Giannoni et al., 2021), and their content varies from 4.6 to 55.2 g/100 g d.p., especially in the stems (Mauromicale et al., 2014). Lignocellulose has a protective function against natural agents and microbial attacks (Shatalov et al., 2017). The most abundant component of lignocellulosic biomass was cellulose, a long-chain structural polymer, present in plant tissues (Shokri & Adibkia, 2013). In the cardoon plant, cellulose was present in a range from 10.33% to 51.7%, with the highest content in the stems (Giannoni et al., 2021), (Ben Amira et al., 2018), (Francaviglia et al., 2016). The cellulosic polymers have been used in many industrial sectors such as in the wood and paper industry, but also in the textile, cosmetic and pharmaceutical industries (Shokri & Adibkia, 2013). Cardoon hemicellulose was used for the production of xylitol because it is composed of 90-95% xylan polysaccharide; hemicellulose was contained from 4.6% to 55.2%, especially in the stems of the cardoon (Giannoni et al., 2021), (Ben Amira et al., 2018), (Francaviglia et al., 2016). Furthermore, fermentable sugars can also be obtained from the saccharification process of cellulosic fibres, such as glucose, used for the production of bioethanol (Shatalov et al., 2017).

Among the carbohydrates most present in the cardoon, lignin must also be considered. Lignina was found in quantities ranging from 8.7 to 28.8%, especially in the stems (Giannoni et al., 2021), (Ben Amira et al., 2018), (Francaviglia et al., 2016). Lignin, in addition to being used as a resin, was highly exploited for the production of biological products, such as antioxidants and polymers. Another application of lignin was a binding dispersing agent in the form of lignosulfates (Lourenço et al., 2015).

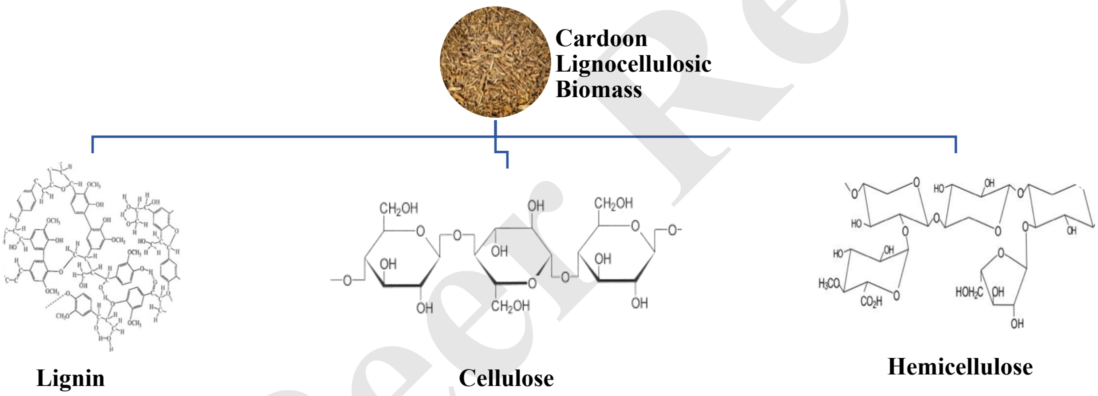

Fig. 6. The lignocellulosic residues of the cardoon (cellulose, hemicellulose and lignin).

3.2 Proteins and Amino Acids

Cardoon is a plant food considered to be low in protein, with a content of approximately 0.7 g/100 g. The fraction of the cardoon containing the highest protein content was the seeds (between 18.1–30.4% dry weight) (Petropoulos et al., 2019), (Mandim et al., 2022), (Mandim et al., 2020), (Francaviglia et al., 2016). In the study by Raccuglia et al., (Raccuglia et al., 2007) seed proteins were identified in a range of values ranging from 191 to 225 g kg^{-1}.

Proteins such as aspartic proteases have been used in dairy technology (Alavi & Momen, 2020). Proteases were added industrially in cheese production to improve consumer acceptability, as well as improve the nutritional intake of the finished product (Ben Amira et al., 2017). Other proteins contained in cardoon flowers were milk coagulating enzymes, called cardosins (Sarmento et al., 2009). The presence of 75% cardosin A (with greater proteolytic activity) and 25% cardosin B in the extract of *C. cardunculus* flowers was found (Barros et al., 2002), with effect on cleavage of kappa casein (Vairo Cavalli et al., 2013).

3.3 Fatty Acids and Sterols

The comparison with the literature highlighted the presence of 30 fatty acids in the vegetal parts of cardoon (flowers, seeds, bracts, heads). Saturated and unsaturated fatty acids were found, and in particular palmitic acid (0.03–55.9%), oleic acid (0.58–46.6%), linoleic acid (C18:2n6c; 0.3–30.6%) and gamma-linoleic acid (0.0–70.41%). These characteristics make *Cynara* oil suitable for human consumption. (USDA, 2021), (Mauromicale et al., 2014), (Ben Amira et al., 2018), (Petropoulos et al., 2019), (Mandim et al., 2022).

Vegetable oils also contain abundant quantities of phytosterols. They can be found both in free form and in esterified form. The most highlighted phytosterols are β-sitosterol, campesterol and stigmasterol. Numerous studies have reported their action against hypercholesterolemia and their antioxidant action, as a prevention against some forms of cancer (Silva et al., 2014). In cardoon sterols were found in different fractions but in low quantities. Tocopherols are part of the unsaponifiable fraction of oils, they are fat-soluble and have an antioxidant action (Kritchevsky & Chen, 2005).

Tocopherols are molecules with a high nutritional and antioxidant action, present mainly in the leaves, but also in the seeds, bracts and heads of cardoon. Some studies have reported the most present tocopherols, α-tocopherol, γ-tocopherol and approximately seven sterols: cholesterol, 24-methylenecholesterol, campesterol, stigmasterol, β-sitosterol, β-sitostanol and Δ5-avenasterol (Mandim et al., 2020), (Ramos et al., 2013). Stigmasterol and β-sitosterol are the main compounds, contained in a concentration range between 12.9 and 58.8 mg/100 and between 13.1 and 70.8 mg/100 g, respectively (Mandim et al., 2022), (Petropoulos et al., 2019). The leaves represent the fraction of the cardoon richest in α-tocopherol (from 39–9 to 100.7 mg/100 g). In seeds, however, this was found to be between 1.210 and 29.620 mg/100, and even less in receptacles α-tocopherol can also be found (n.d. – 0.062 mg/100 g). In heads, it has been reported that the quantities of α-tocopherol vary from 0.25 to 0.619 mg/100 g (Mandim et al., 2020).

Recent research, characterizing seed oil from six populations of cardoon (*C. cardunculus* L. var. *sylvestris*) and a cultivated native cardoon (*C. cardunculus* L. var. *altilis*) in Tunisia, highlighted that that the highest oil yield was obtained from cultivated cardoon (27%) compared to the six wild populations (18–26%), and that the main fatty acid components obtained were: palmitic (11–13%), oleic (23–40%) and linoleic (40–61%); this study also tested the antimicrobial activity of these oils against three bacterial strains: *Staphylococcus aureus*, *Escherichia coli* and *Enterocccus feacalis*. The results showed that all cardoon oils were active against the three bacteria tested, especially those from cultivated cardoon compared to wild ones (Khaldi et al., 2021).

A recent study compared the sterol and fatty acid profile of cold-pressed cardoon seed oil by GC-MS with that obtained by solvent extraction. The research evaluated the total phenolic content and lignan content of other edible vegetable oils (sesame, linseed, olive) and both oils derived from cardoon seeds showed greater activity. Cynara seed oil therefore represents a rich source of ω-6/ω-9 fatty acids (linoleic acid was the abundant compound, followed by monounsaturated and saturated fatty acids), phenolic compounds and lignans, making it a promising vegetable oil with nutraceutical action. The study also analyzed the seed cake, composed by defatted seed residue after oil extraction, which represents approximately 80% of the mass fraction, normally used as organic fertilizer or animal feed, it was shown to have an antioxidant, anti-radical potential and an inhibitory activity of acetylcholinesterase (Varvouni et al., 2021).

In the study of Curt et al., the cardoon seed oil content and fatty acid composition were studied on 18 populations for 3 years. The maximum oil content value recorded was 32.47%, and the main fatty acids were mostly 10.7% palmitic, 3.7% stearic, 25.0% oleic and 59.7% linoleic. The seed cake, obtained as a by-product, was also analyzed and a content of 50.1% carbon, 3.8% nitrogen, 0.8% phosphorus, 5.1% ash and 0.9% potassium were highlighted (Curt et al., 2002)

In the work of Raccuglia et al., (Raccuglia et al., 2011), wheat seeds oils were extracted by Soxhlet from 8 domestic cardoon and 4 wild cardoon, and the oils obtained were characterized for palmitic, stearic, oleic and linoleic acids by gas chromatography. The study highlighted a greater presence of unsaturated acids (oleic and linoleic) compared to saturated ones (stearic and palmitic acids). The main compound characterized was linoleic acid (44.5%), followed by oleic acid (42.6%), palmitic acid (9.8%) and stearic acid (3.1%). The wild cardoon populations reported an oil yield of 289 g kg^{-1}, compared to an average value of 472 g kg^{-1} for the domestic cardoon.

3.4 Organic Acids

Organic acids are primary metabolites present in high quantities in the plant world and significantly interfere with the organoleptic characteristics of fruit and vegetables (flavor, color and aroma) (García-Fraile et al., 2013).

In the seeds, bracts and heads of the cardoon, five organic acids were mainly highlighted: oxalic, quinic, malic, citric and fumaric acids which were detected in lower quantities. The highest total organic acid content was found in the bracts and heads of the (between 1.96 and 15.6 and between 0.89 and 15.7 g/100 g) (Petropoulos et al., 2019), (Mandim et al., 2020)

3.5. Minerals

Even minerals, like all essential micronutrients, cannot be synthesized within the body, but must be supplied through the diet (Gonçalves et al., 2022). In raw cardoon, flowers and seeds, seven minerals were highlighted most: K, Na, Ca, Mg, Mn, Fe and Zn (Ben Amira et al., 2018). In seeds, the detected quantities of Na were low, from 12 to 24 mg/100 g, while the concentrations of K, Ca, Mg and Fe were higher (Petropoulos et al., 2019). Raw cardoons and flowers, on the other hand, had higher quantities of Na, in a range of 170 -–300 mg/100 g (Ben Amira et al., 2018), (USDA, 2021). High amounts of K (1600–1710 mg/100 g), Ca (580–1010 mg/100 g) and Mg (150–170 mg/100 g) were also quantified in the flowers (Ben Amira et al., 2018).

In the study of Curt et al., (Curt et al., 2002) the seed cake, obtained as a by-product, was also analyzed and a content of 50.1% carbon, 3.8% nitrogen, 0.8% phosphorus, 5.1% ash and 0.9% potassium was highlighted.

3.6 Vitamins

Vitamins are very important micronutrients for the health of humans and animals, but they are also essential in metabolic and growth processes in plants (Li & Schellhorn, 2007). Vitamins can be classified into two main groups: fat-soluble (A, D, E and K) and water-soluble vitamins (B vitamins) (Liu et al., 2019). Some of the bioactive effects of cardoon, such as antioxidant activity, are attributed to vitamins (Liu et al., 2019). The most abundant vitamin in cardoon and artichoke was vitamin C, with a concentration of 2.0 and 11.7 mg/100 g, respectively. This represents a fundamental vitamin in protein metabolism and in the biosynthesis of some neurotransmitters (Li & Schellhorn, 2007). Other vitamins were found in lower concentrations in the Asteraceae family such as vitamin A, vitamin E, vitamin A, pyridoxine, thiamine, riboflavin and folic acid, pantothenic acid (0.338 - 0.34 mg/100) and niacin (0.3 - 0.9 mg/100 g) (USDA, 2021).

3.7 Volatile Compounds

Volatile compounds in plants can derive from different biomolecules, including amino acids, fatty acids and carbohydrates (Oliveira et al., 2010), and their type and quantity depends on the species considered. Volatile compounds usually contain nitrogen and aromatic molecules, but also long-chain aliphatic alcohols, sesquiterpene lactones and pentacyclic triterpenes, and are released in response to different stimuli (Vivaldo et al., 2017). Sesquiterpene lactones are another group of secondary metabolites present in plants and responsible for the cytotoxic, antimicrobial and antiviral activity of cardoon (Barbosa et al., 2020). Plants of the Asteraceae family are rich in sesquiterpenoid lactones, a subclass of terpenoids with anti-tumor action including guaianolides, pseudoguaianolide, eudesmanolide, melampodinin a and germacrene (Dhyani et al., 2022). One of the main sesquiterpene compounds present in the stems, receptacle, bracts and leaves of cardoon was cynaropicrin, a guaianolide lactone (Ramos et al., 2013), (Brás et al., 2020); numerous biological activities were attributed to cinaropicrin, such as anti-tumour and anti-inflammatory activity (Brás et al., 2020). Other sesquiterpene lactones identified were Grosheimin, mostly found in leaves, and deacylcinaropicrin, which was found in small concentrations only in cardoon leaves (Ramos et al., 2013).

Long-chain aliphatic alcohols are also among the volatile compounds present in the plant world and have been highlighted at low concentrations in the cardoon (1–5%) (Ramos et al., 2013). A recent study by Kabir et al. showed the antioxidant, anti-tumor, anti-inflammatory activity and hypocholesterolemic effect of octocosan-1-ol. This compound, also used in the food and cosmetics industry, also has an action on lipid peroxidation, on neurological functions and an improvement in athletic performance was also seen in rats trained in physical exercise (Kabir et al., 2020). Pentacyclic triterpenes have also been identified in the flower heads, receptacles, and bracts. These lipophilic molecules were found either in free form as aglycones or in glycosides forms, in a concentration range from 8% to 84%. A recent study reported the main pharmacological effects of these compounds, including antimicrobial and antiviral, but also antitumor, anxiolytic, antidepressant and anti-inflammatory effects (Liu et al., 2019).

Another aromatic molecule found in the cardoon leaves, but in lower quantities, is 3-vanilylpropanol (0.3% - 4%), followed by benzoic acid; only scopolin was found in flower heads and flowers (Ramos et al., 2013). Aromatic compounds, such as triterpenes, have been studied for their antioxidant and antimicrobial actions, and have numerous advantages over antibiotics as growth promoters (Christaki et al., 2012). Ramos et al., in their work studied the main secondary metabolites in the leaves, including guaianolides and hydroxycinnamic acids, such as cynaropicrin and chlorogenic acid (9.5% and 10.4% dry weight, respectively). These represent secondary metabolites, synthesized in plants as part of the defence mechanism, but which have high biological activity (antioxidants, anticancer, hepatoprotective, antimicrobial and anti-hyperlipidemic (Ramos et al., 2014).

3.8 Phenolic Compounds

Phenolic compounds, present abundantly in fruits and vegetables, represent numerous positive effects on human health. Numerous studies have reported their anti-tumour and antioxidant, anti-inflammatory, hypoglycemic, and neuroprotective action (Mandim et al., 2021), (Gonçalves et al., 2019).

Phenolic compounds are divided into classes based on their structure into non-flavonoids (phenolic acids, stilbenes, and lignans) and flavonoids (flavonols, flavan-3-ols, flavones, flavanones, and anthocyanidins) (Liu et al., 2019).

The qualitative and quantitative composition of phenolic compounds in the Asteraceae family depends on several factors (cultivar, climatic conditions, ripening and harvesting period, fractions and age of the plant) (Mandim et al., 2020), (Mandim et al., 2021), (Pandino et al., 2013).

The cardoon mainly presents two phenolic classes: hydroxycinnamic acids such as 5-O-caffeoylquinic acid, 3,5-O-dicaffeoylquinic acid, 3,4-O-dicaffeoylquinic acid and 1,5-O-dicaffeoylquinic acid, also called cynarin, with a prevention of cardiovascular diseases, reported mostly in the receptacle and bracts flavonoids (apigenin, luteolin, luteolin-7-O-glucoside and cyanidin caffeoylglucoside) (Christaki et al., 2012), present mostly in immature inflorescences, in the leaves and flower heads of the cardoon (Ramos et al., 2014), and chlorogenic acid and 1,5-O-dicaffeoylquinic acid. (Pinelli et al., 2007), (Ramos et al., 2014), (Mandim et al., 2020), (Mandim et al., 2021), (Zayed et al., 2020), (Gouveia et al., 2012), (Russo et al., 2017).

Some works in the literature have generally found different biological actions of cardoon extracts: anti-inflammatory (Kammoun et al., 2010), anticancer (Velez et al., 2012) and antimicrobial (Falleh et al., 2008), (Scavo et al., 2019), mainly due to the presence of phenolic compounds.

A recent study investigated the use of membrane technologies, a separation technique used to fractionate liquids from agricultural and food byproducts, such as liquids and wastewater. It is a technique that offers advantages on pressure and temperature and shows high selectivity. This study aims to recover and fractionate phenolic compounds from boiling wastewater generated by the canned cardoon industry. HPLC analysis of residue identified 5-O-caffeoylquinic acid, 3-O-caffeoylquinic acid (chlorogenic acid, CGA), 1,3-dicaffeoylquinic acid (cynarin), apigenin-7-O- glucoside, 4-O-caffeoylquinic acid, 1,5-di-O-caffeoylsuccinylquinic acid (Garcia-Castello et al., 2023). A recent article evaluated the polyphenolic composition and bioactive properties of the flower head constituents (stigma, corolla, bracts, pappus and receptacle) of seven cardoon cultivars. The study highlighted that the bracts had the highest concentration of phenolic compounds (including secoiridoid, secoxyloganin, and apigenin-O-hexuronoside), and the corolla had the greatest variety, with greater antioxidant potential. In addition to the antioxidant, anti-inflammatory action and anti-proliferative capacity against tumour cell lines tested, the antimicrobial capacity was also observed, with all samples presenting an antifungal potential, without any toxic effect. This study also reveals that the results obtained support its promising use as a nutraceutical ingredient and as a substitute for some artificial additives (Mandim et al., 2024).

4. Sustainable food-industry applications

The food sector is growing, and consumers are increasingly looking for healthy foods capable of providing a greater nutritional contribution to their diet. From both a food and commercial point of view, the cardoon, compared to the artichoke, which represents the most cultivated species within the Cynara genus, has a smaller cultivation and production surface area. For example, in 2019, around 19.4 kTon (MAPA, 2022), of cardoon were produced in Spain, around ten times less than the production of artichokes (Garcia-Castello et al., 2023). Despite the lower demand from consumers, interest in the cardoon as an edible vegetable is growing thanks to its nutritional and health benefits, very similar to artichokes. The use of cardoon as a food fortifier has been studied in various works. One of its major uses is the production of goat's and sheep's cheeses. The stems and flowers of the cardoon, for example, were exploited for the production of cheeses (French, Italian, Spanish and Portuguese) such as vegetable rennet thanks to their richness in various proteases (Ben Amira et al., 2017), (Gomes et al., 2019) which gave the cheeses particular organoleptic qualities (creamy consistency and slightly spicy flavour) (Mandim et al., 2023). Cardoon flowers are rich in coagulant enzymes with similar activity to mammalian chymosin and pepsin, such as cardosins A and B, chinarase and cyprosins (Conceição et al., 2018), (Almeida & Simões, 2018), (Barbosa et al., 2020). In particular, cardosins E, F, G and H are dimeric, glycosylated, pepstatin-sensitive enzymes, active at acidic pH (maximum activity around pH 4.3) present on the pistils of *C. cardunculus* L., with cyprosins and cardosins A and B. These find an important industrial application in the preparation of cheeses (Sarmento et al., 2009). The cardoon, thanks to his properties, was used for the valorization of added value aimed at the production of cheeses with Protected Designation of Origin (DOP) (Conceição et al., 2018), (Almeida & Simões, 2018).

The food industry favours the sale of canned cardoons. Boiling the stems produces a significant quantity of wastewater, which may contain numerous bioactive compounds with high environmental, economic and nutritional potential. In the study of Garcia-Castello et al., (Garcia-Castello et al., 2023) new methods were identified to recover these bioactive compounds such as mono- and di-caffeoylquinic acids (Gerschenson et al., 2020), inulin and vitamin C (Pandino et al., 2022), (Garcia-Castello et al., 2022) from cardoon wastewater for their potential use. The seed yield and oil production from the cardoon plant depend on many variables, such as pedoclimatic conditions and cultivation techniques (Foti et al., 1999), (Curt et al., 2002), (Raccuia and Melilli, 2007). The roots, however, represented an important source of inulin, a molecule of interest for various applications, including food (Raccuia and Melilli 2004), (Raccuia and Melilli 2010). Moreover, since ancient times, cardoon leaves have been used as an essence for the preparation of alcoholic beverages (Foti et al., 1999).

5. No-food industry applications

Cardoon has numerous industrial applications, however, approximately 60-85% of the plant fractions are not used, generating thousands of tons of waste worldwide. The main producing countries, such as Portugal, Spain and Italy estimate that approximately 10-30 t/ha (62% stems and leaves and 38% heads) of dry biomass are produced (Barracosa et al., 2019), (Espada et al., 2021), (Raccuia & Melilli, 2007). Raccuia & Melilli evaluated the production of cardoon field residues; approximately 600 days after sowing, the accumulation of biomass, mainly represented by stems, flower heads and leaves (40%, 35% and 25%, respectively) can reach 3968 g·plant^{-1} (Raccuia & Melilli, 2010), with a low moisture content (10–15%) (Lourenço et al., 2015), with a yield per hectare with a range of values ranging from 3.64 to 38.38 t/year (Francaviglia et al., 2016), (Foti et al., 1999), (Gouveia et al., 2012). Due to the environmental impact associated with waste plant material, it is essential to develop a circular economy approach, new applications of by-products and increase the economic value of the species.

At an industrial level, cardoon has multiple uses and new non-food applications are being developed (Fig.7.). From its seeds, which contain 25% oil, the extracted oil can also be used purely as an additive to traditional fuels or treated with various technologies for the production of biodiesel, biomass and bioenergy (biogas such as bioethanol and biomethane), (Ferrero et al., 2020). The high yield of lignocellulosic biomass, low maintenance costs and large-scale availability make the cardoon an interesting raw material for energy production (Mauromicale et al., 2019), (Barracosa et al., 2019) and for the production of bioethanol, biomethane and bio-oil; furthermore, the high thermal capacity makes the cardoon suitable for its application as a solid fuel (Mauromicale et al., 2019). According to the authors, the use of *C. cardunculus* seeds for oil production could be compatible with the exploitation of aerial biomass for energy production and biodiesel production. From an agricultural point of view, the success of this application would lie in the seed yield, presently estimated at 1:3 t seeds ha^{-1} $year^{-1}$ (Curt et al., 2002).

Another application derived from cardoon seed cake residues is the production of pellets for domestic heating (Foti et al., 1999), (Raccuia et al., 2007).

A further application of the cardoon was highlighted in the feed sector, in particular the potential of its products as green fodder for animal feed, thanks to its high content of bioactive substances as proteins (18.52 ± 0.08% mg/100g), fibre (1.22 ± 0.30% mg/100g), phenolic compounds (32.7 ± 0.02 mg/tannic acid equivalent), polyunsaturated fatty acid (PUFA), and a high energy and digestibility coefficient (Barbosa et al., 2020). The solid residue resulting from the extraction of oily achenes has also recently been evaluated as a precious source of fatty acids (Cabiddu et al., 2019), (Zumbo et al., 2022), and seed cake, which showed greater antioxidant capacity and higher total phenolic content (Genovese ert al., 2015), (Petropoulos et al., 2018). Recent work by Zumbo et al. (Zumbo et al., 2022) described feed fortification of the pig diet with pressed cardoon and observed a decrease in intramuscular fat and a lower content of monounsaturated fatty acids. Due to high protein content, also the residual flour can be used for animal feed after oil extraction from grain (Foti et al., 1999). Fresh biomass is suitable to be used as winter forage for livestock feeding (Cravero et al., 2012).

Although knowledge regarding the cosmetic application of cardoon is very scarce, seeds oil has also been used in the cosmetics industry to produce body oils and creams (Barbosa et al., 2020).

Recent studies have also found that cardoon leaves have a bioherbicidal effect against weeds (Scavo et al., 2019), and an anti-mold effect on citrus fruits (Restuccia et al., 2020). Furthermore, the cytotoxicity of the cardoon was recently evaluated, which was found to be highly safe towards healthy cells, and potentially cytotoxic towards cancer cells (Mandim et al., 2020), (Mandim et al., 2021).

The biomass derived from the cardoon plant contains large quantities of cellulose fibres, including lignin and hemicellulose. Thanks to its composition, the cardoon has been widely exploited and studied for the production of wood pulp and paper (Lourenço et al., 2017). A research group evaluated the production levels of three different cardoon genotypes (Altilis, Gigante and Trinaseed) in two different climatic conditions of Mediterranean crops (a flat site and a hilly site). In the flat site the lignocellulosic biomass yield was 19 t ha^{-1} d.m., mainly hemicellulose. In the hilly site, biomass yield was similar (20 t ha^{-1} d.m.) (Ottaiano et al., 2017). Thanks to its high cellulose and hemicellulose content it can be used by the paper industry (Gominho et al., 2011).

In the study of Curt et al., the use of the seed cake as a fertilizer has been proposed because it would also help improve the organic matter content of the soil and provide a significant number of macronutrients to the crop. At an industrial level, it could also be used as animal feed thanks to its protein content, estimated at 24% (Curt et al., 2002).

A study by Francaviglia et al. (Francaviglia et al., 2016), reported the average yields and quality characteristics of cardoon grown in marginal Italian lands, in conditions of low fertilization and with rain irrigation. In particular, in their work, four genotypes, two cultivated genotypes (CDL07 and Gigante) and two wild cardoons, one from Sicily (RCT10) and the other from Latium (Tolfa Mountains) were compared. In detail, the wild genotypes were less productive than the cultivated genotypes in terms of fresh and dry biomass (ash, crude fibre, hemicellulose, cellulose and lignin), 48 and 60% respectively, in terms of grain yield (between 8 and 18 t ha^{-1} and between 1.2 and 2.8 t ha^{-1}, respectively) and in terms of chemical composition: it was highlighted that, in the cultivated genotypes, the oil yields were found to be greater (0.45 t ha^{-1}) compared to the cultivated (0.23 t ha^{-1}). From this research the economic side was also studied; the analysis of the production costs and revenues of the cardoon, compared to other annual herbaceous crops, has demonstrated the low cultivation costs per hectare, and its suitability for inclusion in arable cultivation systems in marginal lands and that the lignocellulosic contents represented by hemicellulose, cellulose and lignin were suitable for energy or paper production.

Fig. 7. Main industry applications of *Cynara Cardunculus*.

6. Food packaging uses

Today there is active research towards new natural compounds from food by-products with antimicrobial, antifungal and antioxidant actions, to be used in food packaging to reduce lipid oxidation and microbial contamination (Andrade et al., 2019), (Castro et al., 2019). Mazzaglia et al. studied the effect of cardoon extract at two concentrations (1% and 3%) added during the preparation of aubergine-based burgers to increase shelf-life. The microbial load and sensory variations of the vacuum-packaged hamburgers were evaluated on the day of processing and after 30 and 105 days of storage. The burger with 3% cardoon extract presented the best result (Mazzaglia et al., 2018). In the study of Mirpoor et al., microbial transglutaminase (mTGase) was tested on proteins from cardoon cake. The cakes were cross-linked with mTGase and used as a matrix to prepare bioplastics for use as peanut snack sachets. These biological materials were evaluated for their technological, mechanical and hydrophilic characteristics. The microbial enzyme influenced the characteristics of the film making it more resistant and less hydrophilic. The biodegradation test demonstrated that the materials could be decomposed under soil-like conditions, indicating that bioplastics can be used as biodegradable materials to protect peanuts and increase their shelf-life, as demonstrated by the decrease in food peroxidase value (Mirpoor et al., 2024). Some authors have highlighted the possible use of cardoon seed oil derived from the inedible plant *Cynara cardunc.ulus*, which grows in marginal areas and contaminated soils in Mediterranean regions and has been successfully epoxidized in fed-batch mode. The inexpensive and environmentally friendly oils have been used as bio-plasticizers of poly(lactic acid) (PLA), a biodegradable thermoplastic polyester that suffers from high stiffness and brittleness, disadvantages that limit its industrial application, to improve its industrial applications as a biodegradable packaging material. The structural, thermal and mechanical properties of films made from a blend of PLA containing 3 wt% of epoxidized cardoon seed oil. The cardoon oils induced the decrease in glass transition temperature due to the increase in PLA free volume, and the increase in thermal stability and ductility of PLA, favouring its use as a bioplastic for packaging materials as a new environmentally friendly and economical plasticizer that can positively contribute to the improvement of PLA properties (Turcu et al., 2019).

In recent years, the search for green and sustainable solutions to improve the energy efficiency of the construction sector has intensified. Recent research has developed an innovative lightweight composite material with thermal insulation properties, composed of cardooon particles and polyurethane (45% by weight of cardoon particles and 75% isocyanate). Furthermore, compared to other common and conventional materials, it has very low emissions of volatile organic compounds and formaldehyde (lower than legal levels), high resistance to biological degradation and a better insulating capacity than plasterboard (Fernandes et al., 2024). Given the growing interest in the adsorption of pollutants on absorbent materials, especially those of plant origin, a recent study evaluated the development of activated carbons based on cardoon leaf waste (Hajji et al., 2023).

7. *Bioactive properties*

Cardoon is widely consumed in traditional medicine for its many medicinal properties. To date, there are many works in the literature that describe its bioactive potential and different pharmacological properties (Fig.8.).

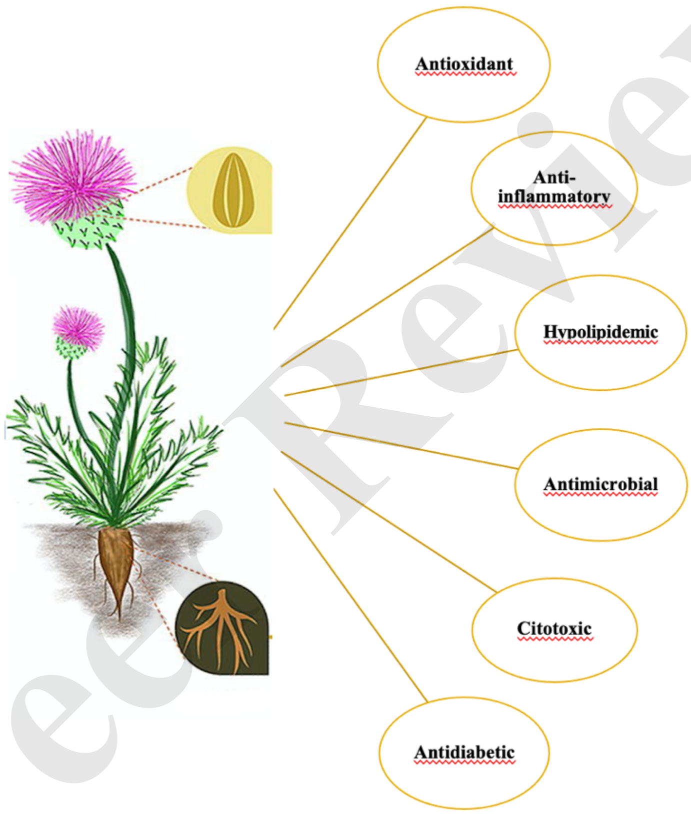

Fig. 8. Main bioactive properties of *Cynara cardunculus.*

7.1 Antioxidant activity

One of Cardoon's most studied bioactive properties is its antioxidant activity. Several studies have focused attention on the different growth steps of the cardoon through enzymatic and colorimetric assays. Based on the studies carried out by Mandim et al., bracts and heads showed a higher action in the intermediate stages of maturation, the petioles and blades demonstrated a greater ability to inhibit lipid peroxidation in the immature stage, and the seeds showed better activity in more advanced growth stages. The oxidative hemolysis inhibition test showed better results in flower heads at lower stages of maturation, different to bracts and seeds which however showed lower IC50 values (Mandim et al., 2021), (Mandim et al., 2020), also confirmed by Petropoulos et al. (Petropoulos et al. 2018). Ramos et al. (Ramos et al. 2014) described higher activities for the receptacle and bracts. It is necessary to evaluate the antioxidant potential based on the extraction methodologies. studies have shown that ultrasound-assisted extraction (UAE) reported higher DPPH and ABTS values compared to the infusion (Kollia et al., 2017). Juaniz et al. (Juaniz et al. 2017) observed an increase in antiradical activity in samples subjected to thermal processes.

Lockowandt et al., highlighted a promising antioxidant activity of cardoon extracts through two tests, the ability to inhibit oxidative hemolysis (OxHLIA) and the formation of thiobarbituric acid-reactive substances (TBARS), using Trolox as a positive control. The results were expressed as IC50 (ability to inhibit 50% of the lipid peroxidation process) (Lockowandt et al., 2019).

Several authors have highlighted the presence of numerous polyphenolic compounds with high antioxidant capacity, especially in cardoon leaves (Falleh et al., 2008), (Chihoub et al., 2019), (Bràs et al., 2015), among which chlorogenic acid and flavonoids are the most common (Pinelli et al., 2007). Flavonoids in leaves are important for the protection of the plant itself because they can absorb ultraviolet (UV) rays, especially UV-B (Pinelli et al., 2007). Pandino et al. (Pandino et al., 2013) identified caffeoylquinic acid as the most common bioactive compound quantified in leaves, with an inhibitory action towards reactive oxygen species, delaying the development of tumors. The presence of caffeoylquinic acid depends on various factors (genetic, environmental, plant manipulation and maturation) (Scavo et al., 2019), (Lombardo et al., 2018). Several authors have reported important properties of these substances such as antioxidant, antimicrobial, anti-inflammatory, anticancer and anti-anxiety (Stumpf et al., 2020), (Chihoub et al., 2019).

Several assays can be performed to measure the antioxidant activity of leaves or their potential to inhibit lipid oxidation. The iron antioxidant reducing power (FRAP) test, the DPPH free radical inhibition test, the β-carotene bleaching test, the thiobarbituric acid reactive substances (TBARS) inhibition test and the reducing power test are some of the most commonly used techniques to evaluate antioxidant activity, directly or indirectly. Numerous authors (Chihoub et al., 2019), (Falleh et al., 2008), have performed these tests and confirmed the antioxidant activity of cardoon leaf extracts thanks to the presence of numerous bioactive compounds previously described. For example, Chihoub et al. compared the antioxidant activity of cardoon leaf hydroethanolic extract and leaf infusion through. The hydroethanolic extract showed higher values for the DPPH free radical inhibition test (0.07 ± 0.00 mg/mL), reducing power (0.27 ± 0.09 mg/mL), β-whitening test -carotene (0.19 ± 0.05 mg/ml) and TBARS inhibition (0.05 ± 0.01 mg/ml) compared to the infusion (Chihoub et al., 2019).

7.2 Anti-inflammatory

The anti-inflammatory activity of cardoon has been demonstrated in numerous studies. Mandim et al., showed the influence of the maturation stage, and in particular that the flower heads, bracts and petioles at a recent stage of maturation had a greater capacity to inhibit the formation of NO (Mandim et al., 2021), (Mandim et al., 2020). On the other hand, blades and seeds presented greater potential at advanced maturation stages. Mateus et al., demonstrated the ability of the aqueous extract of dried cardoon leaves in an induced colitis model to reduce TNF-α levels (Mateus et al., 2021). These results were confirmed by Speciale et al. who highlighted that cardoon extract suppressed NF-κB, activating Nrf2 pathways. The effect was probably due to chlorogenic acid (Speciale et al., 2022) or cynaropicrin (Elsebai et al., 2016).

A recent study by Huarte et al. (2021) demonstrated the ability to inhibit the inflammation caused by lipopolysaccharides in CaCo-2 cells of raw vacuum-packed cardoon compared to cooking, which instead highlighted pro-inflammatory effects, probably due to poor absorption of polyphenols (Huarte et al., 2021).

In a procedure described by Mandim et al., (Mandim et al., 2019), the anti-inflammatory capacity of cardoon extracts was evaluated by measuring their ability to inhibit the production of nitric oxide (NO) induced by lipopolysaccharide (LPS) . The results were promising and were expressed as a minimum concentration inhibiting the production of the proinflammatory mediator (NO) in 50% (IC50 values, μg/mL).

7.3 Antimicrobial and antifungal properties

In several studies, cardoon has been identified as a promising source of compounds inhibiting the growth of bacteria and fungi (Ferro et al., 2018), (Petropoulos et al., 2018). Mandim et al. (Mandim et al. 2020) found that non-viable ones had higher antibacterial potential. The state of maturation also has a significant influence on the antimicrobial potential of the cardoon; petioles showed higher antibacterial potential for immature samples, however, none of the samples tested demonstrated significant antifungal activity (Mandim et al., 2021). Scavo et al. (Scavo et al., 2019) demonstrated that the ethanolic extract showed the best antimicrobial results, and Gram-positive bacteria are more susceptible than Gram-negative bacteria to plant extracts due to the permeability of the bacterial cell barrier. Petropoulos et al. (Petropoulos et al., 2019) highlighted that methanolic extracts of seeds had greater or similar antibacterial activity compared to the control.

The phenolic composition is associated with the antimicrobial potential of the cardoon, particularly the content of luteolin and 5-O-caffeoylquinic acid (Barbosa et al., 2020), (Ferraz et al., 2022). The antimicrobial activity of cynaropicrin has also been studied, with a potential to inhibit the growth of Bacillus cereus, Pseudomonas aeruginosa and Staphylococcus aureus (Ferro et al., 2018).

Añibarro-Ortega et al. (Añibarro-Ortega et al., 2020) tested cardoon extracts, dissolved in 5% dimethyl sulfoxide (DMSO), for the evaluation of antibacterial potential. To evaluate the antibacterial activity, six bacterial strains were used*: Staphylococcus aureus,* *Bacillus cereus, Listeria monocytogenes, Escherichia coli, Salmonella enterica* and *Enterobacter cloacae*. Instead, for the evaluation of antifungal activity, the micromycetes *Aspergillus fumigatus, Aspergillus niger, Aspergillus versicolor, Penicillium funiculosum, Trichoderma viride,* and *Penicillium aurantiogriseum*. Promising results have been shown on these bacterial and fungal strains, expressed as minimum inhibitory concentrations (MIC), bactericidal (MBC) or fungicidal (MFC) (mg/mL), which allow us to conclude how the cardoon can be exploited in this sense.

Falleh et al. linked the antimicrobial activity of cardoon leaves to their richness in phenolic compounds, mainly due to the presence of lutein (Falleh et al., 2008). Kukic´et al. (Kukic´et al., 2008) highlighted the antifungal activity of *C. cardunculus* involucral bract extracts.

7.4 Cytotoxic and hepatotoxic activity

The cytotoxicity of cardoon has been evaluated by several authors and has been demonstrated for tumor cell lines and not for healthy cells (Petropoulos et al., 2018), (Petropoulos et al., 2019). According to Mandim et al., flower heads, bracts, laminae and petioles at intermediate stages of maturation and seeds at more advanced stages have the highest cytotoxic potential (Mandim et al., 2021), (Mandim et al., 2020). Ethanol extracts from bracts and petioles showed cytotoxic potential towards cervical cancer cell line (Mandim et al., 2021), cardoon heads towards lung cancer cell line (Mandim et al., 2020). The seeds had a greater ability to inhibit hepatocellular carcinoma, and blade breast carcinoma (Ferro et al., 2018). Fuhr et al. (Fuhr et al., 2022) showed cytotoxic properties of cardoon leaf extracts towards colorectal cancer cells, while Russo et al. (Russo et al. 2017) studied the effect of a hydroethanolic extract on K562 leukemic cells, in particular, cynaropicrin (Ramos et al., 2013).

Kessler et al. evaluated the cytotoxic and hepatotoxic activity of cardoon extracts by colorimetric assay of sulforhodamine B (Kessler et al., 2022). The extracts were tested against four tumour cell lines: hepatocellular carcinoma, non-small cell lung carcinoma, cervical adenocarcinoma and breast carcinoma. The results of the tests were very promising, the extracts showed a high level of cytotoxicity.

7.5 Antidiabetic and hypolipidemic activity

Antidiabetic activity of the cardoon could be related to the concentration of chlorogenic acid, which has an inhibitory capacity for glucose 6-phosphate, responsible for the regulation of glucose in the blood and caffeoylquinic acid, responsible for regulating the activity of α-glucosidase (Loi et al., 2013).

To search for new solutions to lipid profile dysregulations, the activities of α-amylases have recently been analyzed. Ben Salem et al., (Ben Salem et al., 2017) studied the in vitro inhibitory capacity of α-amylase activity of different extracts (butanol, ethanolic and aqueous) of flowers of *C. cardunculus* var. *scolymus* L. The best results were found in the ethanolic extract (IC50 of 72.22 μg/mL). Furthermore, the same authors administered ethanolic artichoke leaf extract of *C. cardunculus* var. *scolymus* L. to rats to study the possible antidiabetic effect. After supplementation, artichoke leaf extract reduced diabetic rats' α-amylase levels and blood glucose levels. Also, Kuczmannová et al., (Kuczmannová et al., 2016) and Heidarian et al., (Heidarian et al., 2011) showed a reduction in glucose levels and inhibited the formation of glycation end-products. Ebrahimi-Mameghani et al., conducted a clinical study on the effects of artichoke leaf extract supplementation (1800 mg/day) in patients suffering from metabolic syndrome. A decrease in insulin values and insulin resistance was highlighted in patients (Ebrahimi-Mameghani et al., 2018).

8. Conclusions

Cardoon is a plant widely used in the Mediterranean diet and traditional medicine, composed of numerous bioactive compounds such as vitamins, polyphenols, minerals and fatty acids; cardoon cultivation responds to the need for crops that are well adapted to climate change and sustainable. This review provided a complete overview of the chemical-nutritional composition of the cardoon and its applications in the food and industrial sectors. The main metabolic and therapeutic activities were also considered, including anti-inflammatory, antidiabetic, lipid-lowering, antimicrobial and anti-tumor action. In recent times, the industrial uses of cardoon and its by-products have increased in the energy, feed, bioplastics and food packaging sectors. However, especially the cardoon by-products and their industrial application, require further investigation to optimize the uses of this low-cost and simple cultivation Mediterranean plant. The plant biomass coming from stems, leaves and external bracts which represent approximately

80% of the total is identified as a source of compounds that promote health, also promoting economic valorization in a zero-waste circular economy perspective.

CRediT authorship contribution statement

Carla Buzzanca: Writing – review & editing, Writing – original draft, Visualization, Supervision, Software, Methodology, Project administration, Conceptualization. **Vita Di Stefano:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Software, Methodology, Project administration, Conceptualization. **Angela D'Amico:** Writing – review & editing, Supervision, Software, Methodology, Conceptualization. **Alessandro Gallina**: Writing – review & editing, Supervision, Software, Methodology. **Maria Grazia Melilli**: Writing – review & editing, Supervision, Software, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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