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Licium Barbarum cultivated in Italy: Chemical characterization and nutritional evaluation

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PAPER

Abstract

Goji berries are the most cultivated fruit crop in Asian countries as they contain many nutrients and health-promoting bioactive compounds. These health-promoting properties have recently stimulated the interest of food and nutraceutical industries in Europe, so this crop has spread within Italy, which has become the largest European producer. Several works on the chemical composition and biological activities of Chinese goji berries are available. In this review, the chemical and the nutritional profile of goji berries from *Licium barbarum* spp. cultivated in Italy are reported.

Keywords: Goji berries; *Licium barbarum spp*; bioactive compounds; antioxidant properties; anticancer activities

Introduction

Goji berry or wolfberry is a bright orange-red berry produced by perennial plants of the genus *Lycium*, belonging to the Solanacee family (Aronson, 2006). Of late, Goji berries (GBs) used in traditional Chinese medicine are becoming very popular also in the Occidental world because of their properties, such as antioxidant (MA *et al*., 2019), anti-aging (Gao *et al*., 2017), anti-cancer (Ceccarini *et al*., 2016a; Georgiev *et al*., 2019), neuroprotective (Xing *et al*., 2016), antidiabetic (Zhao *et al*., 2020), immunomodulatory (Yang *et al*., 2013), anti-inflammatory (Chen *et al*., 2020), and others activities, such as hormonal profile and reproductive performance in livestock animals (Andoni *et al*., 2021; Brecchia *et al*., 2021; Agradi *et al*., 2022). Among *Lycium* (L.) species (spp), *L. barbarum* spp is definitely the most commercially widespread species given its high nutritional and medicinal value. The *L. barbarum* plant is a perennial plant that mainly grows in the Ningxia Hui Region in North-central China, the Xinjiang region in Western China, and also in Tibet and in Mongolia (Potterat, 2010). This plant is highly tolerant to adverse environmental conditions and grows in salinity regions and at different altitudes ranging from 700 to 2700 m (Kruczek *et al*., 2020).

In China, *L. barbarum* fresh leaves are much used in food dishes such as soups or used as herbal tea (Crawford, 2012) while the fruits are squeezed for their juice or used fresh or dried (Donno *et al*., 2015). The dried fruits and leaves have also been used for medicinal purposes, as a traditional Chinese medicine, for thousands of years (Zhu *et al*., 2013). According to the Traditional Chinese Pharmacopeia (TPC), *Lycium* spp can be used to treat various diseases including blurry vision, glaucoma, diabetes, kidney failure, cancer, cough, asthma, metabolism/energy expenditure, and aging (Amagase *et al*., 2009).

Many studies have shown that goji fruits have antioxidant, hypoglycemic, anticancer, and immunomodulatory effects so that supplementation of a regular diet with these berries can help to prevent many age-related

Table 1. Average nutritional composition (g/100g) of Italian fresh goji berries (mean± standard deviation).

	Moisture	Fats	Proteins	Carbohydrate	Fiber	Ash
Montesano *et al.*, 2018	78±1.5	0.2±0.01	2.5±0.01	16.5±1.8	2.0±0.5	0.8±0.02
Niro *et al.*, 2017	77.4±1.8	1.1±0,05	2.5±0.02	15.3±1.3	2.9±0.8	0.8±0.03

diseases (Gao *et al.*, 2017; Ma *et al.*, 2019; Ceccarini *et al.*, 2016b; Menchetti *et al.*, 2020). These health-promoting properties have also recently stimulated the interest of food and nutraceutical industries in Europe (Bae *et al.*, 2017). This crop has spread within Italy, which has become the largest European producer (Knowles, 2016).

Several papers on the chemical composition and biological activities of Chinese GBs are available (Wang *et al.*, 2021; Lu *et al.*, 2021), less of Italian GBs (Lopatriello *et al.*, 2017). This review aims to analyze the chemical and the nutritional profile of GBs from *L. barbarum* spp. cultivated in Italy and its application as a functional food.

Nutritional composition of Italian GBs

The nutritional composition of fresh GBs cultivated in Italy was investigated by Niro and Montesano (Niro *et al.*, 2017; Montesano *et al.*, 2018). Both research groups analyzed GBs samples from southern Italy. The nutritional composition of Italian GBs is reported in Table 1.

The results are very similar and the small differences may depend on some variables such as different methods of preparation and analysis of the samples.

The nutritional values make GBs an excellent source of macronutrients, especially carbohydrates. They are present as highly branched water-soluble L. *barbarum* polysaccharides and represent 5–8% of the total dry matter of the berries. Several studies indicate that the high biological activity components in GBs are polysaccharides (Amagase and Farnsworth, 2011). The mixture of *L. barbarum* polysaccharides exerts a retinal ganglion cell protection and reduces the oxidative stress in retinal/reperfusion injury (Li *et al.*, 2011; Mi *et al.*, 2012) and in high-fat diet fed mice (Ming *et al.*, 2009) in which a decrease in total cholesterol, LDL-cholesterol, and triglycerides, and an increase in HDL-cholesterol have been observed (Luo *et al.*, 2004). Thanks to the lipid-lowering and hypoglycaemic effects, the GBs exert a protective effect on the cardiovascular system (Ma *et al.*, 2019). Moreover, Yang *et al.* demonstrated the immunomodulatory properties of *L. barbarum* polysaccharides that increased the phagocytosis and nitric oxide production of RAW 264.7 macrophages (Yang *et al.*, 2015).

GBs have a low protein content (2–2.5 g/100g) and therefore they could not be considered a good source for protein. However, it has been shown that these fruits contained 17 of the 20 protein amino acids, including all eight essential amino acids (Lu *et al.*, 2021).

Table 2. Average total carotenoid and zeaxanthin dipalmitate content (mg/100g) in Italian dried goji berries (mean± standard deviation).

	Total carotenoids	Zeaxanthin dipalmitate
Bertoldi *et al.*, 2019	355±49	245±49
Niro *et al.*, 2018	184±4	159±2

Carotenoid composition of Italian GBs

The second highly significant group of biologically active molecules present in GBs are carotenoids, the coloured components of goji fruits. The total carotenoid content of different *L. barbarum* fruits ranges from 0.03% to 0.5% of dried fruits with zeaxanthin dipalmitate representing more than 75% of the total carotenoids (Cenariu *et al.*, 2021). Table 2 shows the total carotenoid and zeaxanthin dipalmitate content, expressed in milligram per 100 g of Italian dried fruits according to Bertoldi and Niro (Bertoldi *et al.*, 2019; Niro *et al.*, 2018).

The study of Bertoldi *et al.* showed that the average total carotenoid content of Asian GBs (197.8 mg/100g) was just over half of the Italian ones (355 mg/100g). These data are of particular importance as it means that Italian GBs have a biological and nutritional value higher than those of Asian origin. Instead, the data obtained by Niro showed levels of carotenoid and Zeaxanthin palmitate similar to those of Asian origin. The discrepancy between the data may depend on the different methods used for their determination or to ecological factors and cultural practices (Arena and Curvetto, 2008).

Goji antioxidative power has carotenoid content (Kulczynski and Gramza-Michalowska, 2016; Chang and So, 2008). Many studies have demonstrated a correlation between antioxidant activity of *L. barbarum* fruit and its antitumor (Potterat *et al.*, 2010; Ceccarini *et al.*, 2016a; Georgiev *et al.*, 2019), anti-inflammatory (Amagase and Farnsworth, 2011; Chen *et al.*, 2020), and immunomodulatory (Yang *et al.*, 2013) activities. Cenariu *et al.* have indicated the cytoprotective activity of a zeaxanthin-rich extract from *L. barbarum* berries on tumor-derived A375 skin cell line through mitogen-activated protein kinase (MAPK) influence (Cenariu *et al.*, 2021).

Mineral composition of Italian GBs

GBs are also extremely rich in many minerals which are essential components for a balanced diet. Indeed, adequate mineral intake is essential for many human vital functions such as oxygen transport, muscle contraction, enzyme activation, blood acid–base balance, bone structure, nerve impulse conduction, heart contraction, antioxidant system activity, and immune system activation (Williams, 2005). Sodium and potassium, for example, are macro elements essential for membrane depolarization and body water balance, calcium for mineral bone structure and muscle and heart contraction, magnesium is a cofactor of more than 300 enzymes and is required for energy production and nucleic acid synthesis (Sá *et al*., 2019). The average values of principal macro elements in dried Italian GBs are shown in Table 3.

It was observed that potassium (K) is the main macro element of the Italian and Asian GBs. Anyway, the K concentration determined by Bertoldi in Italian GBs was about twice the average values found in Asian GBs (Endes *et al*., 2015). High dietary K intake (>3.5g/day) is associated with a decrease in blood pressure as documented in several clinical studies (Binia *et al*., 2015). Sodium (Na) concentrations were very similar in all Italian samples but about a third of that was found in the Asian GBs (Llorent-Martinez *et al*., 2013). Many studies suggest a direct relationship between Na intake and blood pressure values (Mente *et al*., 2014). Indeed, excessive Na intake (defined as >5 g Na per day (WHO, 2012)) has been shown to produce a significant increase in blood pressure and has been linked with the onset of hypertension and its cardiovascular complications (Weinberger, 1996; Strazzullo *et al*., 2009).

Also, phosphorus (P), magnesium (Mg), and calcium (Ca) contents were rather different in the two studies. The P value of the Bertoldi *et al.* study was particularly high even when compared to data obtained for Asian GBs (270 mg/100g). These discrepancies can be due to mineral variation in the soil and water source mineral quality and differences in growing conditions. Referring to Recommended Dietary Allowances (RDA) and Adequate Intake (AI), a daily portion of about 30 g of dried GBs provides on average 6–9% of RDA for Mg and P, 6–9% of AI for K and Na, and 1–2% of RDA for Ca (Bertoldi *et al*., 2019).

Table 3. Average values (mg/100g) of the main macro elements in dried Italian GBs (mean± standard deviation).

	K	Na	Ca	P	Mg
Bertoldi *et al*., 2019	2079±403	264±7	72±17	317±60	134±27
Niro *et al*., 2018	882±239	209±72	101±23	174±32	46±9

K, Potassium; Na, Sodium; Ca, Calcium; P, Phosphorus; Mg, Magnesium.

In addition, GBs can be a good source of microelements. The most abundant micro elements in GBs are reported in Table 4. Iron (Fe) is a very important mineral for living organisms since it participates in a wide variety of metabolic processes such as oxygen transport, electron transport, and DNA synthesis (Lieu *et al*., 2001). Zinc (Zn), copper (Cu), and manganese (Mn) are essential elements that principally act as cofactors of different enzymes, which participate in all the major metabolic pathways (Agget and Harries, 1979; Cox, 1999; Eirkson and Aschner, 2003).

A similar amount of Fe was found by the two research groups and these values were about half of that found in the Asian GBs (Bertoldi *et al*., 2019). Zn, Cu, and Mn contents from Bertoldi *et al*. samples were about two times higher than Asian berries, whereas the Zn, Cu, and Mn values from Niro *et al*. were similar to those of the Asian GBs (Bertoldi *et al*., 2019). Referring to RDA, a daily portion of about 30 g of dried GBs provides on average 20% of RDA for Cu, 15% of RDA for Fe, and 4% of RDA for Zn, whereas referring to AI, the same portion provides on average 10% of AI of Mn (Bertoldi *et al*., 2019).

Toxic trace elements present in Italian GBs

GBs may also contain some toxic elements that can have a negative impact on human health (Bordean *et al*., 2011). Bertoldi *et al*. also investigated Italian GBs for their toxic metal concentrations by comparing them with Asian GBs. The average values of the main toxic trace elements measured in Italian GBs are shown in Table 5.

Regarding arsenic (As), a daily portion (30 g) of Italian GBs provides around 12 μg which is one-third less than Asian goji's As content (18 μg/30g). Daily intake of a portion of 30 g of Italian GBs provides 5.8 μg of cadmium (Cd) which is about twice the Asian goji's average Cd content. Thirty grams of Italian GBs also provides 0.17 μg of mercurius (Hg), a value slightly higher than that found in Asian GBs (0.11 μg/30g). Finally, a daily portion

Table 4. Average values (mg/100g) of the main trace minerals in dried Italian goji berries (mean± standard deviation).

	Fe	Zn	Cu	Mn
Bertoldi *et al*., 2019	3.9±1.8	3.5±1.3	1.3±0.8	1.1±0.2
Niro *et al*., 2018	3.5±1.5	1.5±0.6	0.8±0.2	0.5±0.2

Fe, Ferrum; Zn, Zincum; Cu, Cuprum, Mn, Manganesum.

Table 5. Average values (μg/100g) of the main toxic trace elements in Italian GBs (mean± standard deviation).

	As	Cd	Hg	Pb
Bertoldi *et al*., 2019	40.7±0.5	19.3± 2.7	5.1±0.5	84.3± 5.5

As, Arsenicum; Cd, Cadmium; Hg, Mercurius, Pb, Plumbum.

of Italian GBs provides 25.3 μg of plumbum (Pb) that represent a significant amount of the daily dietary intake (0.02–3 μg/kg bw/day), but it is one sixth of that found in Asian berries (Bertoldi *et al*., 2019). Thus, concerning toxic elements, Italian GBs are better than Asian GBs.

However, caution should be used in taking large amounts of these fruits because excessive intake can overload the body with toxic mineral (Gogoasa *et al*., 2014).

Fatty acid and sterol composition of Italian GBs

Cossignani *et al*. studied fatty acid and sterol composition of GBs samples from Italy, China, and Mongolia in order to distinguish goji samples of different production areas (Cossignani *et al*., 2018).

Table 6 shows average lipid percentage and the average percentage values of saturated (SFA), monounsaturated (MUFA), and polyunsaturated (PUFA) fatty acids from the previously mentioned three origins.

Table 6. Average values (% mol) of fatty acid composition of goji samples of different origin (mean± standard deviation).

	Italy (n=9)	China (n=6)	Mongolia (n=4)
Lipid %	5.1±2.1	2.0±0.7	3.3±1.2
Fatty acid			
C16:0	14.6±4.6	9.5±2.4	11.7±0.6
C16:1	0.6±0.4	0.4±0.1	0.2±0.1
C18:0	2.9±0.8	3.2±0.2	3.3±0.0
C18:1	31.7±19.7	21.2±0.3	20.8±0.1
C18:2 (n-6)	40.5±14.8	56.5±2.9	57.2±0.2
C18:3 (n-6)	0.6±0.4	2.6±0.1	1.3±0.3
C18:3 (n-3)	7.3±6.0	5.1±0.6	3.8±0.2
C20:0	0.5±0.3	0.5±0.0	0.7±0.1
C22:0	0.4±0.3	0.5±0.0	0.5±0.2
C24:0	0.5±0.2	0.3±0.0	0.2±0.0

As can be seen, the lipid percentage of Italian GBs samples was higher than that of Asian samples, in accordance with literature data (Endes *et al*., 2015; Rosa *et al*., 2017). In addition, Italian GBs samples compared to Asian ones are richer in saturated (18.9% vs 14 and 16.4 % of Chinese and Mongolian samples) and monounsaturated (31.7% vs 20.8 and 21.2 % of Chinese and Mongolian samples) fatty acids but poorer in polyunsaturated fatty acids (48.4% vs 64.2 of Chinese and Mongolian samples). Anyway, the PUFA was the most abundant fraction in all samples and the linoleic acid (C18:2 n-6) was the most abundant PUFA acid for both Italian and Asian samples, followed by α-linolenic acid (C18:3 n-3), most abundant in Italian samples with respect to Asian samples (Cossignani *et al*., 2018). The low percentage of lipids combined with the richness in PUFA makes GBs a new dietary source of essential fatty acids, especially linoleic acid.

Cossignani and co-workers also studied the sterol fraction of GBs from Italy, China, and Mongolia. To this end, alkaline hydrolysis was carried out on goji lipid fraction to obtain data about percentage and quantitative composition (mg/100g) of the main phytosterols identified in Italian and Asian samples (Table 7).

It can be noted that Δ5-sterols were the major components compared to Δ7-sterols and that β-Sitosterol was the most abundant sterol in Italian and Chinese samples while Δ5-Avenasterol was the most abundant sterol in Mongolian samples.

β-Sitosterol, the predominant component in Italian samples (53.7%), is known to lower blood cholesterol levels in humans and also for its strong free radical scavenging activity (Lin *et al*., 2014). In addition to these properties, phytosterols possess anti-inflammatory, anti-cancer, and anti-atherogenicity activities (Berger *et al*., 2004).

The nutritional quality of the lipid and sterol fractions of the Italian GBs was confirmed through the determination

Table 7. Average values (% and mg/100g) of sterol composition in goji samples of different origin (mean± standard deviation).

	Italy (n=9)	Italy (n=9)	China (n=6)	China (n=6)	Mongolia (n=4)	Mongolia (n=4)
	%	mg/100g	%	mg/100g	%	mg/100g
Sterols						
Cholesterol	7.4±2.9	3.3±1.8	5.2±0.5	2.9±0.2	4.5±0.4	6.0±0.7
Ergosterol	12.7±3.8	5.4±2.1	13.8±0.2	7.8±0.8	12.8±0.8	16.4±1.2
Stigmasterol	4.4±2.3	2.1±1.8	11.6±1.3	6.4±0.4	6.0±0.9	8.7±1.1
Δ-5,23-Stigmastadienol	3.6±2.8	1.2±1.0	12.6±0.3	6.9±0.3	20.1±1.5	25.8±2.2
β-Sitosterol	53.7±6.5	22.8±5.4	39.4±2.5	21.4±1.0	25.9±2.0	31.7±3.1
Sitostanol	4.8±3.0	2.3±1.9	1.0±0.1	0.6±0.2	0.6±0.2	1.1±0.2
Δ5-Avenasterol	9.7±3.6	3.9±1.3	14.5±1.5	7.8±07	26.5±2.3	35.5±3.5
Δ7-Stigmasterol	0.6±0.5	0.2±0.2	0.8±0.2	0.5±0.2	1.2±0.3	1.9±0.5
Δ7-Avenasterol	2.8±1.8	1.5±1.3	1.2±0.3	0.8±0.1	2.0±0.5	2.7±0.8

of the atherogenicity (AI), thrombogenicity (TI) indexes, and hypocholesterolemic (HI) index since the low values of these indexes (0.1% AI, 0.2% TI, and 10% HI, respectively) showed a good amount of anti-atherogenic lipids in the examined samples (Ulbricht and Southgate, 1991; Fernandez *et al*., 2007).

Total tocopherols and ascorbic acid amounts in Italian GBs

Niro's research group also determined the average total tocopherols (vit E) and ascorbic acid (Vit C) amounts in fresh and dried Italian GBs samples as reported in Table 8.

Taking into account the RDA for vit E, which is 12 mg/day (Regulation EU1169/2011) and RDA for vit C which is 80 mg/day (Regulation EU1169/2011), a portion of dried GBs (30 g) provides about 20% of the RDA for vit E and 16% of the RDA for vit C. Donno *et al*. (2015) reported an amount slightly higher (42 mg/100 g) of vit C in Italian dried GBs from northern Italy.

Health benefits of Italian GBs

Antioxidant properties together with anticancer activity of Italian GBs were investigated.

This berry has been described as a "super-fruit" thanks to its concentrated levels of beneficial substances and anti-oxidant powers. The antioxidant properties of Italian *L. barbarum* fruits (cultivated in Umbria) have been evaluated by determining the total phenolic content (TPC) and the Oxygen Radical Absorbance Capacity index (ORAC) (Ceccarini *et al*., 2016b). The TPC value, expressed as milligram of gallic acid equivalents (mg GAE) per 100 g of dry weight (DW) resulted in 1278.247 ± 29.60 mg GAE/100g DW. These results showed that Italian GBs have a TPC higher than the Asian one (712.01 ±29.12gGAE/100g), whereas the ORAC value, expressed as micromoles of Trolox Equivalent per 100 g DW (μmol TE/100g DW), was slightly lower than the Asian one (22507.03±1402.02 μmol TE/100 g DW vs 26502±3807 μmol TE/100g DW). These data showed that GBs cultivated in Italy have high antioxidant properties.

Moreover, Italian fruits (cultivated in Umbria) have also been tested for their apoptotic and antiproliferative effects on human hepatocellular carcinoma (HepG2) cell line (Ceccarini *et al*., 2016b). To this end, a panel of 96 genes involved in oxidative stress, proliferation, and apoptosis was investigated in HepG2 cells using a quantitative real-time PCR-array analysis. Downregulation of genes involved in tumor migration and invasion together with upregulation of tumor suppressor genes suggests that Umbrian GBs play an anticancer role in vitro and could play a role against hepatocellular carcinoma (Ceccarini *et al*., 2016b).

Table 8. Average total tocopherol and ascorbic acid amounts (mg/100g) in Italian goji berries samples (mean± standard deviation).

	Fresh	Dried
Total tocopherols (Vit E)	2.4±0.04	9.7±0.20
Ascorbic acid (Vit C)	40±2.2	38±0.8

Conclusions

Despite the limited literature data concerning the chemical and nutritional characterization of GBs cultivated in Italy, it is possible to conclude that these fruits are an important source of bioactive compounds. In addition, Italian GBs showed some nutritional differences with those of Asian origin. In particular, Italian GBs show a higher content of carotenoids and potassium in comparison to the Asian one. Finally, Italian GBs contain fewer toxic elements in comparison to the Chinese GBs. It is possible to conclude that GBs, but in particular those of Italian origin, are loaded with important nutrients and antioxidants that can support the diet for a better quality of life.

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