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Review

Acorns as a Source of Valuable Compounds for Food and Medical Applications: A Review of *Quercus* Species Diversity and Laboratory Studies

Emilia Szabłowska [1] and Małgorzata Tańska [2,*]

[1] Department of Food Safety and Technology, Faculty of Computer Science and Technology, University of Lomza, Akademicka 14, 18-400 Lomza, Poland; eszablowska@al.edu.pl
[2] Department of Food Plant Chemistry and Processing, Faculty of Food Sciences, University of Warmia and Mazury in Olsztyn, 10-718 Olsztyn, Poland
* Correspondence: m.tanska@uwm.edu.pl; Tel.: +48-89-523-4113

Abstract: Acorns, the fruit of oak trees of the genus *Quercus*, have been known to people for generations worldwide. In ancient times, they were an important part of culinary traditions and folk medicine. Their exploitation for food over the years has been significantly diminished, which may arise from the high content of tannins responsible for a bitter taste and anti-nutritional properties. However, more and more studies show acorns' potential nutritional and health benefits. Furthermore, new reports are emphasizing the health-promoting properties of tannin-decomposition products. This review aims to present the available studies on the phytoconstituents variation in the acorns of different *Quercus* species and their possible significance for food and medical applications. In this study, the results of lab-scale food processing, as well as in vivo and in vitro experiments, are included. The literature data proved that acorn products (flour, oil, and extracts) are intensively examined due to their dietary, antioxidant, anti-microbial, anti-inflammatory, anti-cancer, and neuroprotective activities provided by their bioactive compounds. The general conclusion is that this raw material can be used more widely in the future as an ingredient in functional foods, supplements, and drugs.

Keywords: acorn flour; acorn extract; biological activity; tannins; oak distribution; bakery products; in vitro experiments

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1. Introduction

Acorns have played an important nutritional role since prehistoric times. Indigenous peoples of many cultures worldwide have incorporated acorns into their diets as a significant ingredient necessary for sustenance and an important part of culinary traditions and folk medicine [1–3]. Throughout history, the importance of acorns has diminished, and in the literature reports, researchers have begun to name them "food of the times of famine" or characterize them exclusively in the category of animal fodder. Also, the high tannin content in acorns began to be seen as problematic, necessitating additional pre-treatment prior to processing [4]. A renewed interest in acorns as a food raw material has been observed recently, which is probably due to the desire to learn about the eating habits and traditions of past generations as part of the trend of "going back to the roots" and writing the history of nutrition as an important part of the history of human development [5]. Also contributing to the increased interest in this raw material is the growing emphasis on sustainable farm development and environmentally friendly industrial processes, including the use of acorns in food production [6].

Acorns are an example of a raw material whose introduction into traditional foods enriches its basic composition with bioactive compounds, such as monounsaturated fatty acids and sterols [7], as well as phenolic compounds and tocopherols, which exhibit strong antioxidant properties [8]. Acorns are also distinguished by their high mineral content, among which iron, zinc, copper, and calcium predominate [8]. In addition, the triterpenes found in acorns are potential anti-diabetic agents and may prevent liver fibrosis [9]. Furthermore, acorns, bark, and leaves have been used in traditional medicine, such as as an antiseptic or for gastrointestinal disorders. On the other hand, oak wood is important in the maturation of wine in oak barrels and in the wood industry because of the wood's color, durability, and protection against fungal decay [10].

Large areas of oak forests and, therefore, the high availability of acorns make this raw material an important source of chemical compounds with nutritional and biological activities. Acorns are being intensively studied for processing into flour and its introduction into food products [11]. Additionally, acorn oil and extract preparation and composition are of interest to many researchers [12–14]. Researchers have also conducted studies to show the link between acorn chemical compounds and their bioactivity in in vitro experiments [10]. Although much information is available in the literature on the bioactive components in different parts of oak trees and their health benefits, comparisons of the acorns of different oak species in terms of their bioactive compounds, especially lipophilic ones, and their potential use in industry are scarce.

This review aims to update the literature data about the distribution of *Quercus* species worldwide, their diversity in terms of bioactive compounds in acorns, and their prospective applications in food and medicine.

2. Origin and Occurrence of Acorns

Acorns are the fruits of oak trees of the genus *Quercus* ssp., known to people for generations worldwide across nations, cultures, and religions [15,16]. It is estimated that the global population of oaks can reach up to 600 different species [17], whose areas of occurrence primarily include Europe, North America, the northern part of Africa, and Asia Minor (Figure 1). The habitats for the occurrence of oaks are both deciduous forests of the temperate zone and evergreen forests of the temperate and subtropical zones, as well as subtropical and tropical savannas [18].

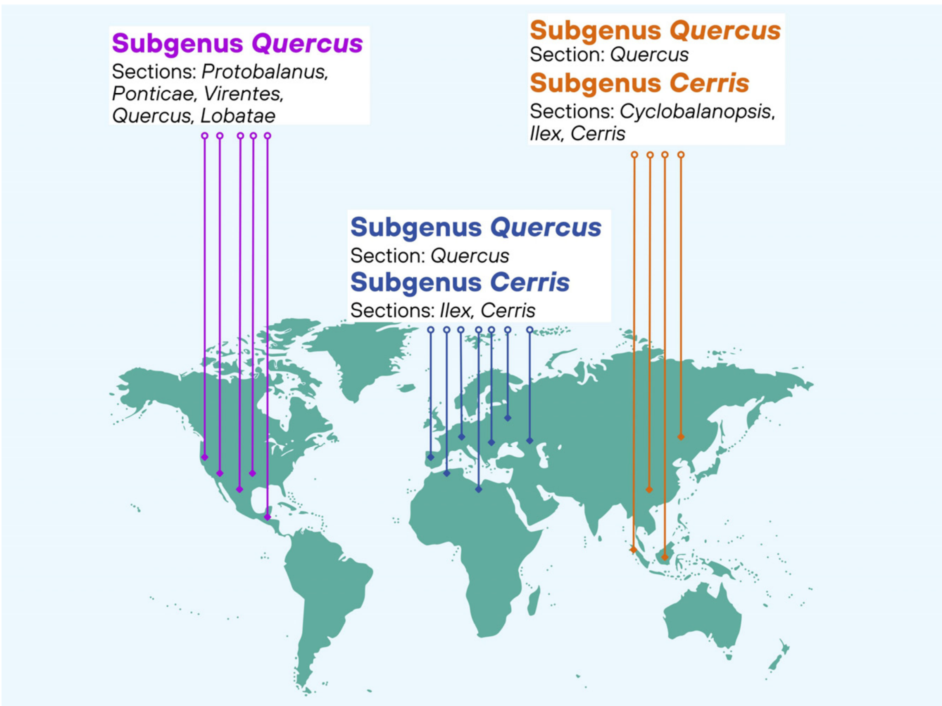

Figure 1. Distribution of oak trees worldwide by subgenus and sections. Source: own elaboration based on Denk et al. [19].

The wide range of oak trees, covering about 40° latitude and 75° longitude, is related to their ability to adapt to varying climatic and soil conditions [20]. As reported by Yang et al. [21] and Wang et al. [20], a large number of inter- and intraspecific varieties of oaks, resulting from inter- and intraspecific hybridization and introgression, make the taxonomic classification of the genus *Quercus* difficult. Over the past 185 years, several attempts have been made to classify oak trees (Figure 2). The most recent classification was proposed by Denk et al. [19] and involved the division of the genus *Quercus* into two subgenera (*Quercus* and *Cerris*), within which eight sections were distinguished. The basis for the division, under the new classification, was based on features of morphology, molecular–phylogenetic relationships, and evolutionary history rather than exclusively morphological features based on which species were classified in earlier studies.

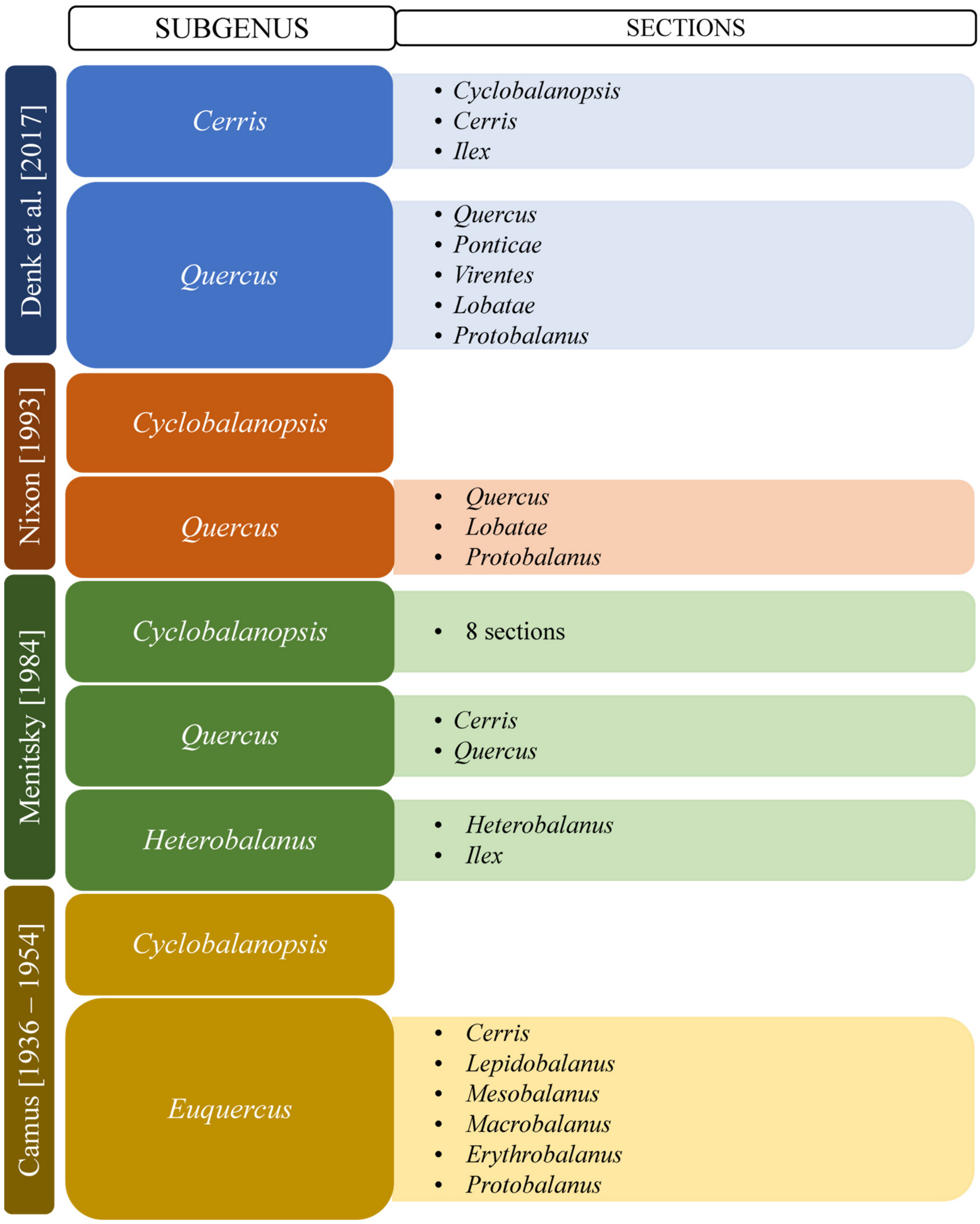

Figure 2. Changes in the taxonomic classification of *Quercus* species over the past 185 years. Source: own elaboration based on Denk et al. following Camus, Menitsky, and Nixon [19].

Oak trees have a long history of cultivation in Europe and other continents, and the practice of oak growing includes both natural forest areas and artificial afforestation made by man [20,22]. For example, in Poland, forested areas cover approximately 9435 thousand hectares (including land associated with forest management) [23], of which oak stands account for about 6% [24]. In China, oak trees account for about 13% of the total natural forest area [20], and in Iran, the area occupied by oak trees is about 6 million hectares [25]. The desirability of cultivation depends on the region, the cultural significance, and the species of oak trees growing in the area. The most commonly mentioned purposes are seed and forage [18,26–31].

3. Impact of *Quercus* Species Diversity on Acorn Morphological and Chemical Characteristics

The wide range of occurrences worldwide and the multiplicity of species influence the varied distribution of *Quercus* species by region (Figure 3). Individual species exhibit significant morphological variability in leaf structure, the structure (Figure 4), and the chemical composition of acorns (Table 1). Factors affecting oaks and acorns' morphological and chemical composition include genetic variation due to species differences and environmental factors, including primarily climatic conditions, adaptive processes, and interdependence with other species and microorganisms [20,32,33].

Figure 3. The diversity of oak trees worldwide is shown in the example of selected countries with growing interest in oak cultivation. Source: own elaboration based on Stavi et al. [30].

Among the characteristics that distinguish acorns of different *Quercus* species are bowl structure, shape, weight (along with the percentage of hardened pericarp), and dimensions (length and diameter) [6,34].

The literature data show that the predominant component of acorns is carbohydrates, among them starch. The variation of starch content in acorns is very high, ranging from 22.03 to 68.15 g/100 g d.m., indicating the degree of maturity of the acorns, as demonstrated in a study by Ferraz de Oliveira et al. [42]. Taib and Bouyazza [43] reported that acorn starch is characterized by an amylose content in the range of 15–39%, and the size of starch granules fluctuates between 2 and 24 μm. The proportion of resistant starch is also significant, at 41.4% [43].

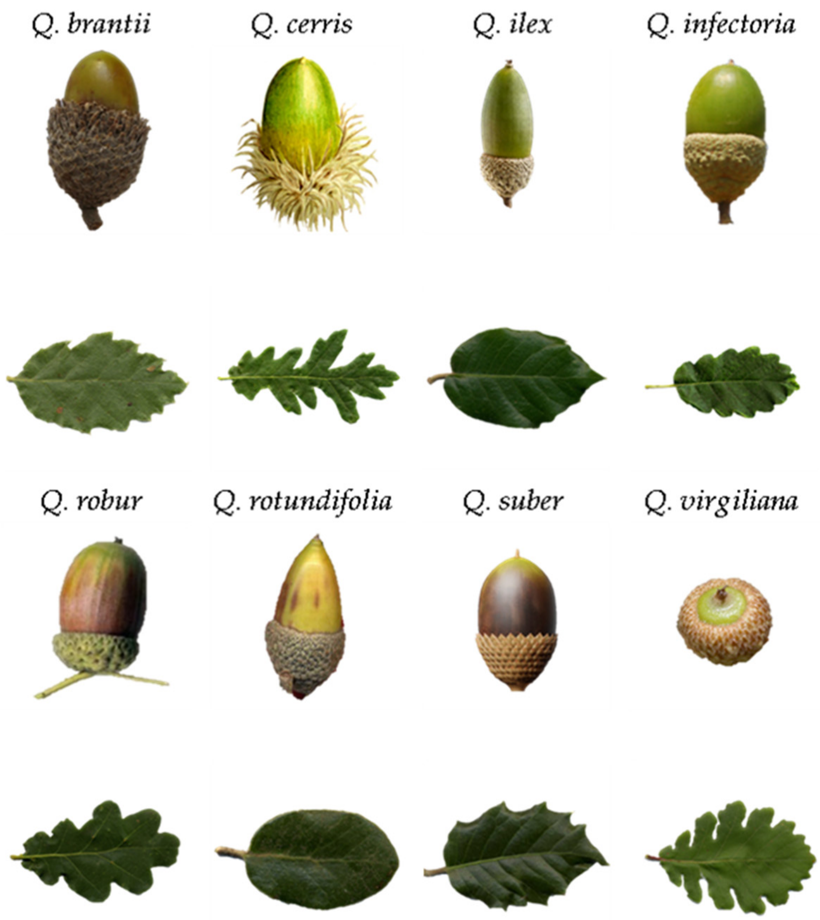

Figure 4. Morphological differences in leaves and acorns of different *Quercus* species. Source: own elaboration based on available images [35–41].

Table 1. Basic chemical composition of acorns of different *Quercus* species.

Quercus Species	Chemical Components					References
	Fat	Protein	Carbohydrates	Starch	Ash	
Q. brantii	0.72	3.37	n.d.	63.00	2.09	[44]
Q. calliprinos	2.31	4.94	77.86	n.d.	1.78	[45]
Q. cerris	1.05	4.3	n.d.	64.55	1.75	[44]
Q. coccifera	2.67	2.54	n.d.	66.2	1.81	[44]
Q. ilex	9.14–14.95	3.90–5.94	8.95–12.47 *	n.d.	1.34–2.02	[46]
Q. infectoria	1.55	4.37	n.d.	68.15	1.95	[44]
Q. ithaburensis	0.76	2.84	58.94	n.d.	3.21	[45]
Q. rotundifolia	8.38–13.51	3.56–4.34	n.d.	47.98–59.95	1.94–2.19	[42]
Q. suber	2.09–8.22	6.19–9.38	n.d.	22.03–60.00	2.12–2.98	[42,44]

* sugar content; n.d.—no data.

Depending on the species, acorns contain from 1.05 to 14.95% fat. In addition to species differences, the fat content can also be affected by origin and related environmental factors, which significantly alter the fat content of the acorns of the species *Q. ilex* [46]. In the case of fatty acid composition, Charef et al. [47] in acorns of *Q. ilex* and *Q. suber* species, Tejerina et al. [48] in acorns of *Q. rotundifolia* species, and Lassoued et al. [49] in acorns of *Q. ilex* and *Q. coccifera* species showed that the predominant fatty acid was oleic acid, the share of which was about 50–60% of total fatty acids. In contrast, a study by Özcan [50] reported that the percentage of oleic acid was similar to or lower than that of linoleic acid in the acorns of species classified into the *Quercus* taxonomic section, while in the acorns of species in the *Cerrus* section, the predominant oleic acid remained, with a maximum share of 54.3% in the acorns of species of *Q. brantii*. Regardless of the proportion of individual fatty acids, it was confirmed that in the oil of the acorns, unsaturated fatty acids are the dominant group [47,48,50].

The protein content of the acorns ranges from 2.54 to 9.38 mg/100 g d.m. The results presented in Table 1 show significant protein content variation depending on the oak species from which the acorns were obtained. Ferraz de Oliveira et al. [42] also showed differences in the protein content of acorns depending on their maturity (*Q. rotundifolia*) and Valero Galván et al. [46] depending on the origin (*Q. ilex*). Özcan [50], analyzing mature acorns from 20 different species, identified 14 different amino acids: 8 exogenous and 6 endogenous. The main amino acids were aspartic acid and glutamic acid, whose contents simultaneously showed the most significant differences between species.

In contrast, the cited author found the lowest content in the case of methionine. The highest content of aspartic and glutamic acids in the acorns of the species *Q. ilex* and *Q. coccifera* was confirmed by Lassoued et al. [49]. The cited authors also showed a high leucine content in acorns.

The ash content of acorns is subject to relatively small fluctuations, reaching a maximum value of 3.21 g/100 g d.m. in the species *Q. ithaburensis* with a dominance of sodium, potassium, and phosphorus [45]. Lassoued et al. [49] also found the highest potassium and phosphorus content in acorns of *Q. ilex* and *Q. coccifera* species, but the contents of calcium and magnesium were also significant (amounting to 118.78 and 135.10 mg/100 g d.m. in *Q. ilex* and 67.51 and 69.63 mg/100 g d.m. in *Q. coccifera*). A variation in mineral content depending on the *Quercus* species was shown by Özcan and Bayçu [51]. In the cited studies, the iron content ranged from 1.9 mg/100 g d.m. in acorns of the species *Q. hartwissiana* to 202.0 mg/100 g d.m. in acorns of the species *Q. petraea*, zinc content from 0.69 (*Q. hartwissiana*) to 36.75 mg/100 g d.m. (*Q. infectoria*), and copper content from 0.9 (*Q. infectoria*) to 10.49 mg/100 g d.m. (*Q. petraea*). Nikolić et al. [52] proved that the content of minerals in acorns depended not only on genotype but also on well-known factors such as the concentration of elements in the soil, their uptake systems by the roots, movement and redistribution within the plant, and the ability to accumulate in seeds.

4. Bioactive Compounds in Acorns

Acorns contain high levels of bioactive phenolic compounds, including phenolic acids, flavonoids, and tannins. Nevertheless, recent scientific reports have revealed numerous other compounds with biological activity, both hydrophilic and lipophilic compounds (Figure 5).

The content of the main hydrophilic and lipophilic bioactive compounds in acorns of various *Quercus* species are shown in Tables 2 and 3, respectively.

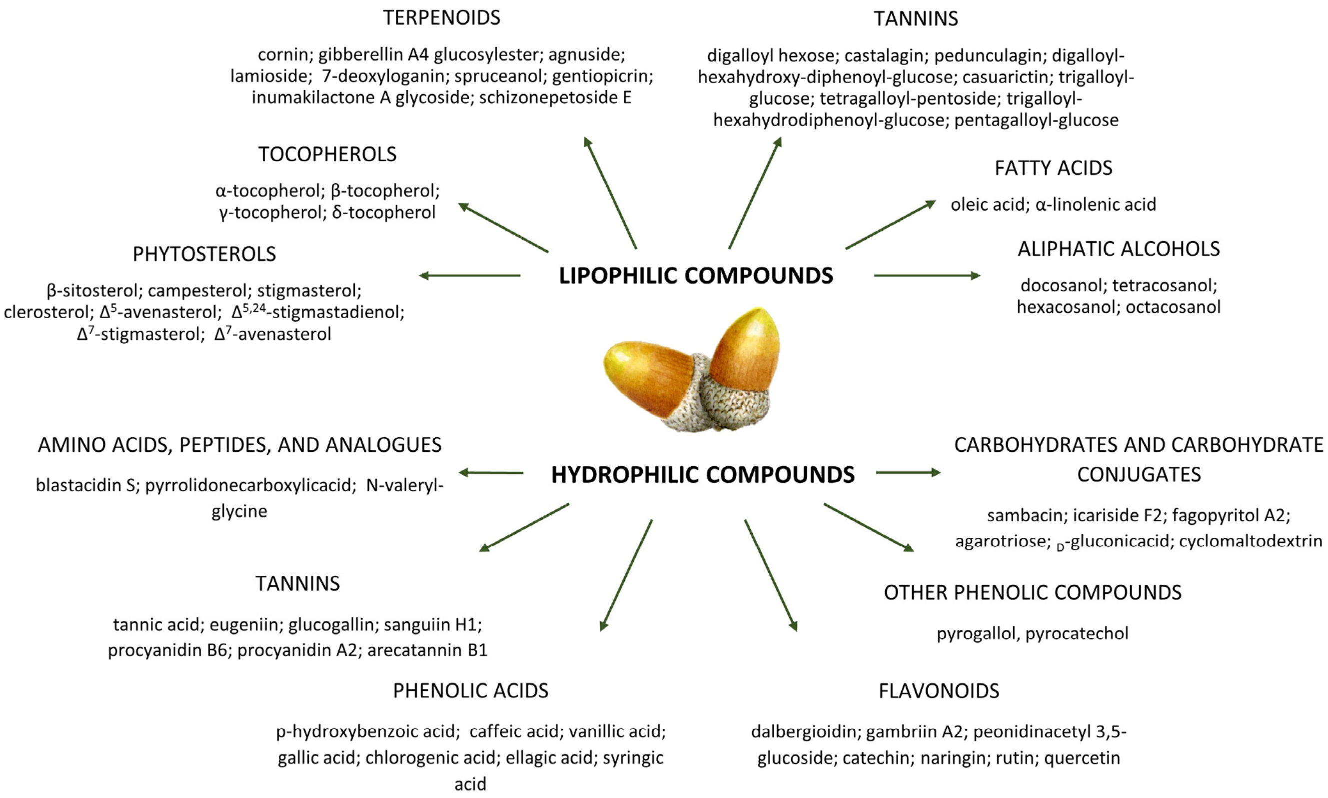

Figure 5. Bioactive compounds most commonly identified in acorns. Own elaboration based on source data [6,10,12,53–62].

Table 2. The content of hydrophilic bioactive compounds in acorns of different *Quercus* species.

Quercus Species	Chemical Group	Subgroup	Content	References
Q. coccifera	tannins [mg/100 g d.m.]	condensed	2670	[44]
Q. ilex	TPC [mg GAE/100 g d.m.]	-	1100.17–5692	[14,63]
	TFC [mg GAE/100 g d.m.]	-	47.3	
	tannins [mg CE/100 g d.m.]	-	903	
Q. robur	TPC [mg GAE/100 g d.m.]	-	22,300	[64]
	tannins [mg GAE/100 g d.m.]	-	20,400	
Q. rotundifolia	TPC [mg GAE/100 g d.m.]	-	840–9163	[42,48]
	tannins [mg CE/100 g d.m.]	condensed	50–140	
		hydrolysable	950–1150	
		gallotannins	740–860	
		ellagitannins	210–290	
Q. suber	TPC [mg GAE/100 g d.m.]	-	13,290–233,350	[14,42,44]
	tannins [mg/100 g d.m.]	condensed	2090	

d.m.—dry matter, TPC—total phenolic content, TFC—total flavonoid content, GAE—gallic acid equivalent, CE—catechin equivalent.

The phenolic compounds found in acorns are phenolic acids (primarily gallic and ellagic acids and their derivatives), flavonoids (including catechin, quercetin, and naringin), and tannins (mainly ellagitannins and gallotannins). The results presented in the literature mostly concern the total content of selected groups of compounds and qualitative profile assessment [65–68]. Therefore, future studies should be conducted to indicate the quantification of individual phenolic acids, flavonoids, and tannins.

The highest content of total phenolic compounds in acorns (up to 233,350 mg/100 g d.m.) was presented by Ferraz de Oliveira et al. [42] for the species *Q. suber* (Table 2). Tejerina et al. [48] in acorns of the species *Q. rotundifolia* determined a relatively low content of total phenolic compounds (840–9163 mg/100 g d.m.), which depended on the period of seed harvesting during the year and over two years, indicating a variation in acorn composition depending on maturity and suggesting a continuous maturation of acorns, both on the tree and after harvesting. The two most common phenolic acids in acorns are gallic acid and ellagic acid [10]. In a study by Rakić et al. [69], gallic acid accounted for up to 0.27% of the dry extract of acorns (previously heat-treated). Molina-García et al. [68] identified 28 different compounds in the phenolic profile of acorns of the species *Q. coccifera*, 14 of which were classified as gallic acid derivatives, including methyl gallate, galloyl derivatives, galloylmethyl gallate, and tetragalloyl–hexoside.

The contents of ellagic and gallic acids in acorns are directly related to the content of tannins, from which they are released by processes including, but not limited to, the action of temperature, enzymes, acids, and alkalis [70]. Tannins are polymerized derivatives of polyphenols with high chemical reactivity and biological activity [70,71]. Tannins cause a bitter taste in the product and show the ability to complex with proteins, polysaccharides, and metal ions, which makes them considered anti-nutrients [2,70]. In acorns, the predominant group is hydrolyzing tannins, especially ellagitannins and gallotannins. In a study by Rakić et al. [64], the content of total tannins in the acorns of *Q. robur* was 20,400 mg/100 g d.m. Tejerina et al. [48] reported the content of hydrolyzing tannins in acorns of the species *Q. rotundifolia* at 950–1150 mg/100 g d.m. (and condensed tannins at 50–140 mg/100 g d.m.), of which gallotannins accounted for up to 860 mg/100 g d.m. and ellagitannins up to 290 mg/100 g d.m. Burlacu et al. [10], among the compounds that make up the profile of ellagitannins in acorns, mention vescalagin, castalagin, and roburins.

Due to interest in acorns as a raw material for extracting oil for food, cosmetic, and pharmaceutical purposes, ongoing research on acorn oil includes the fatty acid composition and the content of tocopherols and sterols [12,72,73]. The predominant homolog of tocopherol in acorns is γ-tocopherol (Table 3), whose content is up to 42.30 mg/100 g d.m. in acorns of the species *Q. robur*. The exception is the species *Q. rubra*, in which the highest content, amounting to 13.26–22.37 mg/100 g d.m., was determined for β-tocopherol [74]. A study by Al-Rousan et al. [72] confirms the predominant content of γ-tocopherol in acorn oil. Taib et al. [13] point to acorn oil as an excellent source of tocopherols, in which the content of these bioactive components, depending on the *Quercus* species, can range from 1440 to 1783 mg/kg of oil. These values are higher than those of well-known oils, such as olive oil (240 mg/kg), sunflower oil (737 mg/kg), or peanut oil (540 mg/kg). It is worth noting that the high content of tocopherols in acorn oil protects against the oxidative changes that occur during storage [75].

In addition to tocopherols, sterols are acorns' second most important unsaponifiable substance [76]. As reported by Al-Rousan et al. [72], the sterol content of acorn oil can be up to 8563 mg/kg of oil. Lassoued et al. [49] identified seven different sterols in the acorns of *Q. coccifera* and *Q. ilex* species, among which β-sitosterol was the dominant one (Table 3). Al-Rousan et al. [72], evaluating the acorn oil of the species *Q. aegilops*, *Q. infectoria*, and *Q. calliprinos*, identified 10 different sterols, among which β-sitosterol was also dominant, followed by Δ5-avenasterol, campesterol, and stigmasterol.

Table 3. The content of lipophilic bioactive compounds in acorns of different *Quercus* species.

Quercus Species	Chemical Group	Predominant Compound	Content of Predominant Compound [mg/100 g d.m.]	References
Q. coccifera	tocopherols sterols *	γ-tocopherol β-sitosterol	4.51 93.77	[7,49]
Q. faginea	tocopherols carotenoids chlorophylls	γ-tocopherol β-carotene lycopene chlorophyll a	4.03 131.2 18.3 400	[7,14]
Q. ilex	tocopherols carotenoids chlorophylls sterols	γ-tocopherol β-carotene lycopene chlorophyll a β-sitosterol	5.22 47.3 14.8 200 91.31 *	[7,14]
Q. pyreneica	tocopherols	γ-tocopherol	3.63	[7]
Q. robur	tocopherols	γ-tocopherol	18.86–42.30	[74]
Q. rotundifolia	tocopherols	γ-tocopherol	5.75–10.79	[48]
Q. rubra	tocopherols	β-tocopherol	13.26–22.37	[74]
Q. suber	tocopherols carotenoids chlorophylls	γ-tocopherol β-carotene lycopene chlorophyll a	3.80 130.1 7.9 300	[7,14]

* percentage [%], d.m.—dry matter.

5. Controversial Role of Acorn Tannins

Phytochemical characteristics of acorns, regardless of species, indicate a relatively high content of tannins (Table 2). Tannins are phenolic compounds with a high molecular weight of 500 to 3000 Da, which are secondary metabolites of plants. Tannins are found in various parts of plants: seeds, fruits, leaves, roots, and bark, and have a protective function, providing protection against herbivores, birds, and insects [77–79]. Based on their structure and chemical properties, tannins are divided into condensed (proanthocyanidins) and hydrolyzed, and in this group, in turn, ellagitannins and gallotannins are distinguished [78,80]. These compounds are often attributed to antioxidant activity [77,81]. However, depending on the chemical structure and physicochemical factors (pH, redox potential, concentration of oxidants and antioxidants, and the action of the enzymes peroxidase and catalase), they may also exhibit pro-oxidant activity [82].

Tannins remain a controversial group of bioactive constituents in plants due to the anti-nutritional properties and adverse health effects that may be observed with increased consumption of tannins on the one hand [79,80] and the increasingly documented preventive and therapeutic effects on human health on the other [77,81,83,84]. Due to their complexation, the primary anti-nutritional effect attributed to tannins is to reduce the digestibility and bioavailability of ingredients in food. Tannins form complexes with both basic nutrients (carbohydrates and proteins) and minerals, such as phosphorus, calcium, magnesium, and iron. The nutritional value of food is also reduced by the complexation of digestive enzymes involved in the digestion of proteins, carbohydrates, and pectin with tannins [80]. Furthermore, Awad et al. [85] report that tannins may themselves undergo enzymatic oxidation, which also increases their toxicity. In addition to the negative aspects associated with the consumption of tannins and their effects on the human body, new reports highlight the health-promoting properties of tannin-breakdown products. For example, ellagitannins, one of the groups of tannins present in acorns, undergo hydrolysis in the human small intestine, and the products of their hydrolysis, primarily ellagic acid, exhibit antioxidant, anti-inflammatory, and neuroprotective effects [83]. In addition, ellagic acid is used by human intestinal microflora as a substrate to produce urolithins, which have been identified as agents in the fight against colon cancer [86–89]. While previous studies have focused on ellagitannins from pomegranates, strawberries, and nuts [86], acorn products may be a new source of these compounds in the diet.

6. Historical and Potential Modern Uses of Acorns in Food

Regardless of the region of occurrence and species of oak, acorns have been one of the more common components of the diet, with historical reports of their consumption relating to such regions and countries as the Mediterranean Basin [3,69,90], Asia Minor and the Middle East, Central America, East and North America [91], and Poland [92] and dating back to the Stone Age (Neolithic) and Bronze Age [2]. Studies on the consumption of acorns in the past, from prehistoric times to the 19th and 20th centuries, point to relatively simple forms of their preparation, depending on the cultural conditions and regional traditions [4,30].

Archaeological studies show the use of acorns in dishes, as stews, and in preparing meals resembling modern-cooked porridge. The role of acorn infusions as coffee substitutes is also mentioned [4,91,93]. From prehistoric times to modern times, one also finds uses for acorns as a raw material in baking bread. Throughout history, the forms of its baking have changed: historical reports indicate the preparation of bread in the form of flat cakes and scones, whose dough was prepared without the addition of yeast, and whose "baking" was carried out in a pan rather than in ovens. Acorn flour was used alone or in combination with cereal flour or flours made from legume seeds [4]. In Sardinia, acorn bread, known locally as "Pan'Ispeli", was prepared from acorn flour mixed with clay and ash, and its preparation involved a ceremony to which religious significance was ascribed [3]. Pignone and Laghetti [93] also point to a tradition of acorn bread baking in Sardinia called "pane di ghiande", the preparation of which was very complex and began with the harvesting of acorns in autumn, drying and roasting, a special method of removing the pericarp by striking acorns enclosed in a pouch made from goatskin, and then involved preparing the seeds by boiling them in water mixed with red clay. The bread was baked from a dough made from overcooked acorns, resembling oatmeal, in the form of pancakes, which were eaten immediately after baking or dried for further storage.

In Asian countries, acorn starch has been used in culinary traditions until modern times and is used to prepare a dish called "dotorimuk", translated as acorn jelly or acorn tofu. Powdered acorns combined with water are also used to make acorn noodles ("dotori guksu"), which resemble soba noodles [94]. Today, acorns have lost their importance as a stand-alone food product or even an ingredient and are most often associated with animal feed [6]. With the increasing importance of healthy lifestyle trends linked to changing diets and the resulting consumption of raw materials and products of organic, natural origin with functional properties, there is also a strengthening of the role of acorns as an alternative and competitive food raw material [18].

In the past, the use of acorns has been associated primarily with their high starch content, and thus the use of acorns as a high-energy ingredient and a substitute for traditionally used high-starch raw materials [2], contemporary applications involve not only the use of acorns as a base or enriching recipe ingredient but also include the potential for use as technological additives, e.g., due to the stabilizing properties of acorn starch (Table 4). The use of acorns as a raw material in the production of oils and coffee or the processing of flour and starch are just some examples of the directions of acorn use that are currently being addressed both by scientists in their research and by food producers in preparing market offerings [3,7,12,43,72,95,96].

Table 4. Studies on acorns of various *Quercus* species in food production.

Quercus Species	Acorn Form/Amount in Product	Food Product Type	Specified Nutritional Advantage	References
Q. aegilops	acorn flour/5–15% substitution of wheat flour	Arabic bread	fiber content increase	[97]
	acorn oil	edible oil	domination of oleic acid, high content of tocopherols (with γ-tocopherol domination), sterols (predominantly β-sitosterol), and phenols	[72]
Q. brantii	acorn flour/5–30% substitution of wheat flour	sponge-fat cake	n.a.	[98]
	acorn flour/15–45% substitution of wheat flour	wheat biscuits	peroxide value decrease; antioxidant activity increase	[99]
	acorn flour/15–45% substitution of corn flour	gluten-free biscuits	peroxide value decrease; antioxidant activity increase	[99]
	acorn flour/25–50% substitution of wheat flour	white yeast bread	satiety index increase; feeling of satiety increase	[100]
Q. calliprinos	acorn oil	edible oil	domination of oleic acid, high content of tocopherols (predominantly γ-tocopherol), sterols (predominantly β-sitosterol), and phenols	[72]
Q. coccifera	acorn oil	edible oil	high content of tocopherols (predominantly β + γ-tocopherols) and phenols (predominantly hydrolyzable tannins); high antioxidant activity	[12]
	acorn flour/30–60% substitution of wheat flour	biscuits	total phenolic content increase	[101]
	grounded acorn kernels	coffee substitute	relatively high content of minerals (K, Mg, P, Fe, Cu, and Zn)	[102]
Q. ilex	acorn flour/10% substitution of wheat flour	biscuits	ash content increase; starch content decrease	[103]
	acorn cotyledons	coffee substitute	high phenol content (predominantly ellagic acid) and antioxidant activity	[104]
	acorn oil	edible oil	high content of tocopherols (predominantly β + γ-tocopherols) and phenols (predominantly hydrolyzable tannins); high antioxidant activity	[12]
	acorn flour/50–75% substitution of barley flour	gluten-free bread	total and insoluble fiber content increase	[105]
	acorn flour/30–60% substitution of wheat flour	biscuits	total phenolic content increase	[101]
	acorn kernels as raw material	HPP beverage	low thrombogenicity and atherogenicity indices; high content of phenols (predominantly gallic acid)	[106]
	acorn kernels as raw material	flour	high fiber and lipids (predominantly unsaturated fatty acids, especially oleic acid) content	[90]
	acorn starch	food additives	n.a.	[107]

Table 4. *Cont.*

Quercus Species	Acorn Form/Amount in Product	Food Product Type	Specified Nutritional Advantage	References
Q. infectoria	acorn oil	edible oil	domination of oleic acid, high content of tocopherols (predominantly γ-tocopherol), sterols (predominantly β-sitosterol), and phenols	[72]
Q. persica	acorn flour/10% substitution of wheat flour	bread	antioxidant activity increase; inhibition of surface moldiness	[108]
Q. rotundifolia	acorn flour/10–15% substitution of wheat flour	bread	n.a.	[109]
	acorn kernels as raw material	flour	high fiber and lipids (predominantly unsaturated fatty acids, especially oleic acid) content	[90]
Q. rubra	acorn oil	edible oil	domination of unsaturated fatty acids, especially oleic acid	[110]
Q. suber L.	acorn cotyledons	coffee substitute	high phenols content (predominantly ellagic acid) and antioxidant activity	[104]
	acorn oil	edible oil	high content of tocopherols (predominantly $\beta + \gamma$-tocopherols) and phenols (predominantly hydrolyzable tannins); high antioxidant activity	[12]
	acorn flour/30–60% substitution of wheat flour	biscuits	total phenolic content increase	[101]

n.a.—not assessed, HPP beverage—high-pressure processing beverage.

The most popular direction remains the use of acorns in formulating bakery and confectionery products as an enriching ingredient, which has been introduced into contemporary baked goods. Ongoing research seeks to obtain bread, cakes, and pastries in which acorn flour will be a source of bioactive compounds and thus have a positive effect on nutritional value, while at the same time, the characteristics of the finished products will be similar to those made from conventional raw materials [96,111].

Historical reports and contemporary work on the use of acorns in food production indicate differences not only in the directions themselves for the use of acorns but also in their proper preparation and pre-treatment, primarily to reduce their tannin content. Bainbridge [91] reports that Indians, indigenous peoples of North America, carried out the de-acornization of acorns by mixing them with iron-rich red earth or wood ash. Pinna [3] states that in Sardinia, acorn bread was prepared from acorn flour mixed with clay and ash, which may also indicate the use of these ingredients in the de-gorging of acorn raw materials. Pignone and Laghetii [93] presented a procedure for baking acorn bread, in which acorns were previously subjected to roasting and leached in water with the addition of red clay. Zocchi et al. [4] have prepared a compilation of traditional methods of processing and using acorns in the Mediterranean and the Middle East. Regardless of the region, acorns were subjected to the debittering process, and the steps used and their complexity probably depended on the variety of oak from which the acorns were extracted and the associated concentration of tannins in the raw material. Debittering usually involves roasting (Calabria in Italy), boiling (Iraq, Afghanistan, Algeria, and Syria), or soaking the acorn nuts in cold water (Iran), followed by drying the seeds.

Acorn debittering, carried out today, is based on similar methods and processes used in the past, namely leaching tannins in water, drying, or roasting [112–114]. Greater attention, however, is being paid to the effectiveness of the treatments carried out and the possibility of their modification for increased effectiveness.

7. Historical and Potential Modern Uses of Acorns in Medicine

Acorns have been used for generations in traditional folk healing methods as a tool to combat, among other things, indigestion, diarrhea, or inflammation [1,30,73]. The possibility of using acorns in the treatment of diseases has been known to man since historical times in various cultures around the world. García-Gómez et al. [95] report on using acorn raw materials and products in the Iberian Peninsula and indicate using acorn drinks (made by boiling crushed, chopped acorns with water) to treat diarrhea. A similar use is presented by Pinto [115] for the acorn coffee substitute, indicating its astringent and antidiarrheal effects. The use of acorns in folk medicine in the Mediterranean region was also described by Vinha et al. [6], indicating their role in treating burns and injuries. The possibility of using acorns has also been known among ethnic groups in California. The people of the Chumash ethnic group used acorn porridge to treat gastrointestinal ailments, which was prepared from the acorns of various species, including *Quercus agrifolia*, *Quercus douglasii*, and *Quercus lobata* [116]. In Turkey, folk medicine indicated a much wider scope of use of the phytochemical potential of acorns, which were administered to people suffering from hemorrhages, chronic diarrhea, bacterial infections (e.g., dysentery), or respiratory problems (including bronchitis, asthma, and chronic cough). One of the ways to serve acorns was to process them into a product called "Gezo", resembling molasses syrup. This syrup was also used preventively to strengthen the immune system [117,118].

Nowadays, research is underway indicating the possibility of using acorns, extracts, and products made from them in the prevention and treatment of, among others, diseases of the circulatory system, nervous system, diabetes, and skin inflammation as an anti-inflammatory, antihypertensive, or antioxidant agent [13,55,119]. Table 5 presents source data relating to the use of the potential of bioactive ingredients found in acorns based on in vitro and in vivo studies. The results obtained by the authors indicate, among others, the possibility of using acorn extracts to inhibit selected enzymes (e.g., liver enzymes, enzymes stimulating the decomposition of neurotransmitters, or enzymes regulating the sugar–insulin metabolism) [120–123], heal skin wounds [124] or prevent inflammation (e.g., in gum diseases) [125]. The health-promoting properties of acorns are due to the presence of phytonutrients in them, among which the most important are phenolic compounds, triterpenes, sterols, tocopherols, and carotenoids [10,13].

Table 5. Studies on the biological activity of acorns of various *Quercus* species.

Quercus Species	Acorn Form	Application Form	Specified Biological Activity	References
Q. acutissima	extract from the acorn kernels with 80% ethanol	in vitro experiment and study on mice—orally administered at a dose of 100 or 200 mg/kg body weight/day	anti-inflammatory activity—inhibition of tumor necrosis factor-a and T-helper 2 (Th2) type cytokines (IL-4 and IL-13)—anti-asthma potential	[126]
Q. brantii	extract from the seed hull with 70% ethanol	mucoadhesive gel for the treatment of periodontitis	antioxidant and antibacterial activity of polyphenols	[125]
	water extract from acorns	intraperitoneally administered at a single dose of 50 mg/kg—study on rats	inhibition of hepatic enzymes (ALT, AST, ALP, and LDH)—prevents liver damage	[121]
	hydroalcoholic extract from acorn internal fruit	in vitro experiment	inhibition of HEWL amyloid formation	[127]
	acorn flour	acorn muffins—oral administration in diet (10 g of acorn flour per day)	reduction of glycated hemoglobin (HbA1c)—anti-diabetic activity of polyphenols	[128]

Table 5. *Cont.*

Quercus Species	Acorn Form	Application Form	Specified Biological Activity	References
Q. brantii	extract from the acorns' inner stratum with 80% ethanol	O/W vaginal cream	antibacterial activity of acorn tannins	[129]
Q. castaneifolia	alcoholic and water extracts from acorns	in vitro experiment	anti-microbial effect of alcoholic extract on *Escherichia coli*, *Salmonella thyphimurium*, *Shigella dysentriae*, and *Yersinia enterocolitic*	[130]
Q. coccifera	extract from the acorn kernels with 70% ethanol	in vitro experiment	inhibition of AChE and BChE—neuroprotective potential	[131]
	extract from the acorn kernels and acorn coffee substitute with 80% ethanol	in vitro experiment	inhibition of AChE and BChE—neuroprotective potential	[123]
Q. faginea	extract from acorn whole fruit, kernel, and pericarp with ethanol-water (1:1, *v*/*v*)	in vitro experiment	antioxidant and antibacterial activity of polyphenols, carotenoids, chlorophylls, and tocopherols	[14]
Q. ilex	extract from the acorn kernels with ethanol	in vitro experiment	inhibition of xanthine oxidase, high anti-proliferative activity on glioblastoma—antioxidant activity of polyphenols, anti-cancer potential cells	[132]
	extract from acorn whole fruit, kernel, and pericarp with ethanol-water (1:1, *v*/*v*)	in vitro experiment	antioxidant and antibacterial activity of polyphenols, carotenoids, chlorophylls, and tocopherols	[14]
Q. infectoria subsp. *boissieri*	extract from acorns with methanol	10% cream with glycerin—study on rats	increase in collagen synthesis and fibroblast and myofibroblast activation	[124]
Q. liaotungensis	extract from dried acorn kernels with 75% ethanol and microporous resins	in vitro experiment	antioxidant and anti-fibrotic activity of galloyl triterpenes	[133]
Q. nigra	extract from acorn whole fruit, kernel, and pericarp with ethanol-water (1:1, *v*/*v*)	in vitro experiment	antioxidant and antibacterial activity of polyphenols, carotenoids, chlorophylls, and tocopherols	[14]
Q. robur	extract from powdered acorn kernels with potassium phosphate buffer solution 10 mM	in vitro experiment	inhibition of α-glucosidase—anti-diabetic potential	[122]
Q. serrata	extract from acorns with 95% ethanol	in vitro experiment	inhibition of NO production by triterpenoids—antineuroinflammatory potential	[134]
Q. serrata var. *brevipetiolata*	Q43 terpenoid isolated from ethanol (70%) acorn extract	in vitro experiment	inhibition of NO synthase and pro-inflammatory cytokines—antineuroinflammatory potential	[135]

Table 5. *Cont.*

Quercus Species	Acorn Form	Application Form	Specified Biological Activity	References
Q. suber	extract from the acorns and leaves with hexane, methanol, and water	in vitro experiment	inhibition of AChE and BChE—neuroprotective potential	[120]
	extract from acorn whole fruit, kernel, and pericarp with ethanol-water (1:1, *v*/*v*)	in vitro experiment	antioxidant and antibacterial activity of polyphenols, carotenoids, chlorophylls, and tocopherols	[14]
Q. variabilis	extract from defatted acorn kernels with 70% ethanol (free polyphenols) and sodium hydroxide hydrolysis (bound polyphenols)	in vitro experiment	inhibition of α-amylase, α-glucosidase, and dipeptidyl peptidase IV—polyphenol activity	[136]

ALT—alanine aminotransferase, AST—aspartate aminotransferase, ALP—alkaline phosphatase, LDH—lactate dehydrogenase, HEWL—hen egg white lysozyme, O/W—oil-in-water emulsion, NO—nitric oxide, AChE—acetylcholinesterase, BChE—butyrylcholinesterase.

The high content of phenolic compounds is important for the health-promoting nature of acorns and products obtained from them. Şenol et al. [123] and Gezici and Sekeroglu [131] indicated the relationship between the content of phenolic compounds in acorn extract and the inhibition of enzymes catalyzing the neurotransmitter degradation reaction: acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). Custódio et al. [137] indicate a particularly high ability of gallic acid for this type of inhibition. The results presented by the authors prove that acorns and products obtained from them can be supportive factors in maintaining the chemical stability of the brain through neuroprotective effects [123].

Wu et al. [136], in research with *Q. variabilis* acorn extract, confirmed the ability of polyphenols to inhibit α-amylase, α-glucosidase, and dipeptidyl peptidase IV enzymes. The authors found a higher ability to inhibit α-glucosidase and dipeptidyl peptidase IV for free phenolic compounds, while bound phenolic compounds exhibited a higher ability to inhibit α-amylase. Among individual compounds, authors highlighted the effects of quercetin, azelaic acid, ellagic acid, and gallic acid. Inhibition of diabetes-related enzymes was also confirmed by Nogueira et al. [122], who obtained positive results of α-glucosidase inhibition via an acorn (*Q. robur*) buffer extract. Promising results related to the influence of acorn phenolic compounds on glycemic control were also obtained by Sasani et al. [128], who conducted research based on the consumption of acorn muffins with acorn flour.

The antioxidant role of phenolic compounds found in acorns can also be used to heal skin wounds. Free radicals and oxidants impair the healing process, leading to changes in the adhesion and distribution of fibroblasts and structural changes in collagen. Phenolic compounds derived from acorns neutralize reactive oxidants, contributing to reducing the wound area, which was confirmed in the research of Uyar et al. [124].

Phenolic compounds in acorns, especially tannins, also have antibacterial activity, which was confirmed in the research of Zare et al. [129], which demonstrated greater effectiveness of a cream used in the treatment of bacterial vaginosis enriched with *Q. brantii* acorn extract (metronidazole + *Q. brantii*) compared to the control group (metronidazole + placebo). The antibacterial effect of acorn extract was also confirmed in the research of Bahador and Baserisalehi [130].

Acorns and their products also contain other antioxidant compounds, including tocopherols, carotenoids, and chlorophylls [14]. γ-tocopherol is the dominant tocopherol form in the tocopherol profile in acorns [7,48,60]. Available research [138,139] indicates that it is a homolog of tocopherol with the highest antioxidant capacity, exhibiting, among others, the ability to trap reactive nitrogen forms and perform a protective function for mitochondria. The carotenoids most noteworthy are β-carotene and lycopene [14]. The antioxidant activity of these substances refers primarily to their ability to trap superoxide and hydroxyl radicals and reactive nitrogen forms [6,140]. These compounds also have protective functions for the cardiovascular system, directly influencing heart rate variability [141].

Biological activity is also demonstrated by triterpenes and terpenoids present in acorns and products made from them, previously unidentified in other raw materials [133–135]. In research conducted by Xu et al. [133], new triterpenes showed antioxidant, anti-proliferative, and anti-fibrotic activity towards hepatic stellate cells, and their activity increased as a result of synthesis with gallic acid (galloyl triterpenes). Huang et al. [135] conducted research on the possibility of using the terpenoid Q43, isolated from the acorns of *Quercus serrata* var. *brevipetiolata*, in the prevention of inflammation of nervous tissues. The mechanism of action included inhibition of the nitric oxide synthase and cyclooxygenase-2 enzymes and limitation of the secretion of pro-inflammatory cytokines.

Available studies regarding the content of bioactive components in acorns and their biological activity indicate that these compounds positively affect human health, which may suggest the usefulness of acorns in the development of pharmaceuticals. It should be noted that it is necessary to conduct comprehensive studies that will evaluate the profile and content of bioactive compounds in acorns and clarify the mechanisms of their effects on the body [10,13].

8. Other Possibilities for Using Acorns

The available literature data, along with the nutritional role of acorns, and their potential for use in the food industry also show their non-food use. Numerous studies treat acorns for feed purposes, which can favorably affect animal health and the sensory characteristics of the meat obtained from them [48,142–144]. Abdel-Tawwab et al. [142] conducted research on the use of acorn (*Q. aegilops*) powder in the breeding of common carp. Feeding fish with enriched feed improved aquaculture and welfare, including hemato-biochemical parameters such as increased white and red blood cell count, hemoglobin and hematocrit values, and decreased total cholesterol and triglycerides. In the study of Mekki et al. [143], acorn concentrates (*Q. ilex*) were used in lamb feeding, resulting in the meat's sensory characteristics: tenderness, juiciness, and general acceptance. Differences in the sensory characteristics of meat from slaughter animals, such as barrows, were also noted by Pugliese et al. [144], who found the effect of feeding with acorn fruits (*Q. cerris* and *Q. pubescens*) on the profile of volatile compounds in Cinta Senese dry-cured ham. The possibilities of using acorns in animal feeding were also indicated by Belkova et al. [145], Sznydler-Nędza et al. [146], Stiti et al. [147], and Tejerina et al. [48].

In addition to being used for feed purposes, acorns are also used in the cosmetics and pharmaceutical industries as a source of bioactive substances. According to Huang et al. [148], acorns can be a raw material for obtaining ellagic acid extract. Mota et al. [149] characterized the acorns of *Q. suber* as a raw material for sourcing phenolic compounds. Such use was also indicated by Kyriakidou et al. [150]. Górnaś [74] indicated the possibility of obtaining γ- and β-tocopherol from acorns (*Q. robur* and *Q. rubra*).

Another direction in using acorns was presented by Karabas [151–153], who researched the possibility of using acorns (*Q. frainetto*) in biofuel production. Nourmoradi et al. [154] also pointed to the possibility of using acorns (*Q. brantii*) in the production of biosorbents [148].

9. Conclusions

Acorns are an easily accessible and cheap raw material known in many regions and cultures that can be used in the food industry, pharmacology, and medicine. Available data show that acorns are rich in bioactive compounds and can be a good health-promoting addition to food products. Moreover, such compounds as antioxidants (i.e., polyphenols, tocopherols, and carotenoids) and triterpenoids, present in acorn extracts, may constitute therapeutic factors due to their biological functions: anti-inflammatory, anti-microbial, anti-cancer, anti-diabetic, and neuro- and gastroprotective. However, the main findings from the recent literature are that the individual species are highly varied in terms of acorn morphological structure and chemical composition. Therefore, conducting further research on the characterization and isolation of bioactive compounds can be extremely important in developing new functional food products, supplements, or drugs. This is mostly related to pharmacological studies, which have been conducted mainly as in vitro experiments, while clinical trials are limited.

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