Current Studies on Lupinus Species Growing in Türkiye

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Introduction

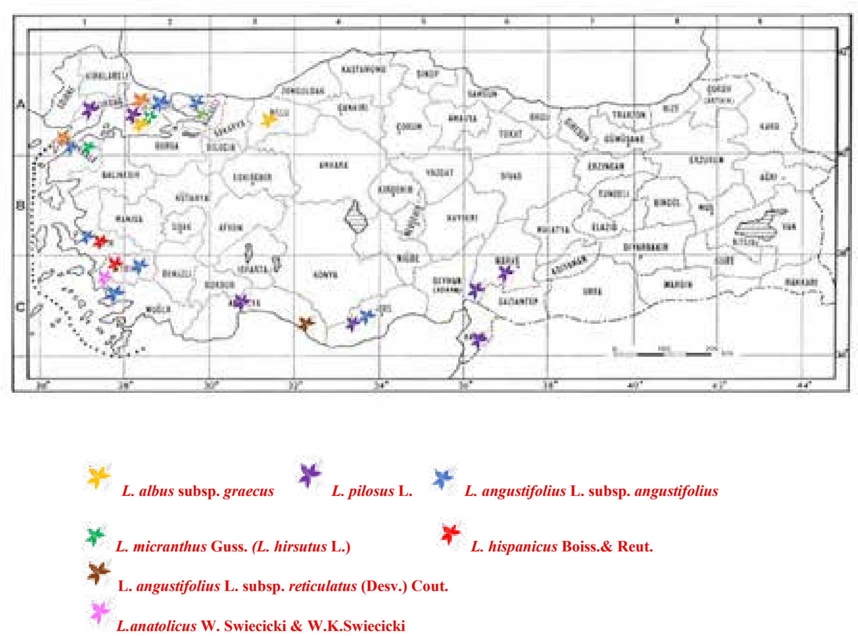
Lupinus L. species (lupin or lupine, Fabaceae family) are wild or cultivated in the Mediterranean, South Aegean and Marmara regions of Turkey and it has been reported in the literature that it is an annual herbaceous plant with thick, hard and bitter seeds (Akbar, 2020; Davis, 1984; Davis et al., 2008; Gross et al., 1976; Güner & Aslan, 2012). The general characteristics of the *Lupinus* genus can be given as follows: annual, hirsute herbaceous; leaves digitate; stipules adnate to the base of the petiole, setaceous; inflorescence racemose, the flowers alternate or verticillate; calyx bilabiate, 4-5-toothed, bracteoles usually persistent, attached to base of calyx; corolla with an obtuse keel; stamens monadelphous; legume a terete, 2-6-seeded, usually hirsute hairy, usually in non calceous soils (Davis, 1984; Davis et al., 2008; Drummond et al., 2012; Mirza et al., 2023).

The *Lupinus* L. plant has nearly 300 species in various countries, besides six species growing in Turkey. Gene banks have been established in different European and Australian countries (https://www.igr.poznan.pl/uploads/resources/Linki%20WS/Lupinus_Collections_Database.pdf; https://www.planthealthaustralia.com.au/wp-content/uploads/2024/01/10-124.pdf) (Swiecicki et al., 2000)

Nine taxa are *Lupinus albus (*white lupine, termiye*)*, *L. albus* subsp. *albus* (Egyptian lupine, Syn: *L. termis* ,termiye), *L. albus* subsp. *graecus* (Syn: *L. graceus*, tavşan baklası), *Lupinus angustifolius* (blue lupine, acı bakla*)*, *L. angustifolius* subsp. *angustifolius* (Syn: *L. leucospermus*, acıbakla) *Lupinus micranthus* (Syn: *L. hirsutus*, pilous lupine, domuz baklası), *Lupinus hispanicus* (Syn: *L.rothmaleri*, delice bakla), *L. pilosus* (Syn: *Lupinus varius*, gavur baklası) and the endemic *Lupinus anatolicus* (mısır baklası) growing in coastal cities in Turkey (Bedevian, 1936; Davis, 1984; Davis et al., 2008; Drummond et al., 2012; Güner & Aslan, 2012). (Figure 1).

Figure 1

Distribution of Lupinus species in Turkey



Among the *Lupinus* species cultivated for medicinal purposes, "Termiye", popularly known as the seed of lupine, has been reported to have strengthening and antihelminthic effects on urinary tract diseases, removal of kidney stones and sand, and also to relieve rheumatism, nerve pain, and headache when boiled in water and consumed. It is known that termiye is consumed as a coffee in diabetic patients in the Konya region (Baytop, 1997, 2021; Tuzlacı, 2011). It is frequently used in floury foods and meat products, as well as in the composition of gluten-free biscuits and bakery products (Leonard et al., 2019; Maghaydah et al., 2013) https://www.fao.org/4/y5019e/y5019e07.htm. Additionally, products containing lupin seeds are sold in cosmetic stores and are also manufactured in various laboratories. (Lupaline®, CO2llageneer®, ACTIMP® Bio) (Caramona et al., 2024).

It is known that *Lupinus* L. was used in Dioscorides' "De Materia Medica" and a work of Hippocrates against inflamed areas and birthmarks or for cosmetic purposes, respectively

(Kurlovich, 2002; Osbaldeston & Wood, 2000). In the Unani system, *Lupinus* species were used for wound healing and anthelmintic purposes. Several scientific studies, both *in vivo and in vitro*, support this finding (Akbar, 2020; Dubois et al., 2019; Prusinski, 2017). Numerous studies on the use of lupin seeds in animal and human diets have shown that they can compete with soybean seeds. Lupine seeds contain about 50% protein, up to 13% fat, and numerous bioactive compounds (Król et al., 2018; Wäsche et al., 2001).

In many countries, including Türkiye, especially in Asia and Europe, the nutritional value (niacin, riboflavin, thiamine) in the production of fermented products (pastry, crisps, bread, and emulsified meat, etc.) is very high in the Lupinus seeds (Erbaş et al., 2005). The antimicrobial effect of dichloromethane extracts of some *Lupinus* species against *Pseudomonas aeruginosa, Klebsiella pneumoniae, B. subtilis,* and *S. aureus* strains was determined (Erdemoglu et al., 2007; Romeo et al., 2018).

There are studies on seed pods of some *L. angustifolius* and *L. albus* cultures, and various extracts prepared from them induced apoptosis in MIA PaCa-2 (human pancreatic carcinoma) (Ishaq et al., 2022). In addition, *L. albus* seeds are known to have hypolipidemic, antiepileptic, and antihelminthic (Vollmannova et al., 2021), antihypertensive (HunieTesfa et al., 2025), and antidiabetic (Aydın et al.,2021), anti-inflammatory (Pereira et al., 2022)**,** and antifungal (Caramona et al., 2024) effects.

Some *Lupinus* wild or cultivated species (*L. albus* and *L. angustifolius*) have been reported to show antioxidant activity (Karamać et al., 2018; Król et al., 2018; Siger et al., 2012)Cammilleri et al.,2024). The species of this plant contains many different primary and secondary metabolites. It is known that its seeds contain a significant amount of phenolic compounds (phenolic acids, flavonoids, isoflavonoids), polyphenols, carotenoids, phytosterols, tocopherols, and are rich in fatty acids (oleic and linoleic acids, etc.) (Ishaq et al., 2022; Yorgancılar et al., 2018)(Özyazıcı.,2022). The above-ground parts of some species (*L. albus, L. angustifolius*) of various genotypes contain alkaloids, including 13-tigloyloxylupanine, lupanine (Chludil et al., 2009). *Lupinus* species have hepatotoxic and teratogenic effects due to quinolizidine alkaloids **(**angustifoline, sparteine(lupinidine), lupinine**)** and piperidine alkaloids (anagyrine, ammodendrine) (Patočka and Ho,2008).

In this chapter, botanical characteristics, traditional uses, chemical composition, bioactivity, and clinical studies of wild or ecotype/genotype *Lupinus* species growing in Turkey, as well as their herbal drugs and side effects, are reported. Also, scientific studies conducted in other countries on these species growing in Türkiye are reviewed.

Ethnic uses of *Lupinus* species in Türkiye

While *L. varius* is used as an ornamental plant, *L. albus* is used as a tonic, cardioactive, and diuretic, as well as in various skin diseases. Its seeds are used as anthelmintics and antidiabetics in the Marmara and Aegean Regions of Turkey, besides in Europe and the Balkans due to their high protein, polysaccharides, and low starch content. *L. luteus* (yellow lupin) is used in the Mediterranean region as a blood pressure-lowering agent, in cardiovascular diseases, and against colon cancer (Ishaq et al., 2022; Khan et al., 2015).

In Konya City and its surrounding provinces, the seeds of lupine, whose bitterness has been removed, are consumed as snacks and used in animal nutrition. Additionally, the stem is preferred as a fertilizer and fodder. *Lupinus angustifolius* seeds are used for the control of obesity and cholesterol in various countries, particularly in Europe, New Zealand, and Australia (Ishaq et al., 2022). The external use of maceration prepared from its sprouts protects ruminants from lice and fleas (Yaşar et al. 2015). Lupin species naturally contain alkaloids, some of which can be bitter and toxic. For this reason, soaking or boiling the seeds in water to remove the bitterness has often been practiced colloquially in traditional medicine (Baltacıoğlu & Özcan Tarım, 2024). Protein powders preferred by vegans are also frequently used. Links to these are provided below;

Patagonia Proteins – Lupine Protein Powder (Andes Cocoa) (https://patagoniaproteins.com/products/lupine-protein-powder-andes-cocoa-2-2-lb)

Raab Vitalfood

(https://www.naturitas.us/p/supplements/sport/proteins/organic-lupine-protein-powder-500-g-of-powder-raab)

Tarwi – Pure Lupin Protein (300g)

(https://tarwi.co/products/protein)

Mikuna – Chocho Lupin Protein Powder

(https://mikunafoods.com)

Pure Inka Foods – Lupin Protein Powder (55% Protein)

(https://cerebro.faire.com/product/p_hvtkzs6dru)

Trace element ingredients and nutritional value of Turkish native *Lupinus* sp.

In a study conducted in Turkey by Yorgancılar et al. (2018), the mineral and physical properties of white lupin (*Lupinus albus* L.) seeds were determined. The study revealed the following concentrations of minerals: phosphorus (0.14%), potassium (0.4%), calcium (0.04%), magnesium (0.06%), iron (11.9 ppm), manganese (533.4 ppm), and zinc (15.8 ppm) (Yorgancılar et al., 2018).

A comparison of the results with those obtained in studies conducted in different countries suggests that the levels of certain nutrients are lower. For instance, in the extant literature, phosphorus has been reported as ranging from 0.43% to 0.72% in white lupins, potassium as ranging from 0.86% to 1.11%, magnesium as ranging from 0.12% to 0.22%, and manganese as ranging from approximately 896 mg/kg (Pereira et al., 2022; Straková et al., 2006). In the Turkish sample, these values were found to be lower, especially for phosphorus, potassium, and magnesium. In general, white lupins cultivated in Turkey exhibit comparable oil and protein content to international data, yet demonstrate lower mineral values. These differences underscore the impact of genotype, soil structure, climate, and cultivation techniques on nutrient content.

In studies conducted on the nutritional value of four different cultures obtained from *L. agustifolius* seeds found in Poland, total oligosaccharides were determined to be 80-97 g/100g, crude protein (79.4-82.3 g/kg), and amino acids lysine (1.7) and methionine (2.7) were found (Kaczmarek et al., 2014).

The highest protein content was found in the lupin varieties belonging to *L. luteus* (ca. 465 g/kg), followed by *L. albus* (ca. 360 g/kg) and *L. angustifolius* (ca. 330 g/kg) (Sujak et al., 2006). In the literature, it is noted that cookies can be produced successfully with lupin flour (Baltacıoğlu & Özcan Tarım, 2024; Obeidat et al., 2013).

Some primary and secondary metabolites of *Lupinus* species in Türkiye

In addition to the important nutritional compounds mentioned above, some *Lupinus* species also contain anti-nutritional compounds (quinolizidine alkaloids) (Sujak et al., 2006). Important main alkaloids found in the literature related to some *Lupinus* species growing in Türkiye are summarized in Table 1. Also, flavonoids (apigenin and luteolin derivatives) were detected in different *Lupinus* species (Czubinski et al., 2019; Vollmannova et al., 2021).

Table 1

Some Important Alkaloids and Other Metabolites in Lupinus Species in Türkiye

PLANT NAME	LOCATION	USED PARTS	ACTIVE COMPOUNDS
Lupinus albus	East Marmara, West Black Sea (Türkiye)	stem, seed, leaf	Lupanine 13-Hidroksilupanine Albine Multiflorine α- isolupanine]

Lupinus angustifolius	Çatalca-Kocaeli in the Marmara Region, the Egean Region, Antalya and Adana	stem, seed, leaf	Apigenin 4-Hydroxybenzoic acid 4-hydroxycinnamic acid Gallic acid protocatechuic acid, caffeic acid *p*-coumaric acid, genistein
Lupinus hispanicus	Aegean Region	seed leaf stem root	Lupinine Gramine
Lupinus micranthus	Çatalca-Kocaeli in Marmara, East Marmara Region	seed leaf stem root	Albine Lupanine Multiflorine 13-α hydrokxylupanine 13-α- hydroxymultiflorine 13- angeloxymultiflorine

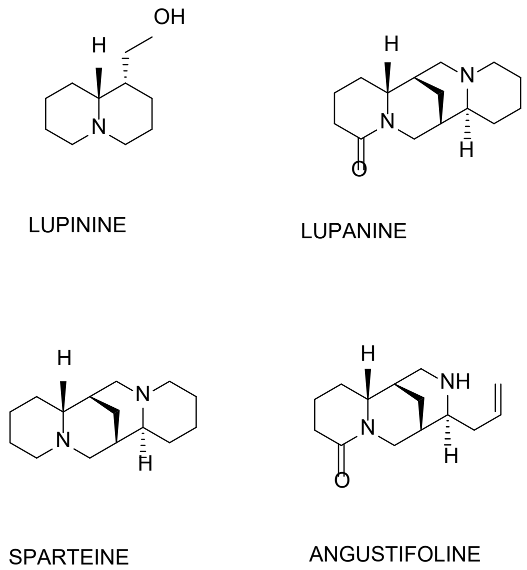
*(References: (El-Adawy et al., 2001; Khan et al., 2015; Maknickienė & Asakavičiūtė, 2008; Martínez-Villaluenga et al., 2009; Pastor-Cavada et al., 2009; Petterson, 2000; Pilegaard, Kirsten; Gry, 2008; Porres et al., 2007; Ruiz-López et al., 2019; Siger et al., 2012; Sujak et al., 2006) Christiansen ve ark. (1997),

It has been reported that the total QA level in Turkish-origin bitter *L. albus* populations is approximately 12–19 g/kg dry matter, with this amount being largely (80–87%) derived from the lupanine alkaloid (Awad-Allah & Elkatry, 2013; Muzquiz et al., 2011; Pilegaard, Kirsten; Gry, 2008). International data indicate that the total QA content in bitter *L. albus* genotypes generally ranges from 4–10 g/kg, reaching up to 11% in some wild accessions, while in sweet lines, it is kept below 200 mg/kg to be suitable for food use ('Outcome of a Public Consultation on the Draft Scientific Opinion on the Risks for Animal and Human Health Related to the Presence of Quinolizidine Alkaloids in Feed and Food, in Particular in Lupins and Lupin-derived Products', 2019; Michael Wink et al., 1995). Wild types may reach levels of up to 2.0%, posing toxicity risks (Kamel et al., 2016). Among the various *Lupinus* species cultivated in Turkey, *L. albus* has received the most extensive study, with research focusing on the total quinolizidine alkaloid (QA) levels present in local 'bitter' genotypes. These levels are consistent with the existing data concerning bitter species on an international scale. Despite the absence of direct quantitative data on *L. angustifolius* and *L. luteus* in Turkey, recent studies have indicated that these species contain QA levels of 13–16 g/kg and 4–13 g/kg, respectively, in bitter genotypes. Conversely, in sweet lines, breeding efforts have successfully reduced these levels to below 0.01% (~100 mg/kg) through selective breeding (Bähr et al., 2014; Cowling & Gladstones, 2000). A study on *Lupinus angustifolius* cultivated in Turkey identified 13a-hydroxylupanine and lupanine as the most significant alkaloids, accounting for around 50.78% and 23.55% of the total alkaloid content, respectively (Erdemoglu et al., 2007). Alkaloid profiles are species-specific; lupanine and 13-hydroxy-lupanine have been identified as predominant in *L. albus* and *L. angustifolius*, while sparteine and lupanine have been found in high concentrations in *L. luteus* (Boschin & Resta, 2013; Frick et al., 2017). Genetic factors and environmental conditions, such as temperature, soil pH, and cultivation practices, influence the variation in alkaloid content of *Lupinus* sp.. Research showed that soil pH significantly affects alkaloid concentration. Higher alkaloid contents are found in environments with a lower pH (Jansen et al., 2012). It is a fact that abiotic stresses, such as drought and elevated temperatures, lead to increased alkaloid synthesis in *Lupinus* species, including specific cultivars such as *Lupinus angustifolius* (Święcicki et al., 2019; Valente et al., 2024). The formula of alkaloids has been given in Figure 2.

In a study, Jansen et al. definitively noted that the alkaloid content decreases significantly at higher pH levels. This clearly suggests that careful management of soil conditions could optimise alkaloid profiles for the desired outcomes (Jansen et al., 2012). For instance, *Lupinus albus* and *Lupinus angustifolius* are categorised as edible varieties with lower toxicity, while many wild types contain alkaloids that are highly relevant to animal and human health (Hassine et al., 2021). For instance, *Lupinus mutabilis* has been identified as a species of particular interest due to its high alkaloid levels, which possess both therapeutic potential and the potential for toxicity if not properly processed (Cortés-Avendaño et al., 2020).

Figure 2

Some Alkaloids in Lupinus Species



Research on bittering methods (soaking, boiling, and ultrasound, etc.) conducted in Türkiye has shown that these processes significantly reduce QA levels in seeds, making them compliant with international standards for food use (Baltacıoğlu & Özcan Tarım, 2024; Chamone et al., 2023; Erbas, 2010)**.** However, it has been reported that QA levels can vary significantly depending on factors such as genotype, growing conditions, plant organ, and analysis method (Bähr et al., 2014; Chamone et al., 2023; Frick et al., 2018; Jansen et al., 2012; Kamel et al., 2016; Muzquiz et al., 2011; Valente et al., 2024). This comparison reveals that the alkaloid levels of *Lupinus* species in Turkey are similar to global variation ranges, but that local genotypes are predominantly of the high-alkaloid 'bitter' form. Consequently, the development of sweet species for food and feed purposes, whilst concomitantly reducing the alkaloid levels of existing bitter genotypes by the effective use of processing methodologies, will constitute a pivotal strategy to increase the agricultural and industrial potential of *Lupinus* in Türkiye. Also, for the extraction of lupin alkaloids (such as Lupanin-type quinolizidine alkaloids), solid-phase extraction methods are utilized, or extraction processes are performed in acidic or basic environments using various apolar or polar solvents (such as methanol-water mixtures**)** (Erdemoglu et al., 2007; Karamać et al., 2018; Muzquiz et al., 2011)**.**

White lupin (Lupinus albus L.) seeds are notable for their high protein content, ranging from approximately 32–48% on a dry weight basis (Dervas et al., 1999; Prusinski, 2017). Approximately 80–90% of lupin proteins consist of the globulin fraction, with the remaining portion comprising albumins and other small protein fractions (Duranti et al., 2008). Among globulins, there are subclasses of α-conglutin (11S), β-conglutin (7S), γ-conglutin (10S), and δ-conglutin (2S), and they are evaluated as functional components in the food industry due to their technological properties (Lam et al., 2018). When evaluated in terms of amino acid profile, white lupin proteins are particularly rich in lysine and also contain high amounts of essential amino acids such as leucine and threonine(Sujak et al., 2006). However, the levels of sulfur-containing amino acids, methionine and cysteine, are relatively low (Prusinski, 2017). These characteristics enhance the potential use of white lupin as both a high-nutritional-value plant protein source and a valuable component in gluten-free food formulations. Nowadays, the extraction of concentrates, isolates, and hydrolysates from lupin seeds is commonly due to their easy digestibility and content of important bioactive peptides. The extraction methods generally used for these protein-based products include alkaline neutral extraction, isoelectric precipitation, ultrafiltration, salt extraction, and ultrasonication and microwave-assisted methods (Lemus-Conejo et al., 2023; Rababah et al., 2023).

If we explain other metabolites and their general methods of obtaining from Lupinus species; the oleic acid content (42.37) was high in *L. albus*, a *Lupinus* species grown in Turkey, while the linoleic acid content (54.06) was higher in *L. pilosus*, both of which were collected from Tunisia, Egypt, and some Mediterranean countries (wild/commercial cultivars) and extracted using a Soxhlet apparatus. The Soxhlet apparatus is also used to remove alkaloids from lupin seed flour. High nutritional value amino acids (lysine, conglutin) and up to 45% protein (glutamic acid, aspartic acid, and arginine) have been identified in some lupins (Akremi et al., 2025; Pereira et al., 2022; Rani & Rani, 2025). On the other hand, the presence of saponins in lupine species has been determined using the ultrasound-assisted extraction method (Bitwell et al., 2023). The volatile oil obtained from flowering shoots of *L. varius* by hydrodistillation was analyzed by GC-MS, and 6,10,14-trimethyl-2-pentadecanone (20.5%) was identified as the main component (Al-Qudah, 2013). In addition, various triterpenes (squalene) and the compounds ursolic acid and lupeol were reported to be present in the oil (Pereira et al., 2022). In a study conducted on the genotypes of *Lupinus albus L.* seeds grown in Konya, Turkey, nearly 100 different compounds were detected in the volatile oils obtained by the HS-SPME (Headspace Solid Phase MicroExtraction) method using four different SPME fibers (Şimşek Sezer et al., 2023).

Biological activities of *Lupinus* species from Turkey

A wide range of therapeutic properties has been reported for *Lupinus* species, particularly in studies investigating their pharmacological effects. These effects include antidiabetic, antioxidant, antimicrobial, anti-inflammatory, and anticancer activities. The therapeutic potential of lupin is largely attributed to its rich composition of bioactive compounds, including flavonoids, alkaloids, polyphenols, and peptides. Numerous studies have elucidated the bioactive constituents and molecular mechanisms responsible for these properties, highlighting the therapeutic relevance of lupin in both pharmaceutical and nutraceutical contexts.

Antioxidant Activity

The antioxidant capacity of *Lupinus* species—especially *Lupinus angustifolius* (commonly known as blue lupin) and *Lupinus* albus (white lupin)—has garnered significant attention due to its potential role in therapeutic applications. These species are distinguished by their bioactive richness, notably peptides and polyphenols, which significantly contribute to their antioxidant effects.Studies have highlighted that protein hydrolysates derived from *L. angustifolius* possess considerable antioxidant properties. The bioactive peptides isolated from these hydrolysates have been shown to improve metabolic markers and protect against oxidative stress by increasing the total antioxidant capacity in animal models of metabolic syndrome (Lemus-Conejo et al., 2020; Santos-Sánchez et al., 2021). These peptides mitigate oxidative damage by reducing inflammatory enzymes and activating endogenous antioxidant mechanisms (Cruz-Chamorro et al., 2021; Santos-Sánchez et al., 2022).

The polyphenolic content of *Lupinus* species also plays a central role in their antioxidant potential. In a comparative study evaluating the antioxidant properties of *Lupinus micranthus*, *L. hispanicus*, *L. angustifolius*, *L.luteus*, and *L. hispanicus* demonstrated the highest antioxidant activity, followed by moderate activity in *L. micranthus* and *L. luteus*. *L. angustifolius* exhibited the lowest antioxidant effect among the species tested (PASTOR-CAVADA et al., 2010). Moreover, lupin seeds have been reported to contain high polyphenol concentrations, showing superior antioxidant capacity compared to other legumes (Karamać et al., 2018). Germination has been shown to enhance the phenolic content and radical-scavenging ability of lupin seeds (Dueñas et al., 2009) by the development of extraction techniques that further optimize the isolation and functionality of these compounds (Tesarowicz et al., 2022).

Extracts from *L. albus* seeds increased plasma glucose levels and decreased oxidative stress markers such as malondialdehyde (MDA) in diabetic rats, particularly at a dose of 10 mg/kg (Yildirim et al., 2020). Ethanolic extracts of *L. albus* demonstrated dose-dependent increases in antioxidant enzymes, including catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and glutathione (GSH). Roasting has also been reported to enhance the antioxidant profile of lupin seeds. Although thermal processing may degrade some bioactive constituents, it promotes the formation of melanoidins—compounds with antioxidant capacity due to their metal-chelation properties—thereby enhancing overall antioxidant potential (Al-Amrousi et al., 2022). Peptides in *Lupinus* species are short amino acid sequences produced through the enzymatic hydrolysis of seed storage proteins from the conglutin families (α, β, γ, δ). These peptides are typically released via *in vitro* gastrointestinal digestion or enzymatic treatment using pepsin, trypsin, alcalase, or pancreatin. *In vitro* studies have demonstrated that lupin-derived peptides exert antioxidant effects, inhibit metabolic enzymes such as ACE, α-glucosidase, and DPP-IV, and reduce the production of pro-inflammatory cytokines by modulating the NF-κB and MAPK signaling pathways (Cabello-Hurtado et al., 2016). The ecological adaptability and nutritional profile of *Lupinus* species, including their content of essential amino acids, lipids, and dietary fiber, render them promising components in diets aimed at mitigating chronic disease risks through antioxidant support (Thambiraj et al., 2019; Yildirim et al., 2020). Consequently, lupin is increasingly recognized not only as a valuable agricultural crop but also as a functional food relevant to public health interventions.

In summary, *L. angustifolius* and *L. albus* have demonstrated significant antioxidant properties mediated by their bioactive peptides and polyphenols. The diversity of extraction and preparation methods further emphasizes their potential as functional foods for enhancing resistance to oxidative stress and promoting overall health.

No studies have yet been conducted on the antioxidant properties of *Lupinus anatolicus*, a species native to Turkey.

Anti-inflammatory Effects

The genus *Lupinus* has garnered considerable scientific attention due to its potential anti-inflammatory properties. Extracts obtained from germinated seeds of *Lupinus angustifolius* and *Lupinus albus* have demonstrated moderate anti-inflammatory activity in both *in vitro* and *in vivo* models. These effects are primarily attributed to high levels of flavonoids, phenolic acids, and tocopherols, which become more abundant following germination. The extracts inhibit key pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β by downregulating the NF-κB signaling pathway. They also suppress the production of prostaglandins and leukotrienes by inhibiting cyclooxygenase-2 (COX-2) and possibly lipoxygenase (LOX) enzymes. *In vivo* studies have reported that *Lupinus* extracts reduce inflammation by mitigating tissue edema, cellular infiltration, and vascular congestion (Andor et al., 2016). Moreover, protein hydrolysates derived from these seeds exhibited similar anti-inflammatory effects in THP-1-derived macrophages. The hydrolysates significantly reduced the production of TNF-α, IL-1β, and IL-6, while increasing levels of the anti-inflammatory chemokine ligand CCL18 (Khan et al., 2015; Millán-Linares et al., 2014). For instance, hydrolysates obtained through enzymatic treatment with alcalase enzyme showed a 45% reduction in TNF-α, 32% reduction in IL-1β, and 43% reduction in IL-6 compared to controls. A separate group treated with alcalase on hydrolysis demonstrated slightly lower inhibition levels. Importantly, CCL18 expression was nearly doubled in cells treated with both hydrolysates. Cruz-Chamorro et al. (2021) further confirmed that lupin protein hydrolysates (LPHs) exert anti-inflammatory effects by inhibiting inflammation-associated enzymes such as phospholipase A2 and COX-2. The study concluded that LPHs significantly attenuated pro-inflammatory cytokine levels in macrophage cultures, underscoring their therapeutic potential.

A systematic review by Castillo et al. (2023) exhibited the potential of *Lupinus albus* constituents in regulating lipid metabolism, which may, in turn, influence inflammatory pathways involved in metabolic disorders. Similarly, Lima-Cabello et al. (2020) identified specific proteins in *L. angustifolius*, particularly γ-conglutin, with promising anti-inflammatory properties. These proteins reduced oxidative stress and inflammation markers in pancreatic cell lines, suggesting a dual role in both nutrition and inflammation. The anti-inflammatory activity of lupin is closely associated with its phenolic content. For example, Danciu et al. (2017) quantified the total phenolic content in lupin seeds and linked it directly to both antioxidant and anti-inflammatory effects. These phenolic compounds modulate oxidative stress and inflammatory cascades, indicating that lupin-enriched diets may provide protective benefits against chronic inflammatory diseases.

In conclusion, strong evidence supports the anti-inflammatory potential of *Lupinus* species, especially through their rich content of bioactive peptides and phenolic compounds. These effects are mediated by suppression of key inflammatory mediators and modulation of intracellular signaling pathways, indicating the potential of lupin as both a functional food and a therapeutic agent in managing inflammation-related disorders.

Antidiabetic Effects

The pharmacological potential of *Lupinus* species in the management of diabetes has gained considerable interest in recent years. Seeds of *Lupinus albus* and *Lupinus angustifolius* are particularly rich in bioactive compounds responsible for notable hypoglycemic properties, making them promising dietary components for glycemic control and prevention of diabetes-related complications. In Egypt, for instance, *L. albus* seeds have traditionally been used by individuals with type 2 diabetes, although the efficacy of this use is not thoroughly documented (Eskander & Won Jun, 1995; KUBO et al., 2000). One of the primary mechanisms by which lupin exerts antidiabetic effects is through modulation of glucose metabolism. Studies have shown that polysaccharides and peptides derived from lupin seeds significantly reduce blood glucose levels in diabetic models. For example, ethanolic extracts of *L. albus* seeds have been shown to lower plasma glucose concentrations and oxidative stress markers, such as malondialdehyde (MDA), while also increasing antioxidant enzyme activity, including superoxide dismutase (SOD) and catalase, in streptozotocin-induced diabetic rats (Yildirim et al., 2020). The γ-conglutin protein in lupin has been related to insulin-mimetic activity in cellular models, supporting its potential to enhance glucose uptake and regulate insulin signaling (Andor et al., 2016). Additionally, the compounds such as 13-α-hydroxylupanine, lupanine, 17-oxolupanine, 2-thiosparteine, and sparteine have demonstrated the ability to increase insulin secretion *in vitro* (Díaz et al., 1990; M Wink, 2005). Traditional uses of lupin in Turkey support its hypoglycemic reputation. For instance, *L. albus* subsp. *albus*, commonly known as “termiye” or “Jew’s foot,” is consumed in Konya and Tekirdağ regions in various forms (raw, boiled, or decocted) to manage diabetes (Akalın & Akpınar, 1994; Koçoğlu Keklik et al., 1996). Similarly, *L. angustifolius* (referred to as “yahudibaklası” in the İzmir region) is traditionally roasted and consumed with hot water for diabetes patients (Ugulu et al., 2009).

Phenolic compounds in lupin seeds, particularly polyphenols, have been shown to control glycemic index and protect against oxidative stress in diabetic patients (Danciu et al., 2017). Germination of lupin seeds enhances these effects by increasing the bioavailability of polyphenols and other bioactive components (Andor et al., 2016).

In a comparative animal study, *L. albus* extracts were found to reduce hepatic and pancreatic damage caused by diabetes. Rats were divided into five groups: healthy control, diabetic control (streptozotocin-induced), gliclazide-treated, *Hyphaene thebaica*-treated, and *L. albus*-treated. Daily oral administration of 700 mg/kg of *L. albus* significantly alleviated diabetic symptoms and tissue damage (Tohamy et al., 2013). Clinical studies have also demonstrated that dietary interventions using lupin can reduce postprandial glucose levels and improve lipid profiles in humans, reinforcing its role in dietary control for diabetes management (Hodgson et al., 2010). These benefits are further supported by the LDL cholesterol-lowering effects of lupin proteins, which stimulate LDL receptor activity (Sirtori et al., 2004).

Lupin seeds also offer functional properties like high-quality proteins and soluble fibers, which improve satiety and reduce postprandial glycemia. Due to their low glycemic index and ability to delay glucose absorption, lupins are well-suited for individuals with type 2 diabetes (Ward et al., 2020). Oxidative stress, a major contributor to diabetic complications, is mitigated by the antioxidant properties of *Lupinus* species. Peptides and polyphenols reduce oxidative damage and inflammation, thereby lowering the risk of comorbidities such as nephropathy and liver fibrosis (Garmidolova et al., 2022; Sayari et al., 2023). A study using *L. angustifolius* extracts demonstrated that it induces antioxidant enzymes and regulates anti-inflammatory cytokines in diabetic conditions (Millán-Linares et al., 2014)..

In conclusion, *Lupinus* species exhibit strong antidiabetic properties through multiple mechanisms, including regulation of glucose metabolism, insulin-mimetic effects, antioxidant protection, and modulation of inflammation. Their integration into dietary strategies offers promising benefits for the management and prevention of diabetes and its associated complications.

There are currently no published antidiabetic effects of *Lupinus micranthus*, *Lupinus hispanicus*, or *Lupinus anatolicus*.

Antihypertensive Effects

The antihypertensive potential of *Lupinus* species, particularly *Lupinus albus* and *Lupinus angustifolius*, has drawn attention as a natural dietary approach to managing high blood pressure. These species contain a diverse range of phytochemicals, including alkaloids, flavonoids, and peptides, which are known to contribute to cardiovascular health by modulating vasodilation and oxidative stress.

Several studies have demonstrated that *Lupinus* seeds influence the nitric oxide (NO) pathway, a critical regulator of vascular tone. Flavonoids and peptides derived from lupin have been shown to stimulate NO production, thereby promoting vasodilation and lowering systemic blood pressure (Hassine et al., 2021). Additionally, *Lupinus* extracts may modulate the renin-angiotensin system (RAS), a hormonal system that regulates blood pressure and fluid balance. Protein fractions such as β-conglutin isolated from *L.*

angustifolius have been reported to enhance NO synthesis and reduce vascular resistance (Lima-Cabello et al., 2019).

Of particular importance are the bioactive peptides in *Lupinus* species, which exhibit angiotensin-converting enzyme (ACE) inhibitory activity. Inhibition of ACE prevents the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor, thereby contributing to blood pressure reduction. Clinical studies and *in vitro* analyses showed that lupin-based food products lead to a decrease in both systolic and diastolic blood pressure (Castillo et al., 2023; Czubinski & Feder, 2019).

Phenolic compounds in lupin seeds also improve endothelial function by increasing the bioavailability of NO and reducing oxidative stress. This effect supports vascular relaxation and helps maintain arterial elasticity (Czubinski & Feder, 2019; Loredo-Dávila, 2012). Additionally, lupin phenolics have been shown to inhibit calcium influx in vascular smooth muscle cells, further supporting their role in reducing vascular resistance and blood pressure (Czubiński & Feder, 2019).

In summary, *Lupinus* species have antihypertensive activity through multiple mechanisms, including ACE inhibition, enhanced NO signaling, calcium channel modulation, and oxidative stress. These properties support the use of lupin as a functional food ingredient in the strategies of hypertension management.

There are no reported studies investigating the antihypertensive properties of *Lupinus micranthus*, *Lupinus hispanicus*, *Lupinus varius*, or *Lupinus anatolicus*.

Hypocholesterolemic Effects

The hypocholesterolemic effects of *Lupinus* species—particularly *Lupinus albus* and *Lupinus angustifolius* —have been widely investigated for their ability to regulate lipid metabolism and manage hypercholesterolemia. These beneficial effects are primarily attributed to the protein composition, bioactive peptides, dietary fiber, and phytochemical content found in lupin seeds.

Lupin-derived peptides also promote cholesterol catabolism and excretion by increasing bile acid production, facilitating the elimination of cholesterol from the body. The high soluble fiber content in lupin seeds contributes further to this effect by binding bile acids in the intestine, thereby interrupting enterohepatic recirculation and enhancing cholesterol clearance (Hodgson et al., 2010; Tesarowicz et al., 2022). In animal studies, lupin protein sources have been demonstrated to have cholesterol-lowering potential. For instance, in a study comparing *L. angustifolius* with casein in pigs fed a high-cholesterol diet, lupin significantly reduced plasma cholesterol levels (Martins et al., 2005). Similarly, Fontanari et al. (2012) reported that both whole lupin seeds and protein isolates significantly lowered serum cholesterol in animal models. This effect was associated with the inhibition of 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA reductase)—the rate-limiting enzyme in cholesterol biosynthesis—regulated via sterol regulatory element-binding proteins (SREBPs) (Fontanari et al., 2012). Both human and animal studies support the efficacy of yellow lupin (*L. luteus*), *L. albus*, and *L. angustifolius* in improving lipid profiles. These effects are believed to result from the unique amino acid composition and structure of lupin proteins. The protein hydrolysates from these species also exhibit antioxidant properties, which help combat oxidative stress, a key factor in the development of hyperlipidemia and cardiovascular disease (Tesarowicz et al., 2022).

Flavonoids, saponins, and other phenolic compounds in lupin seeds further contribute to lipid-lowering effects. These compounds enhance endothelial function and reduce intestinal cholesterol absorption by altering micellar solubility and inhibiting cholesterol transport mechanisms (Zhong et al., 2012). Additionally, regular lupin consumption has been linked to increased satiety, which can support weight management and indirectly impact serum lipid levels (Yildirim et al., 2020).

Dietary interventions involving lupin-based foods have consistently demonstrated improvements in lipid profiles. For example, Hodgson et al. (2010) reported that increasing lupin-derived protein and fiber intake led to reductions in total cholesterol and triglyceride levels in overweight individuals. These outcomes were attributed to the synergistic effects of energy-dense nutrients and bioactive compounds in lupin that act on lipid metabolism pathways (Hodgson et al., 2010).

In conclusion, *Lupinus* species exhibit robust hypocholesterolemic activity through multiple mechanisms, including inhibition of cholesterol synthesis (via HMG-CoA reductase), the promotion of bile acid-mediated excretion, the inhibition of intestinal lipid absorption, and the improvement of antioxidant defenses. These properties reinforce the value of lupin as a functional food for cardiovascular health and metabolic regulation.

There are no reported studies investigating the antihypertensive properties of *Lupinus micranthus*, *Lupinus hispanicus*, *Lupinus varius*, or *Lupinus anatolicus*.

Anticholinergic Effects

In addition to their well-documented antioxidant properties, certain *Lupinus* species particularly *Lupinus luteus* contain bioactive quinolizidine alkaloids, such as lupanine and sparteine, that exhibit mild anticholinergic activity. These alkaloids have drawn scientific interest due to their potential pharmacological applications in neurological disorders, especially those involving cholinergic dysregulation, such as Alzheimer's disease.

Research suggests that lupanine and related compounds act as reversible inhibitors of acetylcholinesterase (AChE), the enzyme responsible for the breakdown of acetylcholine in the synaptic cleft. By inhibiting AChE, these alkaloids can increase the availability of acetylcholine at synaptic junctions, thereby enhancing cholinergic neurotransmission. This mechanism underpins the rationale for their potential use as adjunct therapies in neurodegenerative conditions characterized by acetylcholine deficiency (Hassine et al., 2021).

Although their anticholinergic effects are generally considered mild compared to synthetic cholinesterase inhibitors, the natural origin and additional bioactivities of these alkaloids—such as antioxidant and antimicrobial effects suggest they may contribute to multifunctional therapeutic strategies. However, the therapeutic window is narrow, as these same alkaloids are also associated with toxicity risks at higher concentrations, including neurotoxicity and cardiotoxicity (Ozkaya et al., 2021).

In summary, alkaloids such as lupanine and sparteine present in *L. luteus* exhibit mild anticholinergic effects through AChE inhibition, supporting their potential role in managing neurodegenerative diseases. Further studies are needed to determine their safety profile, optimal dosing, and efficacy in clinical settings.

There are no reported studies investigating the anticholinergic properties of *Lupinus micranthus*, *L. hispanicus*, *L. varius*, *L. angustifolius*, or *L. anatolicus*

Anticancer Effects

The anticancer potential of *Lupinus* species—especially *Lupinus albus* and *L. angustifolius*—has attracted growing scientific attention due to their diverse phytochemical content, including flavonoids, alkaloids, peptides, and dietary fiber. These compounds are known to exert anticancer effects via multiple cellular and molecular mechanisms.

A particularly noteworthy compound is genistein, an isoflavone in lupin, which has been shown to inhibit the proliferation of various cancer cell lines, including ovarian carcinoma (SK-OV-3) cells. Genistein induces apoptosis through cell cycle arrest and the activation of pro-apoptotic factors such as caspases, as well as modulation of the MAPK/ERK signaling pathways that regulate cell proliferation and survival (Antosiak et al., 2017).

Additionally, the octapeptide GPETAFLR, derived from hydrolyzed *L. angustifolius* protein, has been found to exert immunomodulatory effects that contribute to anticancer activity. This peptide enhances anti-inflammatory responses and promotes immune surveillance by skewing monocyte differentiation toward the M2 macrophage phenotype, which is associated with tissue repair and immune regulation (Montserrat-de la Paz et al., 2019). The antioxidant properties of lupin phytochemicals, particularly polyphenols and flavonoids, are believed to prevent carcinogenesis by reducing oxidative stress and preventing DNA damage. Danciu et al. (2017) demonstrated that high total phenolic content in lupin seeds correlates with the inhibition of tumor cell growth by oxidative stress suppression(Danciu et al., 2017).

Lupin proteins have also been linked to improved lipid metabolism, which may reduce the risk of cancer. Given the established association between hyperlipidemia and various malignancies, the cholesterol-lowering properties of lupin seeds (Fontanari et al., 2012) may have indirect anticancer benefits.

Furthermore, the dietary fiber content of lupin contributes to its anticancer potential, especially in the context of colorectal cancer. Dietary fiber binds bile acids and promotes their excretion, reducing their potential carcinogenic effects in the colon (Danciu et al., 2017). In addition, fiber supports gut microbiota health, which has been linked to immune system modulation and tumor suppression.

In conclusion, *Lupinus* species exhibit multifaceted anticancer effects mediated through antioxidant activity, immune modulation, apoptosis induction, and dietary fiber functions. These findings underscore the potential of lupin-derived compounds as natural adjuncts in cancer prevention and management strategies. Further research is warranted to clarify their mechanisms and explore clinical applications.

There are no reported studies investigating the anticholinergic properties of *L. micranthus*, *L. hispanicus*, *L. varius*, or *L. anatolicus*.

Antimicrobial, Antifungal, and Antiparasitic Effects

Lupinus species have demonstrated broad-spectrum antimicrobial properties, making them a subject of increasing interest in the search for natural antimicrobial agents. These effects are primarily attributed to the presence of various bioactive compounds, including alkaloids, polyphenols, flavonoids, peptides, and saponins found in lupin seeds.

Ethanolic extracts of *Lupinus albus* and *Lupinus angustifolius* have been shown to possess potent antibacterial properties against both Gram-positive and Gram-negative bacteria, including *Escherichia coli* and *Bacillus subtilis* (Rani & Rani, 2025). The antimicrobial action of phenolic compounds is largely related to their ability to disrupt bacterial cell membranes, inhibit essential metabolic enzymes, and interfere with nucleic acid synthesis.

The efficacy of both germinated and ungerminated seed extracts of lupin has also been validated *in vitro* models. These extracts exhibited significant reductions in microbial loads, suggesting a potential role in controlling foodborne pathogens and promoting food safety (Andor et al., 2016). Specific isoflavones and cinnamic acid derivatives in lupin extracts are believed to enhance this antimicrobial action(Andor et al., 2016).

Additionally, alkaloid-rich extracts from lupin have demonstrated strong antibacterial activity against antibiotic-resistant clinical isolates such as *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*—pathogens commonly associated with hospital-acquired infections (Romeo et al., 2018).

Fermentation of lupin proteins further enhances their antimicrobial activity. For example, fermentation with Lactobacillus species reduced the molecular weight of *L. angustifolius* proteins, thereby increasing their bioactivity against microbial pathogens (Bartkiene et al., 2019). Saponins another class of lupin phytochemicals—exhibit antimicrobial action by disrupting microbial membrane integrity and leading to cell lysis (Ishaq et al., 2022).

The anthelmintic properties of lupin alkaloids have also been documented. *In vitro* studies verified that alkaloid extracts from *L. albus* inhibit the migration of larvae from parasitic nematodes such as *Haemonchus contortus* and *Teladorsagia circumcincta*, both of which are major gastrointestinal parasites in ruminants. This effect was attributed to the interaction of alkaloids with the nematodes' acetylcholine receptors, disrupting neuromuscular function (Dubois et al., 2019).

Regarding antifungal effects, extracts of *Lupinus albescens* demonstrated high antifungal activity against *Fusarium oxysporum* and *F. verticillioides*, pathogens responsible for significant crop losses. Supercritical CO_2 and liquefied petroleum gas extraction methods yielded extracts that inhibited fungal growth by over 60%, suggesting potential for use as eco-friendly fungicides (Confortin et al., 2019). Further analysis of quinolizidine alkaloids in *Lupinus* species revealed that their antifungal efficacy varies based on chemical structure. Targeted extraction and chemical characterization could pave the way for the development of novel antifungal agents (Cely-Veloza et al., 2022, 2023). Lupin alkaloids have also shown efficacy against *Candida albicans* and other opportunistic fungi, with studies highlighting their broad-spectrum antifungal potential (Erdemoglu et al., 2007).

In addition, silver nanoparticles (AgNPs) synthesized using *Lupinus albus* extracts have demonstrated acaricidal, larvicidal, and repellent activity against the camel tick (*Hyalomma dromedarii*). These nanoparticles caused 100% mortality at specific concentrations, significantly reduced egg-laying parameters, suppressed acetylcholinesterase (AChE) activity, and elevated oxidative stress levels in target organisms (Majeed et al., 2023).

Furthermore, allelopathic interactions between lupins and neighboring plant species suggest that their root exudates may have antifungal properties, contributing to soil health and plant disease resistance (Georgieva et al., 2015; Prass et al., 2022; Wurst et al., 2010).

In conclusion, the antimicrobial, antifungal, and antiparasitic effects of *Lupinus* species are multifactorial and involve a rich array of phytochemicals. These findings support the potential use of lupin-based extracts as natural antimicrobial agents in food preservation, animal health, crop protection, and even human therapeutics.

Immunomodulatory Effects

The immunomodulatory potential of *Lupinus* species has gained increasing scientific interest, particularly regarding their ability to modulate cytokine production, support immune cell function, and mitigate inflammatory responses. These effects are primarily attributed to the presence of flavonoids, alkaloids, peptides, and other secondary metabolites found in lupin seeds.

Flavonoids—abundant polyphenolic compounds in *Lupinus*—are well known for their antioxidant and anti-inflammatory properties, but they also play a critical role in immune modulation. These compounds can regulate the release of pro-inflammatory cytokines such as interleukin-1 (IL-1) and interleukin-2 (IL-2), which are crucial for T-cell activation and proliferation (Hoensch & Weigmann, 2018; Kamboh, 2015). By inhibiting overactivation of immune effectors, flavonoids help maintain immune balance and reduce the risk of autoimmune reactions. Mierziak et al. (2014) further highlighted the role of plant flavonoids in environmental stress and immune signaling (Mierziak et al., 2014).

Alkaloids, particularly lupanine, also contribute to immunomodulatory effects by exerting metabolic and antimicrobial actions. Lupanine has been shown to regulate glucose metabolism by modulating KATP channels and insulin gene expression, while also enhancing host defense mechanisms (Wiedemann et al., 2015). This highlights the complex interplay between metabolic regulation and immune function, where phytochemicals simultaneously improve systemic and immune health.

Tannins found in lupin seeds have also been related to the stimulation of macrophage activity and enhanced cytokine secretion. These effects are consistent with studies demonstrating that plant-derived secondary metabolites exhibit antiviral properties and support immune responses against a broad spectrum of pathogens (Jumaa et al., 2021).

The GPETAFLR peptide, derived from *L. angustifolius* protein hydrolysate, has demonstrated dual anti-inflammatory and immunoregulatory effects. In monocyte-derived osteoclasts, this peptide downregulated pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, while simultaneously upregulating anti-inflammatory cytokines IL-4 and IL-10. Additionally, in microglial cells and high-fat diet-induced obese mice, GPETAFLR was shown to promote M2 macrophage polarization and reduce neuroinflammation, thus supporting central nervous system (CNS) homeostasis (Millán-Linares et al., 2014; Montserrat-de la Paz et al., 2019).

Other studies have focused on specific lupin varieties such as *L. albus*, whose protein and lipid compositions contribute to improved immune status. Dietary consumption of these legumes has been associated with decreased levels of inflammatory markers, reinforcing their potential as functional foods aimed at immune enhancement (Carvajal-Larenas et al., 2016; Khan et al., 2015; Pastor-Cavada et al., 2010; Yildirim et al., 2020).

The globulin γ-conglutin, one of the major proteins in lupin seeds, has also been associated with improved metabolic and immune outcomes. It plays a role in energy metabolism in muscle tissue and may activate immune-related signaling cascades (Rosa Lovati et al., 2012).

Animal studies have further demonstrated that *Lupinus* extracts can modulate immune responses, increasing levels of pro-inflammatory cytokines (interferon-gamma (IFN-γ)), while decreasing levels of immunosuppressive cytokines (IL-10). This immunostimulatory balance may enhance host resistance to infections and inflammation (Gaur et al., 2008).

A noteworthy application of lupin in animal health includes its use in aquaculture. For example, Weiß et al. (2020) demonstrated that incorporation of lupin seed meal into the diet of white-legged shrimp (*Litopenaeus vannamei*) improved immune function, indicating that the immunomodulatory benefits of Lupinus species extend across species(Weiss et al., 2020).

In conclusion, *Lupinus* species exhibit pronounced immunomodulatory activity through multiple phytochemicals that influence cytokine profiles, macrophage polarization, and immune system regulation. These findings support the development of lupin-based dietary strategies to enhance immunity and prevent immune-related disorders in humans and animals.

Side Effects

Despite the numerous health benefits associated with Lupinus species, potential adverse effects must be considered, particularly those related to their alkaloid and allergenic content. The most significant concern is the risk of toxicity due to quinolizidine alkaloids—naturally occurring compounds found especially in L. luteus, L. angustifolius, and L. albus. These alkaloids may lead to neurotoxic effects, allergic reactions, and gastrointestinal disturbances if consumed in excessive amounts or without proper processing.

Some lupin varieties contain alkaloid levels that exceed the recommended safety threshold of 200 mg/kg, as established by food safety authorities (Boukid & Pasqualone, 2022). Unprocessed or poorly processed seeds of such varieties have been linked to acute poisoning symptoms, including nausea, vomiting, tremors, convulsions, and impaired motor coordination (Boschin et al., 2008; Frick et al., 2017). In particular, lupanine and sparteine have been identified as the primary neurotoxic agents.

L. angustifolius, while considered a "sweet" lupin species, can still contain significant amounts of lupanine, which has been associated with anticholinergic symptoms when consumed raw or inadequately prepared (Daverio et al., 2014; Ozkaya et al., 2021). Lupin proteins, particularly α- and β-conglutins, are also known allergens. Sensitization to lupin has been reported, *in particular* among individuals allergic to peanuts or soybeans, due to cross-reactivity. Clinical cases have documented mild symptoms (e.g., bloating, rash) as well as severe reactions such as anaphylaxis after lupin ingestion in peanut-sensitive individuals (Peeters et al., 2009; Sanz et al., 2010; Villa et al., 2020).

Additionally, the high fiber content of *L. albus*, *L. angustifolius*, and *L. luteus*—particularly α-galactosides—can cause gastrointestinal side effects such as bloating, flatulence, abdominal pain, and diarrhea in individuals with sensitive digestive systems (Zraly et al., 2007). These effects are responsible for the fermentation of fibers in the colon, resulting in gas production.

Severe cases of poisoning have been documented in both children and adults following the ingestion of lupin products containing high levels of alkaloids, reinforcing the importance of appropriate processing methods such as soaking, cooking, and fermentation to reduce alkaloid concentrations to safe levels (Bloothooft et al., 2025; Yeheyis et al., 2011). Although thermal processing may reduce allergenicity to some extent, it does not eliminate it (Villa et al., 2024). Even though "sweet" lupin cultivars have been developed to contain low levels of alkaloids, the unintentional consumption of wild or improperly labeled high-alkaloid varieties still poses a risk (Gresta et al., 2017).

In summary, while *Lupinus* species offer considerable health benefits, attention must be given to their potential side effects, particularly alkaloid toxicity and allergenicity. Ensuring the consumption of properly processed low-alkaloid cultivars is essential for safe use in both human and animal nutrition. Continued monitoring and consumer education remain important for minimizing health risks.

Specific studies on the adverse effects of *Lupinus micranthus* are limited.

Teratogenicity

Although *Lupinus* species are generally considered safe when properly processed and consumed in moderation, certain alkaloid-rich varieties have been associated with teratogenic effects, particularly in livestock. Chronic exposure to quinolizidine alkaloids—specifically anagyrine and ammodendrine—has been shown to cause developmental abnormalities during gestation (S. T. Lee et al., 2008).

These effects have been primarily reported in the context of North American lupin species such as *Lupinus leucophyllus* and *L. sulphureus*. In livestock, exposure to these alkaloids during early pregnancy has been linked to a condition known as "crooked calf disease," which involves skeletal deformities and joint malformations (S. T. Lee et al., 2008; Stephen T. Lee et al., 2007, 2019). The teratogenic outcomes are influenced by the alkaloid concentration, duration of exposure, and physiological status (e.g., body condition) of the pregnant animals(Boschin & Resta, 2013; Green et al., 2013).

Studies have explored non-invasive biomarkers (e.g., analysis of hair, earwax, nasal mucus, and oral fluid) to monitor livestock exposure to teratogenic lupin species, highlighting practical approaches for early detection and prevention in animal husbandry (Stephen T. Lee et al., 2019). Importantly, such teratogenic effects have not been documented for lupin species commonly cultivated in Turkey, including *L. albus*, *L. angustifolius*, *L. luteus*, or *L. anatolicus*. However, due to the structural similarities among quinolizidine alkaloids across species, the potential for reproductive toxicity cannot be entirely excluded without species-specific toxicological evaluation.

In conclusion, teratogenic effects have been primarily associated with specific alkaloids in wild lupin species, especially in livestock exposed during critical periods of gestation. Although no such effects have been reported for *Lupinus* species cultivated in Turkey, continued vigilance, proper species identification, and alkaloid profiling are essential to ensure safety in both human and veterinary contexts.

Discussion

Lupinus species, particularly ***Lupinus albus*** (white lupin), have emerged as prominent subjects in both nutritional and pharmacological research due to their broad spectrum of biological activities. As members of the Fabaceae family, lupins are recognized for their high protein content, abundant dietary fiber, and low-fat levels, making them an attractive alternative food source for both human and animal consumption (Pereira et al., 2022).

The richness of lupin seeds in bioactive compounds—such as alkaloids, flavonoids, peptides, and polyphenols—has positioned them as potential nutraceuticals: natural products that exert beneficial effects in the prevention and management of chronic diseases. A growing body of evidence from animal studies supports their pharmacological effects, including antioxidant, antidiabetic, anti-inflammatory, and lipid-lowering properties (Andor et al., 2016).

In the context of animal health and nutrition, lupin seeds offer multiple advantages. Their high protein and fiber content **contribute** to improved digestion, enhanced immune status, and better nutrient utilization. These attributes make lupin-derived feed an effective and sustainable alternative to traditional protein sources in livestock production systems. Research has shown that the inclusion of lupin meal in animal diets improves feed conversion ratios, promotes weight gain, and supports overall animal health (Pereira et al., 2022).

The method of processing lupin seeds significantly influences their bioactive potential. For instance, fermentation with probiotic bacteria such as ***Lactobacillus*** species has been shown to enhance the nutritional profile of lupin flour and improve its palatability and digestibility in **animal nutrition.** Additionally, **these** processing methods can increase the bioavailability of peptides and other functional compounds, expanding the potential of lupin as an ingredient in nutritionally enriched food and feed products (Bartkiene et al., 2019; Pereira et al., 2022).

Furthermore, the versatility of *L. albus* and *L. angustifolius* as both food and functional agents is reflected in their promising pharmacological profiles. These species provide not only nutritional support but also therapeutic effects in the context of metabolic disorders, immune dysfunction, and oxidative stress. Their applications range from clinical nutrition to veterinary medicine, making them valuable in both human health and animal husbandry.

In conclusion, *Lupinus* species—particularly *L. albus* and ***L. angustifolius***—exhibit a wide range of beneficial properties that align with the growing demand for sustainable, plant-based nutraceuticals. Their role in promoting health, managing chronic conditions, and enhancing animal welfare highlights their dual utility as both food and medicine. Pharmacological and biological activity studies conducted on Lupinus species naturally occurring in Turkey are quite limited in number and scope in the existing literature. This limitation prevents the full elucidation of the biological activity profiles, mechanisms of action, and potential therapeutic applications of these species. However, it is notable that ***Lupinus*** species are distinguished by their abundant phytochemical content, encompassing alkaloids, phenolic compounds, proteins, and bioactive peptides. These characteristics suggest a potential for action against various diseases, including anticancer, antioxidant, anti-inflammatory, antimicrobial, and metabolic disorders. Consequently, there is an imperative for multi-centre, interdisciplinary research that characterises the phytochemical composition of different ***Lupinus*** species cultivated in Turkey in detail, conducts comprehensive biological activity analyses in cell culture and animal models, and transfers the obtained data to clinical studies. Such studies are of great importance for revealing the pharmaceutical potential of local plant genetic resources and for developing new opportunities for biotechnological and industrial applications. Further investigations are needed to fully integrate lupin-based strategies into veterinary and clinical practice, particularly in the context of developing functional food and sustainable livestock production.

Additionally, scientific studies should be complete, including drug-plant or plant-plant interactions, mutagenicity, contraindications, route of administration, dosage, use in pregnancy and lactation, pediatric use, and preparations or herbal products containing *Lupinus* species in Turkey.

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