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LESPEDEZA CAPITATA: DE LA LEGUMĂ LA MEDICAMENT

LESPEDEZA CAPITATA: FROM LEGUME TO MEDICINE

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Rezumat: *Extractele din plante au jucat un rol fundamental în medicină și farmacognozie de secole, adăpostind o varietate de compuși bioactivi cu potențial terapeutic. Acest domeniu, dedicat explorării proprietăților medicinale ale produselor naturale, investighează compozițiile chimice variate ale acestor extracte. De la remedii antice la medicamente moderne, acestea au fost indispensabile în îngrijirea sănătății. Numeroase medicamente, inclusiv aspirina și morfina, își au rădăcinile în sursele vegetale. Astăzi, extractele obținute din plante precum ginsengul, echinaceea și turmericul sunt apreciate pentru proprietățile lor de stimulare a imunității și antiinflamatorii. Lespedeza capitata, o leguminoasă nativă de pe continentul american, este centrul acestui articol datorită compușilor săi, care au prezentat rezultate promițătoare. Rezultatele noastre au arătat că această specie conține diferiți polifenoli cu proprietăți antioxidante sporite. Remedii pe bază de plante profită adesea de efectele antimicrobiene și antioxidante ale extractelor. În plus, compușii fitochimici din aceste extracte oferă un viitor promițător pentru tratamentul diverselor afecțiuni, de la diabet la cancer. Procesele standardizate de extracție garantează potența și uniformitatea produselor medicinale din plante, consolidând și mai mult fiabilitatea lor în îngrijirea sănătății. Cercetările în curs de desfășurare asupra extractelor din plante continuă să dezvăluie potențialul lor terapeutic, stimulând descoperirile de medicamente noi și progresul în îngrijirea sănătății la nivel global.*

Cuvinte-cheie: *farmacognozie, extracte vegetale, medicamente derivate din plante, fitocompuși, Lespedeza capitata.*

Abstract: *Plant extracts have been pivotal in medicine and pharmacognosy for centuries, housing an array of bioactive compounds with therapeutic potential. This field, dedicated to exploring the medicinal properties of natural products, delves into the varied chemical compositions of these extracts. From ancient remedies to modern pharmaceuticals, they have been indispensable in healthcare. Numerous drugs, including aspirin and morphine, find their roots in plant sources. Today, extracts obtained from plants like ginseng, echinacea, and turmeric are esteemed for their immune-boosting and anti-inflammatory properties. Lespedeza capitata, a legume native to the Americas is the focus of this article thanks to its compounds which have shown promising results. Our results showed that this species contains various polyphenols with good antioxidant properties. Herbal remedies often capitalize on the antimicrobial and antioxidant effects of plant extracts. Additionally, phytochemicals within these extracts offer promising avenues for treating diverse ailments, from diabetes to cancer. Standardized extraction processes guarantee the potency and uniformity of medicinal plant products,*

further bolstering their reliability in healthcare. Ongoing research into plant extracts continues to reveal their therapeutic potential, fostering novel drug discoveries and advancements in global healthcare.

Keywords: *pharmacognosy, plant extracts, plant-based drugs, phytochemicals, Lespedeza capitata.*

Introduction

In the past decade, forage legumes have garnered attention for their positive impacts on domesticated animals and the environment, particularly in terms of phytoremediation. Consequently, numerous plant species from the *Fabaceae* family have been scrutinized for their abundant polyphenol content, a group of metabolites widely recognized as antioxidants. Among these species, *Lespedeza*, a group of wild plants used as legumes and native to the Americas and certain Oriental countries, has been of particular interest due to its traditional medicinal uses. Several reports have highlighted the presence of various beneficial compounds in *Lespedeza* species, including flavonoid glycosides, lignans, sterols, alkaloids, organic acids, coumestans, and terpenoids. *Lespedeza capitata* **Figure 1**, commonly known as Roundhead Lespedeza and native to eastern North America, has been underexplored despite its folk medicine tradition as a diuretic, anti-inflammatory, and antirheumatic agent in the USA, Korea, and China. Indigenous peoples in these regions historically used its roots or extracts thereof as antidotes for poisoning. Although less studied compared to other *Lespedeza* species, extracts from the leaves and stems of *L. capitata* are utilized for urinary tract and kidney disorders [1].

Fig. 1. *Lespedeza capitata* pressed plant from the Smithsonian Museum of Natural History (USA) [2]

Results and discussions

The quest for natural ingredients is increasingly captivating the pharmaceutical industry. Plants with rich ethnobotanical backgrounds, extensive phytochemical pedigrees, and abundant biomass availability are natural candidates for such studies. In the pursuit of discovering new active principles for medicine, attention has turned towards forage legumes, members of the *Fabaceae* family. These agricultural crops possess the remarkable ability to fix nitrogen through symbiotic relationships with bacteria housed in rhizobium root nodules.

Forage legumes are known to be abundant in various secondary metabolites, including alkaloids, cyanogenic glycosides, flavonoids, coumarins, phenolics, condensed tannins, triterpenoid saponins, and lectin peptides. Consequently, they represent a promising reservoir for extracting bioactive compounds with potential applications in skincare and human health. Roundhead lespedeza (*Lespedeza capitata* Michx), on which not many studies have been made and which has been used for centuries for its medicinal properties by the indigenous people of the Americas is the perfect candidate for our study.

Lespedeza capitata, a perennial shrub indigenous to eastern North America, has been historically utilized as forage for livestock. Traditional knowledge from native North Americans documents the root's use as an antidote to poisoning and the stems' application in moxibustion for treating neuralgia and rheumatism. The plant is notably rich in flavonoids and tannins, believed to contribute to its therapeutic properties. Experimental and clinical investigations have revealed the positive effects of *L. capitata* on tissue drainage, kidney and cardiovascular ailments, as well as its potential in managing diabetes. Additionally, its Asian counterpart, *L. cuneata*, has been studied for its skin moisturizing properties and protective effects against photoaging. These findings suggest that *L. capitata* may also hold promise for enhancing skin health and resilience. Despite the extensive historical use of these plants, there remains a significant gap in understanding their active principles, mechanisms of action, and specific effects for *in vivo* applications [3].

The chemical profile of the investigated extract was analyzed using liquid chromatography with a Transcend TLX-1 Vanquish Flex system coupled with the Orbitrap Exploris 480 high-resolution mass spectrometer. Compound Discoverer 3.3.1 software, part of the CENEMED platform, was utilized for the identification of small compounds. The method employed a gradient of 0.1% formic acid (A) and methanol (B) from 95:5 to 10:90 over 20 minutes, with a partial loop injection of 10 µL and a flow rate of 300 µL/min. A Hypersil Gold C18 column (50 x 2.1 mm, 1.9 µm) was maintained at 40°C. The instrument settings included electrospray ionization (ESI) in negative ion mode (-p), with a mass range from m/z 100 to 1500 at a frequency of 5 Hz, a negative voltage of 3.0 kV, and an ionization temperature of 350°C. Integration and detection were performed using Compound Discoverer 3.2 software, evaluating both targeted and untargeted modules. Peaks with a rating of at least 7.4 were considered and verified against the Thermo m/z Vault, NIST, and ChemSpider databases.

The general compound profile revealed a predominant presence of flavonoid derivatives, particularly quercetin derivatives, along with some polyphenol carboxylic acids such as chlorogenic acid (m/z = 353.08) and rosmarinic acid (m/z = 359.16), the rusting chromatogram is depicted in figure 2 and their chemical structures being represented in Figure 3. Previous studies have also noted the prevalence of similar compounds, notably flavonoid glycosides and condensed tannins. However, a comprehensive chemical composition of this species is still lacking, with some studies predating

2005. It is essential to consider that our results are specific to the investigated extract, which is a commercially obtained and selectively extracted product. Therefore, they may not encompass the full spectrum of components present in the plant [1, 4].

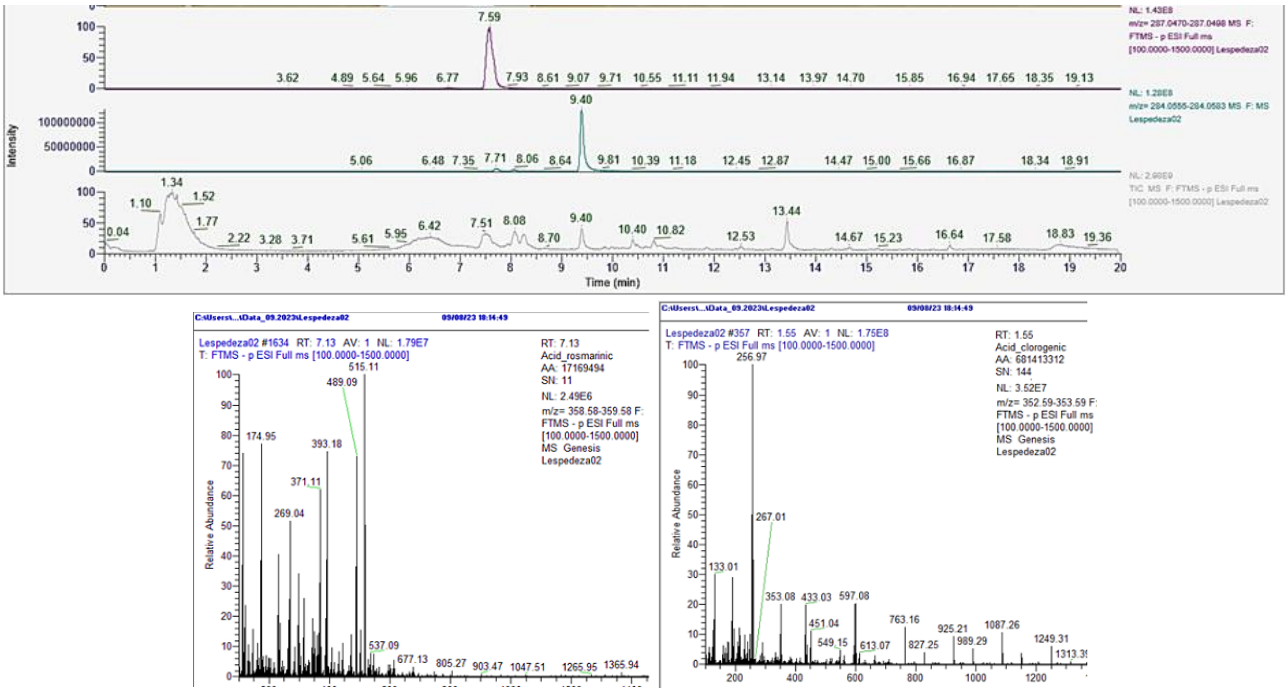

Fig. 2. General LC-ESI-MS chromatogram for *Lespedeza capitata* extract indicating the highest peaks, and the spectra for rosmarinic and chlorogenic acids[1]

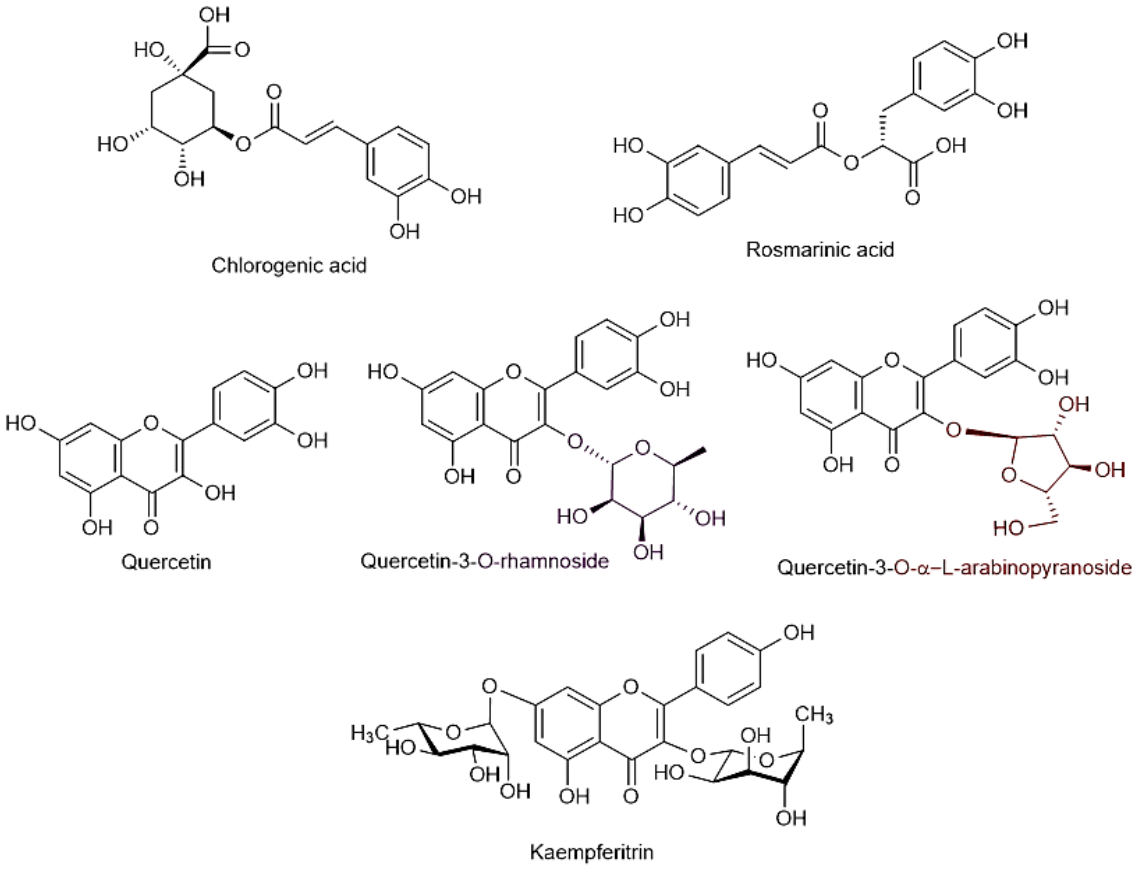

Fig. 3. Chemical structures of the compounds identified in *Lespedeza capitata* extracts

Biological activity and mechanisms: Lespedeza demonstrates various effects on ectoderm derivatives, including the skin and kidneys. Studies have shown significant stimulation of fibroblast and keratinocyte growth, increased collagen synthesis, and a lipolytic effect on adipocytes with *Lespedeza capitata* extract. This suggests the potential use of *Lespedeza* medicinal preparations for stimulating skin cell regeneration, anti-aging therapy, and inducing lipolysis due to its flavonoid content [5].

Kaempferitrin (depicted in *Figura 3*) is a naturally occurring flavonoid glycoside primarily found in *L. capitata* leaves. Previous investigations by researchers have highlighted the hypoglycemic properties of a certain n-butanol fraction extracted from another legume: *Bauhinia forficata* (*Leguminosae*) leaves in alloxan-induced diabetic rats. Additionally, research has indicated that kaempferitrin exhibits an immediate hypoglycemic effect in diabetic rats, although it did not alter the glucose tolerance curve compared to tolbutamide sulphonylurea. Among the aglycone and glycosylated flavonoids extracted from *Bauhinia forficata* leaves, kaempferitrin was the sole compound found to possess a hypoglycemic effect in diabetic rats, prompting further detailed examination. The study was undertaken to explore the prolonged impact of kaempferitrin on blood glucose levels in diabetic rats, as well as its *in vitro* effects on ^{14}C-d-glucose uptake and ^{14}C-leucine incorporation into protein in the soleus muscle of normal rats [6].

Furthermore, it has been found that *Lespedeza* extracts enhance diuresis, reduce edema, decrease azotemia and albuminuria, increases sodium excretion, and to a lesser extent potassium. The plant-based extracts promote renal filtration and excretion of nitrogenous products in urine. These effects are attributed to its flavonoid content, which normalize capillary permeability in the glomeruli and exhibit a mild diuretic effect without significant electrolyte loss, unlike synthetic diuretics. The advantages of phytotherapy in normalizing glomerular capillary permeability complement the action of renin-angiotensin system inhibitors (RAASi), which form the basis of renoprotection in modern nephrology. *Lespedeza* flavonoids improve protein-energy metabolism, exhibiting nephroprotective effects and slowing the progression of chronic kidney disease (CKD) while maintaining normal excretory function. Initial clinical trials carried out in France indicate that injectable extracts derived from round-head lespedeza may decrease azotemia in individuals with different forms of renal failure. However, the precise mechanism through which round-head lespedeza operates remains undetermined. A particular investigation revealed that procyanidins sourced from round-head lespedeza demonstrated inhibition of angiotensin-converting enzyme. Moreover, it has been observed to be non-toxic when administered at standard therapeutic dosages. Typically, it is administered as a tincture, with a recommended dosage of 2-5 ml three times daily.

Moreover, *Lespedeza* extract enhances the action of RAAS inhibitors synergistically, which is particularly relevant in patients with CKD stage 5. Even in CKD stage 10, maintaining a small dose of RAASi or using RAASi with extrarenal elimination in combination with *Lespedeza* extract shows promising results in clinical practice [4, 7].

Antioxidant activity: The phyto-complex present in the extract displayed twice as much activity against ferrous ions compared to its activity against DPPH radicals. This finding is intriguing as ferrous ions participate in the Fenton reaction, which generates hydroxyl radicals within living organisms. Hydroxyl radicals are highly reactive and known to cause damage. Additionally, other Lespedeza species, such as *L. bicolor*, have shown substantial antioxidant activity, with IC50 values

ranging from 50 to 200 μg/mL. Interestingly, root samples exhibited superior antioxidant activity compared to aerial parts of the plant [1].

Conclusions

In conclusion, Lespedeza species, particularly *Lespedeza capitata*, hold significant potential in various fields, including cosmetics, the pharmaceutical and agricultural industry. With its rich phytochemical profile, including flavonoids and polyphenols like quercetin derivatives, chlorogenic acid, and rosmarinic acid, Lespedeza extracts show promising biological activities. These include stimulating fibroblast and keratinocyte growth, enhancing collagen synthesis, inducing lipolysis, and promoting diuresis while reducing edema and azotemia [8].

Moreover, Lespedeza extracts exhibit antioxidant properties, with a noteworthy preference for ferrous ion inhibition, which may contribute to mitigating oxidative stress-related damage. These findings underscore the potential of Lespedeza extracts in skincare formulations, anti-aging therapies, and nephroprotective strategies, particularly in the context of chronic kidney disease.

However, further research is warranted to elucidate the specific mechanisms of action, identify additional bioactive compounds, and explore the full therapeutic potential of *Lespedeza* species. Nonetheless, the existing evidence suggests that Lespedeza extracts hold promise as natural remedies with diverse health benefits, offering opportunities for future therapeutic development and clinical application.

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