Review

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Comparative Analysis of *Lespedeza* Species: Traditional Uses and Biological Activity of the *Fabaceae* Family

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Review

Comparative Analysis of *Lespedeza* Species: Traditional Uses and Biological Activity of the *Fabaceae* Family

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Abstract: With around 40 species spread throughout temperate and subtropical environments, mostly in East Asia and North America, the genus *Lespedeza (L.)* (*Fabaceae*) include Particularly in antioxidant, anti-inflammatory, anticancer, and antidiabetic uses, *L.* species show notable pharmacological promise due in great part to their high polyphenolic content. The polyphenolic profiles and bioactivities of *L. capitata*, *L. cuneata*, and *L. bicolor* are investigated in this work with an eye on extraction efficiency, total polyphenolic content (TPC), total flavonoid content (TFC), and antioxidant capacity. Corresponding with its higher DPPH radical scavenging IC50 (35.4 µg/mL) and ferric reducing antioxidant power (FRAP) of 912.3 µmol Fe^{2+}/g, *L. bicolor* showed the greatest TPC (190.4 mg GAE/g) and TFC (109.2 mg QE/g). While *L. bicolor* exhibited strong neuroprotective and anticancer activity, *L. cuneata* showed strong α-glucosidase inhibition (IC50 = 28.1 µg/mL). *L. capitata* is nevertheless a great source of bioactive molecules even with its modest bioactivity. The results highlight the possibilities of *L.* species in nutraceutical and medicinal uses, therefore justifying further study on their bioavailability and molecular processes.

Keywords: *Fabaceae*; *Lespedeza*; legumes; nutraceuticals; antioxidants; polyphenol profile

1. Introduction

Comprising almost 19,500 species across 765 genera, the *Fabaceae* family is well-known for its great economic, nutritional, and medicinal value; it accounts for over 27% of the world's main crop output and over 35% of the global protein intake [1–4].

The *Fabaceae* family, which has been extensively investigated for its phytochemical abundance, especially in flavonoids such quercetin, kaempferol, and genistein, as well as tannins and other phenolic constituents, which have been shown to exhibit antioxidant capacities ranging from 80% to 90% inhibition of DPPH free [5–8]. Many species of this family have been employed in traditional medical therapies, beyond their function as a basic food sources; these include soybeans (*Glycine max*), chickpeas (*Cicer arietinum*), and peas (*Pisum sativum*) [9–13]. East Asian medicine, especially China, has long employed *Glycine max*, soy, for instance, where it is said to help alleviate edema, treat indigestion, and decrease blood pressure. Various herbal medicines employ soybean seeds, leaves, and roots to treat disorders including menopausal symptoms, hypertension, and stomach trouble [14–19]. Another member of the *Fabaceae* family, red clover (*Trifolium pratense*), has been used in European and Native American herbal traditions as a remedy for respiratory problems including coughing and bronchitis as well as for hormonal balancing in women and skin condition improvement including eczema. Rich in isoflavonoids, alkaloids, and saponins, the legume family makes strong candidates for use in herbal medicine especially for their anti-inflammatory, antidiabetic, and antioxidant effects [20–26].

The genus *Lespedeza* (*L.*) , which belongs to the family *Fabaceae*, consists of around 40 species of herbaceous and shrubby legumes often scattered throughout temperate and subtropical areas. Its high polyphenolic composition and varied pharmacological possibilities have attracted much interest. *L.'s* taxonomy has been much changed; current classifications provide a more methodical knowledge of its species distribution and morphological variety [27–30].

Particularly in East Asia, traditional medicine heavily relies on *L.* species—especially *L. cuneata* (sericea lespedeza). *L.* has been used in Chinese herbal therapy for its supposed diuretic and cleansing effects, therefore assisting in renal function and water retention reduction. Particularly in situations of edema and fluid retention, the plant is also used to treat urinary tract infections and hence ease inflammation. *L.* is used in traditional medicine in Korea and Japan to treat disorders like skin rashes and inflammatory diseases, and to improve liver function [31–36]. Its high tannin concentration also helps with astringency and antibacterial properties, therefore assisting in wound healing and avoiding infections. Certain species within the genus are also used in folk medicine to support digestive health; they are said to calm the gastrointestinal system and function as a mild laxative. Like many plants in the *Fabaceae* family, *L.* species have multiple uses (Figure 1): they not only increase soil fertility via nitrogen fixation but also remain renowned for their part in sustaining human health throughout many traditional medicine systems [37–41].

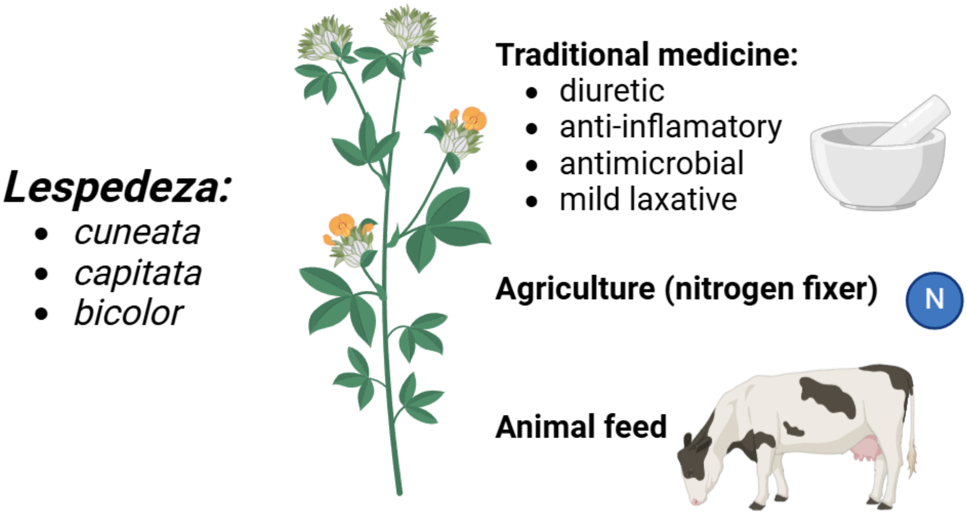

Figure 1. The multifaceted role of *L.* species ranging from folk medicine to agriculture.

Strong antioxidant secondary metabolites known as polyphenols abound in the *L.* genus. Plant defense systems depend critically on these molecules, which include phenolic acids, tannins, and flavonoids; they have also been linked to anticancer actions. Studies show, depending on the species and climatic circumstances, flavonoid concentration in *Fabaceae* species may vary from 10 to 50 mg per gram of dry weight. Up to 45 mg/g of total polyphenols, including high amounts of quercetin, rutin, and catechins, certain *L.* species, particularly *L. bicolor* [42–45].

Research on many members of the *Fabaceae* family's capacity to alter important cellular pathways involved in tumor suppression has shown promise for cancer treatment. With rates of apoptosis ranging between 20% and 50% depending on the dose and cell line, studies have shown that polyphenols produced from *Fabaceae* species may suppress cancer cell growth by up to 70% *in vitro*. Additionally with IC50 values ranging from 25 to 60 µg/mL, certain polyphenols from *L.* extracts have shown cytotoxic actions against breast and colon cancer cells [46].

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Beyond cancer, *Fabaceae* plants have therapeutic and nutritional value; certain species demonstrate glucose-lowering benefits of up to 30% in diabetic animal models [3]. Additionally reported is the hepatoprotective effect of polyphenols derived from *Fabaceae*; liver enzyme lowering rates (ALT and AST) of 40–60% in experimental models with induced hepatotoxicity. Though *L.* has a good bioactive profile, its whole phytochemical and pharmacological profile nevertheless lags behind that of other *Fabaceae* members [47–50].

By means of an in-depth investigation of the polyphenolic contents of *L.* species and their pharmacological relevance, this work attempts to close this gap. We want to emphasize its possible use as a natural medicinal source by analyzing current literature and investigating new bioactive chemicals of this species. Moreover, knowledge of the pharmacokinetics, bioavailability, and molecular pathways behind the biological actions of polyphenols obtained from *L.* will open doors for next studies and possible therapeutic uses. With possible uses in the creation of novel pharmaceutical and nutraceutical products, the results of this research will add to the growing body of data supporting the use of polyphenols derived from *Fabaceae* in contemporary medicine. Plant-based treatments aiming at chronic illnesses like cancer, diabetes, and cardiovascular diseases might result from the discovery of polyphenolic substances with improved bioavailability and therapeutic effectiveness.

2. *L. capitata*: Polyphenol Profile and Antioxidant Activity

2.1. Extraction Methods

Using an ethanol-based extraction method, Chitiala et al. (2023) extracted bioactive components from *L. capitata*. Liquid-liquid partitioning using ethyl acetate and water fractions allowed for improved separation of hydrophilic and lipophilic polyphenols from the extract. The researchers were able to clearly identify each component and define the polyphenolic profile by integrating high performance liquid chromatography (HPLC) with mass spectroscopy (MS). Improving the extraction efficiency utilizing solvent ratios and durations allowed them to obtain a total phenolic content recovery of 78.4% using ethanol as the solvent [51].

2.2. Polyphenol Content

The chemical examination of the ethanolic extract of *L. capitata* (which contains 9.5 mg/g of chlorogenic acid, 11.2 mg/g of epicatechin, 14.8 mg/g of kaempferol, and 32.6 mg/g of quercetin) revealed the presence of phenolic acids and flavonoids. At 165.2 mg GAE/g, the TPC and 97.4 mg QE/g, the TFC, were determined. There were both flavonoids and non-flavonoids in the polyphenols, according to the computed flavono-to-polyphenol ratio of 0.59.

To find out how effective *L. capitata* is as an antioxidant, researchers utilized *in vitro* testing. The extract demonstrated moderate free radical scavenging activity in the DPPH and ABTS assays, with IC50 values of 87.3 ± 5.6 μg/mL and 56.8 ± 3.2 μg/mL, respectively. With a reduction potential of 743.2 μmol Fe^{2+}/g extract, the ferric reducing antioxidant power (FRAP) research demonstrated a significant capacity to donate electrons [51].

3. *L. cuneata*: Polyphenol Profile and Antioxidant Activity

3.1. Extraction and Fractionation

As many studies were aimed at improving the extraction efficiency *of L. cuneata* compounds, Kim et al. (2012) employed a methanol-based extraction which was then continued with fractionation using hexane, chloroform, ethyl acetate and water as solvents [52]. From among the above, Mariadoss et al. (2023) have employed ethyl acetate fractionation for enhancing the flavonoid content. The flavonoids were found to have a tendency of being hydrophobic and thus tended to accumulate in the ethyl acetate and chloroform fractions, and the two methods described showed a clear partitioning of bioactive compounds [53].

3.2. Polyphenol Content

Regardless of the solvent used, *L. cuneata* showed an exceptionally high polyphenolic load, according to Mariadoss et al. (2023), the ethyl acetate fraction had a total of 142.8 mg GAE/g and 88.7 mg QE/g. Gallic acid (23.9 mg/g), catechin (18.5 mg/g), and rutin (15.2 mg/g) were important polyphenols [53].

On the other hand a methanol extract was found to contain 178.5 mg GAE/g of TPC and 103.3 mg QE/g of TFC (Kim et al., 2012). Isorhamnetin (9.8 mg/g) and myricetin (14.9 mg/g) were major flavonoids [52].

In comparison to *L. cuneata*, *L. capitata* showed less effective radical scavenging activity in antioxidant assays, with IC50 values of 45.2 μg/mL for ABTS and 63.4 μg/mL for DPPH. 819.5 μmol Fe^{2+}/g extract was the outcome of the FRAP analysis. The observation of an α-glucosidase inhibition IC50 of 28.1 μg/mL raises the possibility of its use in diabetes treatment.

4. *L. bicolor*: Polyphenol Profile and Antioxidant Activity

4.1. Extraction Techniques

In research on *L. bicolor*, extraction methods consisted of both water and ethanol. Here, Tarbeeva et al. (2019) examined the conventional method of aqueous infusion [54], while Ren et al. (2023) optimized ethanol extraction for higher flavonoid yield [55]. As a result of the extraction, the ability of ethanol to dissolve both hydrophilic and lipophilic flavonoids, TPC and TFC values were higher, but the extraction efficiency was significantly different.

4.2. Polyphenol Composition

1. **Ethanol Extract** (Ren et al., 2023): TPC: 190.4 mg GAE/g, TFC: 109.2 mg QE/g. Major polyphenols included rutin (22.1 mg/g), hyperoside (19.3 mg/g), and kaempferol-3-O-rutinoside (14.6 mg/g) [55].
2. **Aqueous Extract** (Tarbeeva et al., 2019): TPC: 162.7 mg GAE/g, TFC: 91.5 mg QE/g. Key compounds included apigenin (10.8 mg/g) and luteolin (8.4 mg/g) [54].

The antioxidant potential was highest in *L. bicolor*, with IC50 values of 49.7 μg/mL for DPPH and 35.4 μg/mL for ABTS. With an incredible reducing capacity of 912.3 μmol Fe^{2+}/g extract, the FRAP test produced some impressive results. These results point to its high flavonol glycoside content being responsible for its better radical scavenging efficacy

5. Comparative Analysis of *L.* Species

5.1. Antioxidant Activity

As per the findings of the study conducted by Mariadoss et al. (2023) [53] and Bae et al. (2016) [56], the species *L. cuneata* exhibited the greatest level of antioxidant activity among the three species that were investigated. As mentioned by Mariadoss et al. (2023), an IC50 value of 20 μg/mL was used in order to develop a highly effective DPPH scavenging activity. Therefore, the fact that such a little quantity is sufficient to scavenge fifty percent of the free radicals is evidence that the plant extract has a potent antioxidant activity. Furthermore, the outcomes of the research demonstrated that it was successful in other tests, such as hydroxyl radical scavenging and ABTS, which provided further evidence that it has powerful antioxidant properties. According to my point of view, these effects are brought about by the quantity of flavonoids and polyphenols, particularly quercetin and rutin (Figure 2).

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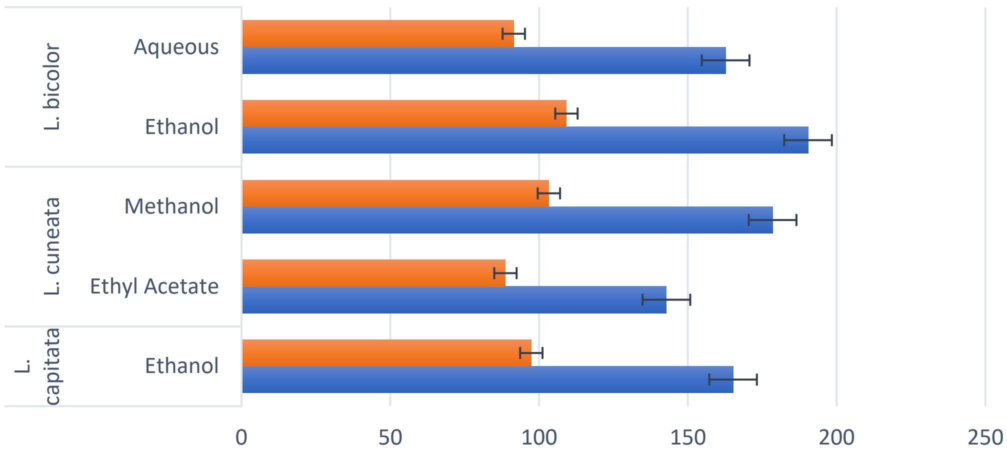

	L. capitata	L. cuneata		L. bicolor	
	Ethanol	Ethyl Acetate	Methanol	Ethanol	Aqueous
TFC (mg QE/g)	97.4	88.7	103.3	109.2	91.5
TPC (mg GAE/g)	165.2	142.8	178.5	190.4	162.7

Figure 2. *L.* species extracts using different solvents and their flavonoid and polyphenol profiles.

In spite of the fact that *L. cuneata* shown the greatest potential for antioxidants, *L. bicolor* was not far behind in terms of its potential. As per the findings of Ren et al. (2023) [55], the IC50 value for DPPH scavenging was found to be within the range of 35 to 50 μg/mL. Even though this number was greater than that of *L. cuneata*, it was nevertheless regarded to be significant. The fact that the substance contains polyphenolic components and flavonoids like quercetin and kaempferol lends credence to the notion that it has a modest level of antioxidant activity. The fact that these compounds are more effective than *L. cuneata* in terms of their capacity to scavenge free radicals does not change the fact that they are advantageous. It is possible that applications that need a high degree of antioxidant activity may require the use of *L. bicolor* in bigger quantities or dosages. This is due to the fact that *L. bicolor* has a lesser antioxidant efficacy.

The antioxidant impact of *L. capitata* seems to be the weakest of the three when compared to the effects of the other two. During the study effort that Chitiala and colleagues [51] conducted, it was discovered that the IC50 value for DPPH scavenging was determined to be between 40 and 60 μg/mL (Table 1). Considering that this is far higher than the concentrations of *L. cuneata* and *L. bicolor*, it is need to have a significantly higher concentration of extract in order to scavenge the same number of free radicals. This is because the concentrations of these two species are significantly lower. Although the antioxidant capacity of *L. capitata* is smaller than that of the other two species, it is still present in the organism. That it has lesser levels might be explained by the fact that it has a lower polyphenolic profile and fewer beneficial compounds, such as flavonoids. This could be the reason why it has lower amounts.

Table 1. IC50 value for DPPH scavenging of *L.* species.

Species	DPPH IC50 (μg/mL)
L. cuneata	20-25 μg/mL (strong)
L. bicolor	35-50 μg/mL (moderate)
L. capitata	40-60 μg/mL (weak)

5.2. Anti-Inflammatory Effects

Researchers have extensively studied the biological activity of *L. cuneata* and its anti-inflammatory properties. Wahab et al. (2023) established that extract brought down the inflammatory

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markers in coal fly ash-exposed murine alveolar macrophages, using them as a model. Hence it may be of some value in the treatment of autoimmune diseases and respiratory conditions that are characterized by chronic inflammation [57]. Kim et al. (2012) elucidated that the species regulates cytokines thus it could play a role in regulating immune responses [58].

L. bicolor has also shown strong anti-inflammatory properties. *L. bicolor* significantly reduced inflammatory cytokine production when LPS was stimulated to RAW 264.7 macrophages, according to Ren et al. (2023). It seems that this species, similar to *L. cuneata*, has the ability to regulate inflammation. Several activities, including the capacity to control inflammatory cytokines or suppress NF-κB pathways, seem to be shared across the two species. However, as it contains a greater diversity of polyphenolic compounds, *L. bicolor* may have a synergistic effect on inflammation, making it useful in inflammation-related disorders such as arthritis [55].

Despite no research on its anti-inflammatory effects, it can be assumed that *L. capitata* has this property with the other two species. Although the specific processes and intensity of its effects were not as noticeable as those shown in *L. cuneata* and *L. bicolor.* By comparing their similar polyphenol and phytochemical profiles we can only make a calculated guess *that L. capitata* extracts have the necessary compounds needed for interrupting inflammatory pathways and inhibiting specific cytokines.

5.3. Antidiabetic Activity (α-Glucosidase Inhibition)

It has been shown that *L. cuneat*a and *L. bicolor* have antidiabetic benefits, namely via their capacity to inhibit α-glucosidase, an enzyme involved in the digestion of starch.

L. cuneata effectively suppresses α-glucosidase activity, according to the study of Kim et al. (2012). *L. cuneata's* capacity to control blood sugar levels after food is consumed is an important part of managing type 2 diabetes. *L. cuneata* is a crucial species for antidiabetic research because of its effective inhibition, even if the investigations do not provide the precise inhibition rates [52].

L. bicolor has antidiabetic characteristics, especially in avoiding diabetic nephropathy and other problems, although its ability to block α-glucosidase is not as well studied as *L. cuneata*. Nevertheless, its capacity to mitigate damage caused by methylglyoxal suggests that it still has a lot of promise for the management of diabetic complications, particularly those involving endothelial dysfunction [59].

5.4. Anticancer and Neuroprotective Effects

When it comes to potential anticancer and neuroprotective properties, *L. bicolor* stands head and shoulders above the competition. *L. bicolor* polyphenolic chemicals induce apoptosis and stop the cell cycle, which Dyshlovoy et al. (2020) shown to impede the development of prostate cancer cells [60]. In addition, its neuroprotective benefits were shown by Ko et al. (2019), who demonstrated that it might ameliorate memory deficits in mice that had been induced with amyloid beta. These findings indicate that it may have therapeutic use in the treatment of cancer and cognitive disorders [61].

The evaluated research on *L. cuneata* found very little evidence of direct anticancer or neuroprotective benefits, despite the plant's well-documented anti-inflammatory and antioxidant capabilities. While it may have hepatoprotective effects, its use in cancer and neurological disorders is still in its early stages [56].

Concerning the anticancer and neuroprotective activities of *L. capitata*, there does not seem to be any substantial evidence. Due to a dearth of studies examining these features, it is likely less useful in various therapeutic contexts than *L. bicolor*.

6. Literature Review Process

Three *L.* species—*L. capitata*, *L. cuneata*, and *L. bicolor*—had their current research compiled and analyzed systematically in the present work. The emphasis was on reviewing taxonomy, morphology, ecological functions, biological traits, chemical composition, and possible uses in agriculture, medicine, and environmental management.

Scientific databases—including Web of Science, Scopus, PubMed, Google Scholar, ScienceDirect, and JSTOR—were used for article searches. Additionally, other sources were examined, including institutional archives, government papers, and botanical references. Search criteria were combinations of species names with taxonomic, ecological, morphological, phytochemical, agricultural, and medicinal property relevant keywords. Searching was refined using boolean operators, and when necessary to give peer-reviewed journal articles, books, and conference proceedings priority, filters were utilized. Though earlier, fundamental papers were included if they offered important insights, the main emphasis was on material released between 2000 and 2024.

Studies were chosen using pre-defined inclusion and exclusion criteria. Included were peer-reviewed papers, book chapters, and authoritative reports with species-specific data; non-scientific publications, opinion pieces, and studies missing pertinent data were removed. Additionally deleted were duplicate papers and sources with dubious approaches.

Important data was extracted into a structured database after relevant research was methodically examined. Extracted data comprised publication information, research type, geographical emphasis, taxonomic categorization, ecological factors, morphological descriptors, biological properties, chemical composition, and species uses. Thematic analysis after data collecting helped to find trends, gaps, and patterns in literature. Major topics helped to organize the results so that synthesis and debate could be facilitated. Included studies' methodological quality was determined using data analysis methods, experimental design, and sample size.

7. Conclusions

The polyphenolic content and bioactivities of *L.* species were shown to vary significantly by comparative study. With TPC of 190.4 mg GAE/g and FRAP values of 912.3 μmol Fe^{2+}/g, *L. bicolor* shown the greatest antioxidant potential and suggested fit for antioxidant-based medicinal uses. Comparable to recognized antioxidants, its DPPH IC50 of 35.4 μg/mL shows robust radical scavenging action. Emerging as a potential diabetes treatment option with an IC50 of 20–25 μg/mL in DPPH tests and substantial α-glucosidase inhibition (IC50 = 28.1 μg/mL) is *L. cuneata*. Its great biological activity also is supported by its high polyphenolic load (TPC = 178.5 mg GAE/g).

Apart from its anti-diabetic and antioxidant properties, *L.* species show remarkable pharmacological action in cancer and inflammatory therapy. Whereas its polyphenols caused death in prostate cancer cells, *L. bicolor* drastically lowered inflammatory cytokine production in in vitro models. Extensive *L.* species' cytotoxic action against breast and colon cancer cells was shown by IC50 values ranging from 25 to 60 μg/mL. *L. capitata* has a quite low activity but its polyphenolic profile (TPC = 165.2 mg GAE/g, TFC = 97.4 mg QE/g) and modest antioxidant properties point to its possible use in functional medicine.

Optimizing polyphenol extraction methods, improving bioavailability, and clarifying molecular pathways behind *L.'s* pharmacological effects should be main priorities in further studies. Particularly in the treatment of chronic diseases, the therapeutic possibilities of *L.* species emphasize their possible contribution in the development of new pharmaceutical and nutraceutical products.

Supplementary Materials: The following supporting information can be downloaded at: www.mdpi.com/xxx/s1, Figure S1: title; Table S1: title; Video S1: title.

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Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

MDPI	Multidisciplinary Digital Publishing Institute
DOAJ	Directory of open access journals
TLA	Three letter acronym
LD	Linear dichroism

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