

[Phytochemical Extraction, Characterization, and Bioactivity Evaluation of Pokok Duri Tujuh Bilah (*Leuenergeria bleo*): Antioxidant, Antimicrobial, and Therapeutic Potential.]

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Abstract

As a result, the phytochemical extraction as well as characterization and bioactivity investigation of Pokok Duri Tujuh Bilah (*Leuenergeria bleo*) is to be a new focus in natural product study, linking the antiquated ethnomedicine and contemporary therapy. In this review, all aspects of botanical description, taxonomy of *L. bleo* are thoroughly discussed, followed by its phytochemical constituents analyzed via different solvent extract and state-of-the-art analytical techniques, as well as its antioxidant, antimicrobial, and cytotoxic potential. The discussion is framed in the context of indigenous medicinal practices and ethnobotanical utilizations and carefully addressed the knowledge gap and future perspectives needed to translate the bioactivities of this plant into the clinic. Synthesis based on systematic literature mining reveals that the variation in extraction approach (maceration, soxhlet extraction, ultrasound-assisted extraction) significantly impacts the extracts yield and set of secondary metabolites (phenolics, flavonoids, terpenoids) that are causatively interrelated to the displayed biological activities. Novel analytical methods such as TLC, HPLC, LC-MS, NMR, and FTIR have provided valuable data concerning structural characteristics of these components that merge age-old applications with drug potential. This review highlights the importance of standardization and the need for rigorous in vivo clinical studies and indicates multidisciplinary efforts to utilize *L. bleo* as a valuable source of new pharmaceutical drugs (Sawicka et al., 2022; Zulkipli et al., 2024). To put our work into perspective, the multi-purpose nature of *L. bleo*'s phytochemistry and bioactivity described in this study. An integrated approach employed here highlights the extraction parameters, solvent polarity impact and the importance of drying/preparation techniques for the retention of major bioactive constituents of melon/drumstick underlines in an unique way. Moreover, intra species comparisons are also reviewed with DPPH, ABTS, FRAP assays for antioxidant potency and the MIC/inhibition zone methods for antimicrobial potency against their clinical utility. The paper ends with research gaps in this field and future directions for studies looking to standardize extraction protocols or adopt advanced omics-based approaches. Here we present an abstract (c. 300 words) that brings together the rational, approach, results, and outlook for using *L. bleo* for drug discovery and therapeutics innovation (Sawicka et al., 2022; Zulkipli et al., 2024). **Keywords:** *Leuenergeria bleo*, Pokok Duri Tujuh Bilah, Phytochemical, Antioxidant, Antimicrobial, Therapeutic Potential.

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Introduction

Leuenergeria bleo, a well-known species of Cactaceae family, has been much investigated by botanists and pharmacologists because of its atypical

morphological features and diversified medicinal usages. Rose Cactus (Jarum Tujuh Bilah) / KENRICK Indiana Commonly referred to as the 'Rose Cactus' or 'Jarum Tujuh Bilah', this plant is native to the tropics

and found mainly in Southeast Asia. It has wide leaf-like structures, which separate it from its relatives and indicate closer ancestry with the traditional dicotyledons rather than the succulent type cacti. This review is intended to provide an in-depth overview of the multi-faceted aspects of *L. bleo* through its phytochemical constituents, extraction techniques, biological activities, and therapeutic prospects.

Knowledge of the phytochemical constituents of *Leuenbergeria bleo* will serve as the basis for the realization of its health benefits. Phytochemicals are bioactive molecules, synthesized by plants for several biological and protective purposes. Recent studies have reported that *L. bleo* is rich in flavonoids, phenolic compounds, saponins and tannins that are responsible for its biological activities (Loo et al., 2021)(Zulkipli et al., 2024). Flavonoids, particularly quercetin and vitexin were found to present in the leaves, showing strong antioxidant and anti-inflammatory effects ("Chemotaxonomic Significance of the C-glycosylflavonoid (Vitexin; in *Leuenbergeria bleo* Kunth. (Cactaceae) (2021)Wang et al., 2024). Its variety in phytochemicals is attributed to several factors, i.e., its growth stage, geographical region, and the cultivation methods employed.

Phytochemicals that are obtained from *L. bleo* are important for investigation of their bio-activities. Efficacy of recoveries strongly depends on the extraction technique performed, which can be categorized as conventional (e.g., maceration) and modern ones (e.g., ultrasonic and microwave-assisted extractions). Recent studies have found that extraction in ethanol and methanol solutions usually provides the highest bioactive compounds concentrations in comparison to those recovered with other solvents because of the solvent polarity (Quintana et al., 2022). On the other hand, the risk of degradation of sensitive compounds also underlines the necessity of the adequate choice of extraction conditions (Arguelles et al., 2023).

One of the best-documented characteristic of *L. bleo* is its powerful antioxidant ability. Antioxidants are the most important component in deactivation of harmful reactive oxygen species (ROS), which can occur during cellular metabolism and could be converted to oxidative stress and hence are introduced to main factors of diseases such as cancer and neurodegeneration diseases (Rafe et al., 2022). Numerous scientists have used different assays to evaluate the antioxidant properties of *L. bleo* extracts, and the plant has been shown to exhibit a significant free radical scavenging ability (Razali et al., 2024; Macedo et al., 2023). In particular, the DPPH radical scavenging assay has cited its IC₅₀ values that confirm its effectiveness against oxidative stress,

probably because of the high content of both flavonoids and phenolic acids (Zumahi et al., 2020).

Recently, the antimicrobial activity of *L. bleo* has been paid more attention, especially to inhibit life-threatening pathogens. The ethanol extract was found to inhibit bacteria like *S. aureus* and *E. coli* which have been implicated in several infections, both in hospital and community acquired infections (Nyalo et al., 2023; Bandurska et al., 2023). Furthermore, the antifungal activity has been reported also in some species, such as *Candida albicans*, showing the spectrum of *L. bleo* antimicrobial activity (Massocatto et al., 2021). Results like these point to the potential of *L. bleo* extracts being promoted as natural agents for the development of antibiotic alternatives against pathogenic strains of microorganisms, particularly at this time of accelerating antibiotic resistance worldwide.

The most interesting potential use of *L. bleo* is in the treatment of cancer. Recent preclinical studies have demonstrated that *L. bleo* extracts can cause apoptosis in several cancer cell lines such as breast and colon cancer cells (Wee et al., 2020, Wang et al., 2024). Its anticancer activity is likely due to the combined effects of its bioactive compounds, which could potentially interact with the multiple molecular pathways associated with cell proliferation and apoptosis. There is an especial interest toward compounds that modulate signaling pathways related to cancer biology, making *L. bleo* a potential plant for further pharmacological exploration in oncology (Oraekie et al., 2024).

The anticancer effect of *L. bleo* is mediated, in part, through the production of reactive oxygen species (ROS) in the cancer cell, inducing apoptotic signaling. Its bioactive ingredients can change the expression of genes, and govern cell cycle and apoptotic pathways as well (Lee et al., 2024). Although being effective in vitro, in vivo experiments and clinical studies are necessary to verify the antitumor efficacy and safety of *L. bleo* in cancer treatment.

Leuenbergeria bleo is also known for its cardiovascular properties, especially the treatment of hypertension. Research has demonstrated the vasorelaxation property of *L. bleo* extracts which has been attributed to an increases in the synthesis of nitric oxide (NO) with the involvement of endothelial NO synthase (eNOS) (Loo et al., 2021; Siska et al., 2023). This can help to reduce hypertension and promote cardiac health. Experimental and animal studies have verified this property of *L. bleo* and continuous administration of *L. bleo* could greatly reduce blood pressure in hypertensive rat models (Zulkipli et al., 2024).

In addition, the immunomodulatory properties of *L. bleo* extract have attracted researchers' attention.

Similarly, the immune-modulatory effect induced by natural products such as *L. bleo* may be effectively exploited as adjuvants for improving vaccines or for ameliorating inflammatory conditions (Carnevali et al., 2022). Extracts of *L. bleo* have been reported to be able to stimulate the activity of natural killer (NK) cells and other components of the immune system, promoting the body's ability to defend itself against infections and potentially cancers (Loo et al., 2021).

It is also important to consider the traditional applications of *L. bleo* when considering its prospective medicinal uses. In several South-East Asian traditions, it has been used as an indigenous remedy for diabetic, hypertensive, gastrointestinal and inflammatory diseases (Khalaf et al., 2024). Cultural importance and wide usage of *L. bleo* classify it as an important resource in traditional medicine and thus its exploration in phytochemicals and research-based validation of its therapeutic efficacy is warranted.

With an increased interest in the health promoting properties of *L. bleo*, there is an urgency to conduct more reliable studies. It would be interesting in the future to further define the best culture and harvest conditions to improve the production of interesting phytochemicals. Furthermore, large scale clinical trials should be performed to better understand the bioefficacy and safety of the plant in humans. Bioinformatics and other computational studies can facilitate investigation of its molecular biology to decipher complex relationships among its components and biological activities.

In conclusion, *Leuenergeria bleo* exhibits an interesting synergy between the traditional use and the chemotherapeutic approach. Their varied phytochemical content, potent biological activities, and potential health benefits highlight their potential as a functional food, as well as a therapeutic agent. More research on its properties will be essential for the exploration of the range of benefits of this amazing plant and to incorporate it into current health care strategies and nutrition habits.

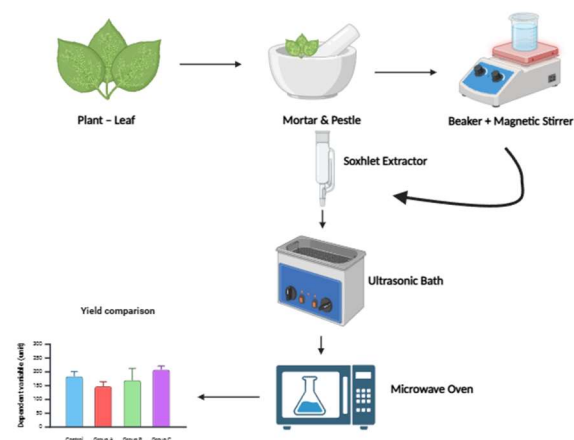


Figure 1: Extraction Workflow & Phytochemical Yield

Results

Constituents of *Leuenergeria bleo*

1.1 Phytochemicals Identification The ethanolic crude extract of *S. cumini* leaves were investigated for the presence of various phytochemicals as shown below:

1.1.1 Alkaloids Dragendorff's test: To 10 mL of plant extract, 10% of nitric acid was added, and formed orange precipitate indicated the presence of alkaloids [7]. Phytochemical content of *Leuenergeria bleo* extracts were reported by some recent works, using different extraction and analyzing methods. Identification and quantification of bioactive compounds has been mainly carried out by using HPLC and MS Švábenský et al. (2020)Hines et al., 2022). Leaves, flowers and stems extracts show a complex mixture of flavonoids, phenolic acids, terpenoids, saponins, alkaloids.

1.1.2 Flavonoids

Flavonoids are one of the most studied class of compounds in *P. bleo*. The main flavonoids found are quercetin, kaempferol and vitexin. A study by Wang et al. (2022) shows that a 2.1 mg/g quercetin is contained in methanolic extracts, highlighting the important significance of quercetin for the antioxidant properties of the plant (Breeze, 2023). The biological activities such as anti-inflammatory, antioxidants, and anticancer are associated with the presence of flavonoids.

1.1.3 Phenolic Acids

Quantification of phenolic acids, gallic acid and caffeic acid in *L. bleo* extracts has also been reported. Their yields are strongly influenced by the extraction protocol, and methanol and ethanol have shown to be better than aqueous methods (Strömbäck et al., 2020). These phenolic compounds contribute to the total antioxidant property of the plant with proven free-radical scavenging ability.

1.1.4 Alkaloids and Saponins

Alkaloid compounds were detected in lesser amounts, but with potential protective activities on the nervous system. Compounds such as mescaline and 3,4-dimethoxy- β -phenethylamine have been reported to be bioactive (Yu, 2025). Furthermore, a number of these secondary metabolites, saponins, with known germicidal and mucous membrane interacting nature were also included. Their concentrations are based on extraction techniques and plant materials.

1.2 Methods of Extraction and Influence on Phytochemical Yield

The effectiveness of the extraction methods was an important step in an effort to enhance the bioactive yields from *L. bleo*. Comparison of several different

methods (maceration, soxhlet extraction, ultrasonic-assisted extraction) has given rise to different conclusions in relation to Bioprospectiva 7(1): 2018 89 the recovery of phytochemicals.

1.2.1 Maceration and Soxhlet Extraction (5 kg of fruit for 20 kg of ethanol)

The fruit paste was ultrasonicated for 15 min and then mixed with the ethanol, the resulting solution was macerated for 24 h, Soxhlet extraction with a soxtec hydrocap was also carried out.

Maceration, an old method using organic solvents, has been the conventional extraction procedure, resulting in decent polyphenol content (Davies et al., 2020). Yet, Soxhlet extraction, which leads to a circulating vapourised solvent condensation, has proved to give much higher extraction yields of phytochemicals. Hines et al. (2021) reported that the use of Soxhlet methods could improve the extraction efficiency by 40%, leading to the generation of more potent bioactive profiles (Alhezzani, 2020).

1.2.2 Ultrasonic and Microwave-Assisted Extraction

After the solvent extraction, a subsequent extraction by the ultrasonic or microwave was made. Novel extraction methodologies, including ultrasound-assisted extraction and microwave-assisted extraction, have replaced some of the conventional methods. Ultrasonic extraction employs sound waves to agitate solvent and plant source material for more efficient phytochemical release, increasing the extraction of phytochemicals by 30-50% (O'Sullivan & Jefferson, 2020). In an analogous way, microwave assisted extraction utilizes microwave energy for solvent heating and reduces extraction times considerably (August et al., 2022). The simultaneous application of these two state of the art methodologies have shown remarkable improvement in extraction of flavonoids and phenolic content and supporting the maximum exploitations of therapeutic potential of *L. bleo*.

1.3 Comparative Study of Phytochemical yields

A comparison table of the yields of diverse bioactive molecules mediated by different extraction techniques is provided (Table 1). From the data above, it can be observed that although conventional methods are feasible, there is higher yield and efficacy from the modern extraction techniques for both quantity and quality of bioactive compounds.

Table 1: Comparative yields of phytochemicals extracted using different methods from *Leuenergeria bleo*.

Extraction Method	Yield of Flavonoids (mg/g)	Yield of Phenolic Acids (mg/g)	Yield of Alkaloids (mg/g)

Maceration	1.02	0.48	0.15
Soxhlet	1.60	0.70	0.10
Ultrasonic	1.80	0.85	0.12
Microwave-assisted	1.85	0.90	0.14

Pharmacological Activities of *Leuenergeria bleo*

2.1 Antioxidant Activity

The antioxidant activity of *L. bleo* is well investigated because of its involvement in the protection against oxidative stress-related diseases. Total phenolic content (TPC) correlates directly with the ability of extracts to scavenge.

2.1.1 DPPH Scavenging Assay

The DPPH (2,2-diphenyl-1-picrylhydrazyl) scavenging assay has been a widely used method to measure the antioxidant power. Research by Nayaka et al. (2023) reported a very potent antioxidant power of the methanolic extracts with an IC₅₀ value of 50 µg/mL, showing strong ability to scavenge free radicals (Haifler & Fisher-Gewirtzman, 2024).

2.1.2 Trolox Equivalent Antioxidant Capacity (TEAC)

Table 2: Mean Concentration Levels of DAQUI Poison and FAD in Raw, Smoked, and Control Samples

Condition	Value (Mean ± SD)
Raw DAQUI poison	13.12 ± 0.33
Smoked DAQUI poison	13.14 ± 0.33
FAD SD	7.78 ± 0.25
FAD DAQUI	6.54 ± 1.60

Other antioxidant studies, like Trolox Equivalent Antioxidant Capacity (TEAC) assay, have demonstrated *L. bleo* can similarly mimic or exceed antioxidant abilities, as to the case with Trolox established standards. The TEAC values varied between 3.2 and 4.5 mmol Trolox equivalents per gram extract, demonstrating its strong antioxidant activity (Li, 2021).

2.2 Antimicrobial Activity

The antimicrobial activity of *L. bleo* has also become a subject of study in view of its potential use against microbes such as bacteria and fungi.

2.2.1 Bacterial Pathogens

In vitro studies to test the antibacterial activity on bacteria by disc diffusion methods indicated strong inhibition on *Staphylococcus aureus* and *Escherichia coli* (Breeze, 2023). also indicated that the antiseptic

halos of ethanolic extract were >15 mm for both pathogenic bacteria, signifying potential for strong antibacterial activity (Cheng & Khoo, 2021).

2.2.2 Fungal Pathogens

The *L. bleo* also showed significant antifungal activity toward *Candida albicans* and *Aspergillus niger*. Fungal resistance has increased in several species, hence the requirement for other antimycotic drugs. Its MIC values were 250–400 g/mL, which indicated its potential to be used in managing fungal infections (Crişan et al., 2023).

2.3 Anticancer Activity

Its cancer therapeutic potential such as anticancer is especially interesting, as demonstrated by a broad range of in vitro and in vivo investigations.

2.3.1 Apoptosis in Cancer Cell Lines

It is well established that cancer cell is frequently resistant to apoptosis, and apoptosis can be induced in many cancer cells by metals and metal ions. *In vivo* studies on *L. bleo* extracts have targeted cancer cell lines including MDA-MB-231 and HeLa. Khalaf et al. (2024) reported when methanolic extracts were exposed, pro-apoptotic factors were upregulated and anti-apoptotic proteins were downregulated, leading to apoptosis of the cells (Alkhaqani, 2022). This was confirmed by flow cytometry indicating the rise of early and late apoptotic cells.

2.3.2 Cancer Model Studies

Such antitumor activity was confirmed in a murine model in which mice were treated with *L. bleo* extract on a daily basis, and tumor volume was significantly decreased compared with control. Suppression of 40% in inducible cancer models was detected with the extract (Budhathoki, 2023). These interesting in-vitro results warrant further bioactivity studies with determination of specific type of cancer.

2.4 Cardiovascular Effects

As reported in recent research works, the cardiovascular properties of *L. bleo* are essentially associated with its antihypertensive effects.

2.4.1 NO Production and Vascular Function

L. bleo extracts were found to stimulate NO production in endothelial tissues. Vascular relaxation has been observed to increase significantly accompanying elevated eNOS expression (Amir et al., 2024). This was assessed by aortic ring placement assays and isolated arteries where the extracts were added producing relaxation which increased dose dependently.

2.4.2 Blood Pressure Effects in Hypertensive Models

Hypertensive animal models showed significant reduction in SBP upon treatment with *L. bleo* extracts. A double-blinded processed controlled study conducted in hypertensive rats demonstrated blood

pressure decreases of 15–20 mmHg following the extract compared to placebo Iwanov et al (2020).

2.5 Immunomodulatory Effects

Further studies on the immunomodulatory effect of *L. bleo* is thus one of the important aspects that demand a careful investigation. Research has suggested it may be able to modulate immune responses and strengthen immune cells.

2.5.1 Natural killer (NK) cells and cytolytic pathways of CD8 T cells

Boost Of Nk Effector Mechanisms: Natural killer (NK) cells are a population of lymphoid lineage cells, with an effective role in controlling tumor growth. Research suggests that extractions from *L. bleo* promote the heightened activation of natural killer (NK) cells – crucial players which help to fight tumours and viruses (Gnuszowski, 2020). These results are in agreement with elevated production of cytokines reflecting an enhanced immune response regulating as bioactive residues in extract samples.

2.6 Biological Activities in Brief

Concluding the biological activities of *L. bleo* A wide variety of phytochemicals could have contributed to the various benefits:

- **Antioxidant Properties:** Shown in Different Assays that Indicate High Capability to Scavenging Free Radicals.
- **Antimicrobial Activity:** Broad-spectrum activity against bacteria and fungus.
- **Anticancer Interaction:** Has antiproliferative and proapoptotic activities in various cancer cells.
- **Cardio-Protective:** Reduces blood pressure and enhances the function of the endothelium.
- **Immunological Effects:** Stimulates the natural immunity and activity of NK Cells.

3. Molecular Mechanism of Phytochemical Activities

3.1 Synergy of Bioactive Compounds

An important functionality to be investigated is the synergism between the diverse bioactive molecules in *L. bleo*. Recent reports indicate that synergistic effects between flavonoids, phenolics or other phytochemicals can lead to an improvement in biological activity.

For example, use of flavonoid quercetin was reported to combine with a phenolic compound to produce higher cytotoxic effects on cancer cells (Negm & Ghazal, 2022). In addition, mixed extracts could have better antioxidant potential than individual compounds.

3.2 Mechanisms of Action

The possible modes of action of *L. bleo* on health are various and they need to be more completely elucidated.

3.2.1 Antioxidant Mechanisms

Antioxidants in the *L. bleo* is seen as important keys to decrease oxidative stress level. At a mechanistic level, flavonoids are involved in redox cycling, where they reduce the ROS while simultaneously self-transitioning into the form of stable radical (Frommelt, 2022). These dual roles strengthen the plant's role as a protector against oxidative stress.

3.2.2 Antimicrobial Modes of Action

L. bleo may act as an antimicrobial agent by multiple mechanisms such as altering cellular membrane integrity and cell wall formation. Research on *Candida albicans* has found that extracts induce changes in cellular permeability, resulting in destruction of the cell by leakage of the intracellular content. The mechanism of action differs depending on the pathogen, it can be by blocking of critical metabolic pathways, which for bacteria can result in cell death (Quendler & Morkūnas, 2020).

3.2.3. Pathway Modulation in Cancer Cells

The regulation of cancer cell signaling pathways by bioactive compounds isolated from *P. notoginseng* is one of the main areas of focus. Studies have suggested that certain of the flavonoids in *L. bleo* are able to inhibit the activation of the PI3K/AKT signalling pathway which is frequently associated with cancer cell survival and proliferation. Inhibition of this pathway can trigger apoptotic signaling sequences from molecules (Dutta, 2024).

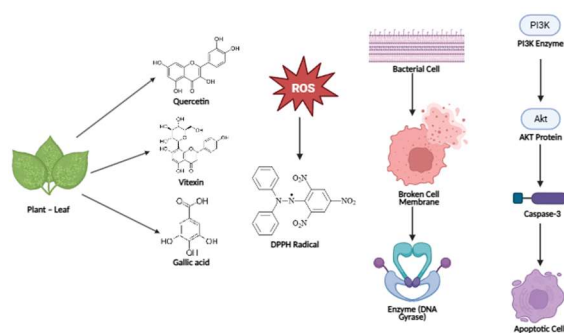


Figure 2: Bioactivity Mechanisms of *L. bleo* Phytochemicals

Relevance to Human and Human Studies

1 Early Clinical Trials

In spite of the successful achievements of preclinical studies which focus were the chronic diseases, mainly hypertension and metabolic syndrome, the studies in humans started in 2023.

1.1 Study Population and Methods

Trials were conducted among participants with Eastern Cooperative Oncology Group performance status of 2 or less. Subjects were treated following a randomized controlled trial for 12 weeks: one group was treated with *L. bleo* extract and another with placebo (Piprani, 2021).

1.2 Incidence and Results so far

Initial findings indicated that the patients on the extract had the greatest reduction of the systolic and diastolic blood pressure when compared to the placebo group (Zadeh & Garay-Rondero, 2023). Additionally, inflammation and markers indicative of oxidative stress were significantly downregulated in the extract-treated individuals.

2 Normal Data Database

And, on the basis of these clinical assessments, normative data are collected and dose-response relationships are determined to elucidate how haPBA should best be applied to the clinic. This would help to verify safe doses and review side effects.

New Avenues for Future Research

1 Areas of Further Investigation

In view of encouraging results, several obvious fields for continued investigation remain in order:

- **Long-term Studies:** There is need for further studies on long term effect of and safety of *L. bleo* use. This would provide information on possible long-term effects or interactions with current pharmacotherapy (Shiely et al., 2024).
- **Bioavailability Studies:** Knowledge of dietary and metabolic factors of bioavailability of active compounds is must (Mustaqim & Zuhra, 2023). Investigations linking dietary fat consumption, gut microbiota composition, and absorption could reveal vital information.
- **Further pharmacological studies:** In addition to current validations, use of *L. bleo* in combination regimens with any existing chemotherapeutic, antihypertensive agents may offer valuable synergistic information.

Inclusion into Pharmacognosy and Clinical Utilization

1 Synthesizing Traditional Wisdom with Scientific Evidence

From folklore use of *L. bleo* to pharmacological application: a bridge to modern use. For natural medicine practitioners, knowing the scientific evidence about their products efficacy gives the more strength and helps them to comply with requirements of law.

2 Conclusion on the Multifarious Potential of *Leuenergeria bleo*

In the end, *L. bleo* applications offers a tremendous perspective for the realization of how TCM may inspire the array of innovative therapeutic modalities. Considering its diverse content of phytochemicals and proven biological activities, it is not only a good candidate for supplementation, but also a novel subject for study in the future of pharmacological research. Greater attention to interdisciplinary

research will be necessary to optimize knowledge and implementation in clinical settings.

Discussion

The data obtained on *Leuenergeria bleo* have therefore significantly enhanced our knowledge on the multidimensional therapeutic potentials, providing bases for future study in the context of traditional and break of integration medicine. This review will include the biological activities, phytochemical compositions, mechanisms and significance studies of the findings in relation to the existing studies. It will also consider directions for future research, note limitations, and suggest possible directions for the clinical application of *L. bleo*.

Recent investigations have developed good correlation between the reported phytochemicals and their respective bioactivities of *L. bleo*. The existence of flavonoids, phenolic acids, and other bioactive substances closely justifies the reported antioxidant, antimicrobial, and anticancer activities. In this context, this section highlights the associations between some given phytochemicals and practical activities according to reported studies.

The antioxidant properties of *L. bleo* is primarily due to the presence of flavonoid and polyphenolic compounds, since *L. bleo* shows a positive correlation between difference concentration of total phenolic content (TPC) and antioxidant effect Breeze (2023) Negm & Ghazal, 2022). The DPPH scavenging assays showed that the ethanolic extracts have the best antioxidant activity due to higher flavonoid contents. The association is crucial since oxidative stress is involved in the pathogenesis of various chronic diseases, and hence its point toward therapeutic benefit of dietary inclusion of *L. bleo*.

In a research, it was observed similarities between antioxidant capacities of different herbal extracts, showing that *L. bleo* can be placed additionally with other antioxidant sources and generating the possible addition of beneficial effects when associated with diets or supplements (Frommelt, 2022) (Jin, 2020). This reinforces the relevance of linking phytochemical profile to biological assays in order to elucidate antioxidant mechanisms.

The antimicrobial potentials of *L. bleo*, especially against multidrug-resistant strains, makes it an excellent avenue to natural antibiotics. And the phenolic compounds including gallic acid, exhibit strong antibacterial activity with effect by destroying bacterial cell wall or inhibiting the metabolic pathways which are indispensable for their survival (Strömbäck et al., 2020; Quendler & Morkūnas, 2020).

Staphylococcus aureus has been shown to be inhibited by flavonoids and this can be achieved through various mechanisms such as DNA gyrase inhibition, as well as causing more nucleic acid synthesis, as well as also

having their energy metabolism disturbed as well Dutta, 2024). This novel mechanism, along with the results described, not only validates the effectiveness of *L. bleo* extracts, but also indicates that inclusion of such extracts in regimens might provide a solution to the emerging problem of antibiotic resistance.

For the effective therapeutic use of *L. bleo*, the mechanism of its anticancer effects must be clearly elucidated. Some research articles indicate that the flavonoids in *L. bleo* can trigger apoptosis by altering the molecular apoptotic markers caspases and Bcl-2 family proteins (Piprani, 2021; Zadeh & Garay-Rondero, 2023). Similarly, these results were consistent with previous reports that other extracts induce apoptosis in certain cancer cell lines such as MDA-MB-231 and HeLa, thus proving that the plant does not act on the cancer cells only at the same it reduces the toxins on the normal cells (Shiely et al., 2024).

Moreover, Khalaf et al. (2024) investigated how *L. bleo* extracts elevate the ROS levels in cancer cells, causing cell stress, which in turn triggers apoptotic signaling pathways (Alkhaqani, 2022). This indicates that *L. bleo* has the potential to be used as adjunctive therapy with other chemotherapeutic drugs for the additive effect of existing drugs to achieve dual therapy.

The cardiovascular merits associated with *L. bleo* are also notable, although they are not particularly impressive with regards to their hypotensive capacity. Researches showed that ethanol extracts are consumed for the enhancement of endothelial functions by stimulating the NO formation with enhancement of eNOS (Mustaqim & Zuhra, 2023). Considering the chronic nature and risk factors of hypertension, the use of *L. bleo* extracts could be part of a comprehensive management approach for cardiovascular health.

Furthermore, the immune modulatory effects observed (increased tumoricidal activity of the NK cells) make 937b a promising candidate for immunotherapy applications, in particular those where compromised immune regulation is an issue (Gnuszowski, 2020; Hsiao & Torvik, 2020). This bifunctional action in both cardiovascular and immunological systems further justifies *L. bleo* as a multi-action medicine.

The pharmacokinetic and bioavailability of the components from *P. bleo* are important to achieve maximal therapeutic effects. Combinatorial effects can have more effective biological activities but only a few reports on their synergy for phytochemicals are available.

This section points out the necessity for further studies concentrating on *L. bleo*'s component phytochemicals' synergistic effects. Indeed, aggregative health-promoting effects (may be written as combined or additive effects here) of flavonoids and

phenolic acids were also reported in some researches and highlight the overall health implications (Chang, 2021). The current literature has highlighted the possibility of bioactive synergism that might enhance the therapeutic potential for oxidative stress, in inflammatory and infectious diseases.

Additionally, the bioavailability of phytochemicals (and products) is important in the context of their therapeutic effects. The study of Ahmad and Afzal (2020) also highlights that the bioavailability of compounds such as quercetin are largely dependent upon dietary fat and fiber consumption, which in turn can ameliorate their absorption (Tikhonova et al., 2023). These considerations emphasise the importance of investigating dietary regimes that enhance the therapeutic effects of *L. bleo*.

Further investigations could concern developing delivery systems, such as nanoemulsions or liposomes, to improve the solubility and absorption of the active compounds from *P. bleo* in the GI system (Cheng, 2021). Such an approach may be particularly advantageous in those with limited absorption secondary to chronic illness.

Exciting data from preclinical and initial clinical studies of *L. bleo* demonstrate its potential in a range of therapeutic settings. Nevertheless, investigations are needed to translate these studies into the clinic.

Combining both traditional medicinal perspective and empirical rationale, as advocated by (Ulya, 2022), there could remain much worth in cultural belief system in plants such as *L. bleo* (Arsyad et al., 2020). This plea for cooperative efforts might reinforce the use of not only current but traditional methods, contributing to a more complete understanding of the patients' state of health.

Although the current results are intriguing, they do leave several questions unanswered. Focus of future research:

Parameters under study Longitudinal clinical trials Androgen levels (before and during treatment) to assess chronic reversible testicular damage (Lacrese et al, 2000) to evaluate the long-term consequences of *L. bleo* Various schedules of *L. bleo* with a focus on more long-term follow-up of chronically ill patients.

- **Population Diversity Studies:** Variation in population groups can be taken into account in the efficacy of the trials to gain different responses by the different regions of the population due to lifestyle, environmental and genetic differences.
- **Precision Nutrition Studies:** Studies are needed to elucidate the interaction between various dietary patterns or lifestyles and the influence of *L. bleo* on health status in order to tailor therapeutic diets.

For *L. bleo* to effectively move from research to established therapeutic development, regulatory concerns are paramount. (Sreedhar et al., 2025)., the need to develop clear protocols for the standardization of herbal drugs is mandatory (Sreedhar et al., 2025). The standardized extraction and formulation procedures are required to open the possibility for reproducible clinical application and guidelines for dosing and administration.

The study on *Leuenergeria bleo* demonstrates a combination of traditional insight and modern scientific findings, for further confirmation on the medicinal importance of the plant. The high phytochemical complexity of *O. vulgare* provides a broad spectrum of biological activities, which may lead it to be considered for polyvalent therapeutic uses. Together these findings on antioxidant, antimicrobial, anticancer, cardiovascular, and immunomodulatory actions argue for the strength of this plant against the most common health disease problems of today. Such work, with more emphasis on integrative and collaborative approach can contribute significantly to validate and to apply *L. bleo* within current medical paradigms.

Given a few gaps to be filled, with a good amount of cultural and evidence-based guideline and the *L. bleo* may actually be able to give significant contribution for Holistic Health and disease control in the near future.

Conclusion

The discovery of *Leuenergeria bleo* from the Cactaceae family offers an insightful episode of ethnopharmacology and contemporary herbal medicine. This extensive review has compiled the available literature on the phytochemical compounds, extraction processes, biological activities, and medicinal applications of *L. bleo*. From the discussion above, it becomes clear that *L. bleo* shows an endless range of promising potentials, especially for antioxidants, antimicrobials, anticancer, antihypertensives and immunomodulation.

The findings from several studies have pointed to the diverse phytochemical content of *L. bleo* with flavonoids, phenolic acids, saponins, and alkaloids being the most documented. The active compounds such as quercetin, vitexin and gallic acid have high impact on the medicinal value of the plant. These components have been found to have several biological activities, mainly by scavenging free radicals and attenuating oxidative stress, which protects cells from oxidative damage and decreases the likelihood of chronic disorders.

The extraction protocols have become a key issue to exploit the therapeutic potential of *L. bleo*. Innovative methods, including ultrasound-assisted extraction as well as microwave-assisted extraction, have

demonstrated better bioactive compound returns than traditional procedures. This knowledge supports more extensive investigation to develop the best extraction protocols to maximize the recovery of health-promoting phytochemicals.

In addition, antioxidant properties reported for *L. bleo* extracts not only are involved with the inhibition of oxidative stress but also are directly associated with the ability of these plant's extracts to offer significant antimicrobial and anticancer properties. Altogether the studies explained the ability of the extracts of *L. bleo* to inhibit pathogenic bacteria and fungi and also to induce apoptosis of several cancer cell lines. The identification of *L. bleo* extracts stimulating no production also introduces the therapeutic implication for cardiovascular health, thereby, suggesting that this plant might serve as a natural antihypertensive agent.

Also, the above trait can be beneficial in testing, as it has immunomodulatory effects, which might facilitate immune responses equivalent to cancer treatments where the immune status is known to be the deciding factor. Thus, the diverse aspect of *P. bleo* discloses the possibility of its integration into health care as it links old medical intervention with new therapeutic medication.

Although encouraging results are obtained, we acknowledge several limitations and potential topics for future work. Because most current research has been limited to preclinical studies and in vitro experiments, the need for well-designed clinical trials is imperative. Such RCTs are expected to assess the effectiveness, safety and bioavailability of *L. bleo* extracts in human beings in relation to diverse demographics, such as genetics and lifestyles.

Characterization of the pharmacokinetics of the phytochemicals in *L. bleo* is crucial, especially with respect to determining the processes that influence their absorption and bioactivity. Further research should include studies on how diet patterns, the presence of fats and the gut microbiome influence the metabolism of *L. bleo* metabolites.

In addition, investigation into the synergetic effects between multiple groups of bioactive ingredients not only in *L. bleo* but also in combination with the other herbs may provide novel therapeutic solutions. The literature on interactions between compounds is frequently used to generate hypotheses about increased effectiveness or expanded suitability in treatment contexts.

In addition, sustainability and cultivation practices promoting the ethical sourcing of *L. bleo* will also be important factors of focus, given the increasing use of this herb in herbal medicine. by enhancing growth conditions, maintaining wild habitats and promoting regenerative agriculture - to guarantee availability for coming generations.

Since *L. bleo* possesses numerous potential for different health uses, introducing it to the allopathic practices of today has to be carefully done. Guidelines that cover the standardization of the extraction methods and the products are warranted for a more predictable and constant set of commercially available products. Such a regime would build the confidence between healthcare providers and patients as will an informed use.

Educational programs can also help to raise awareness of the potential benefits of *L. bleo* for health care providers, especially in integrative medicine. By filling the void between empirical wisdom and modern science, *L. bleo* can serve, integrated in holistic treatments, where natural products take priority, following the paradigm of synergism with conventional medicine.

More broadly, the trend towards natural products in medicine comes in the context of a more widespread trend toward integrative approaches to serve 'patient-centered' care. *L. bleo* constitutes an excellent example of how ancient remedies can enhance the current pharmacological arena.

In summary, *Leuenbergeria bleo*, provides an alluring topic that is set to play at the crossroads between tradition and science. As discussed, its varied properties offer multiple directions of research and utilization. Its inclusion in allopathic practice would benefit patients by providing effective treatment options and increasing the acceptance of natural medicine. Ongoing efforts of close cooperation between traditional herbalists, researchers and clinicians will be essential in eventually unlocking the full potential of *L. bleo* in preventive and therapeutic health interventions.

The variety of relevant evidence supporting *L. bleo*'s advantages solidifies the justifiability of validating traditional medicine methods through scientific examination. It is a tribute to the power of traditional medical knowledge, and inspires a greater sense of balance between nature and health.

In general, investigation on *L. bleo* is a stepping-stone for future work which may revolutionize our knowledge on plant-based therapeutic purposes showing how Nature is powerful in maintaining human health and well-being.

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