Exploring the Therapeutic Treasure Trove of Bergenia ligulata: Unveiling the Potential of Indian Rhubarb

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ABSTRACT

Bergenia ligulata, commonly known as Indian rhubarb or Paashaanbhed, is a perennial herb native to the Himalayan region and widely distributed in the alpine regions of India, Nepal, and Bhutan. It belongs to the family Saxifragaceae and is characterized by large, leathery leaves and pink flowers. Traditionally, various parts of Bergenia ligulata have been used in Ayurveda, traditional Chinese medicine, and folk medicine systems for their medicinal properties. One of the key bioactive constituents identified in Bergenia ligulata is bergenin (C₁₄H₁₆O₉), a naturally occurring glycoside. Bergenin, also known as cuscutin or isocynodontin, is a white crystalline compound that exhibits a wide range of pharmacological activities. It has drawn significant attention from researchers and pharmaceutical industries due to its diverse biological properties and potential therapeutic applications. Bergenin has been the subject of numerous scientific studies exploring its antibacterial, antifungal, antioxidant, anti-inflammatory, hepatoprotective, antidiabetic, and other pharmacological activities. These properties make bergenin a promising candidate for the development of novel therapeutic agents for various ailments. In this article, we aim to provide a comprehensive overview of Bergenia ligulata, with a focus on bergenin, including its biological source, traditional uses, pharmacological importance, extraction methods, solvent selection, and analytical techniques for quantification. Additionally, we will delve into the analytical significance of High-Performance Thin-Layer Chromatography (HPTLC) in the extraction and quantification of bergenin from Bergenia ligulata.

Keywords: Bergenia ligulata, High-Performance Thin-Layer Chromatography (HPTLC), Extraction methods, and Solvent selection.

INTRODUCTION

Bergenia ligulata, also known as Indian rhubarb or Paashaanbhed, is a perennial herbaceous plant belonging to the family Saxifragaceae. It is indigenous to the Himalayan region and is found abundantly in the alpine regions of India, Nepal, and Bhutan. The plant typically grows in damp, shady areas, along streams, and in forest clearings at elevations ranging from 2,500 to 4,000 meters above sea level.[¹] The morphology of Bergenia ligulata is characterized by large, fleshy, and ovate leaves that are leathery in texture and often have a reddish tint. The plant produces erect flower spikes bearing small pink flowers with five petals. Bergenia ligulata is known for its robust growth and ability to thrive in harsh mountainous climates. Traditionally, various parts of Bergenia ligulata have been used in folk medicine systems for their medicinal properties.[²] The rhizomes and roots of the plant are particularly valued for their therapeutic benefits and have been employed in traditional remedies for urinary disorders, kidney stones, gastrointestinal ailments, and inflammatory conditions. The rich phytochemical composition of Bergenia ligulata contributes to its medicinal properties. Bergenin, the major bioactive compound
found in the plant, along with other secondary metabolites such as flavonoids, tannins, and phenolic compounds, accounts for its pharmacological activities.\[3\] The cultivation and sustainable harvesting of *Bergenia ligulata* have garnered attention to meet the growing demand for medicinal plants while conserving biodiversity and supporting local communities. Efforts are underway to promote the cultivation of *Bergenia ligulata* as a valuable medicinal crop and to explore its potential for economic development in the regions where it is endemic.

**Phytochemistry of *Bergenia ligulata***

*Bergenia ligulata*, commonly known as Paashaanbhed or Indian Rhubarb, is a medicinal plant with a rich chemical composition. The primary bioactive constituent of *Bergenia ligulata* is bergenin (also known as bergeninol or cuscutin), a polyphenolic compound belonging to the class of ellagic acid derivatives. Bergenin is primarily found in the rhizomes of *Bergenia ligulata* and contributes to its pharmacological properties.\[4\]

**Chemical Structure:** Bergenin is chemically characterized as 4-O-glucopyranosyl-2,3,4-trihydroxybenzopyranone, with a molecular formula C₁₄H₁₈O₉ and a molecular weight of 326.29 g/mol. It consists of a glucose moiety attached to the C-4 position of a benzopyran one-ring.\[5\]

**Other Phytoconstituents:** Besides bergenin, *Bergenia ligulata* contains various other phytochemicals with pharmacological significance, including flavonoids, tannins, saponins, alkaloids, and triterpenoids. These secondary metabolites contribute to the overall therapeutic effects of *Bergenia ligulata* extracts and formulations.\[6\]

**Mechanism of Action:** The pharmacological effects of bergenin are attributed to its ability to modulate various cellular pathways and biochemical processes. Bergenin exerts anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines and mediators, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and nitric oxide (NO). Additionally, bergenin demonstrates antioxidant activity by scavenging free radicals and enhancing the activity of endogenous antioxidant enzymes, such as superoxide dismutase (SOD) and catalase (CAT).\[7\]

**Traditional Uses and Pharmacological Importance**

*Bergenia ligulata* and its bioactive constituent bergenin have been valued for centuries in traditional medicine systems for their diverse therapeutic properties. Across various Indigenous healing practices, this herb has been employed to address a wide range of ailments, owing to its potent pharmacological effects.\[8\]

**Reported activity:** The pharmacological importance of *Bergenia ligulata* and bergenin extends beyond these mentioned areas, with ongoing research exploring their potential in cancer therapy, metabolic disorders, and other health conditions. The elucidation of their mechanisms of action and therapeutic potential continues to fuel interest in these natural remedies.\[9\]

**Urinary Disorders and Kidney Stones:** One of the primary traditional uses of *Bergenia ligulata* is in the management of urinary disorders, including urinary tract infections (UTIs), cystitis, and nephrolithiasis (kidney stones). The plant is believed to possess diuretic, anti-inflammatory, and antimicrobial properties, which help alleviate symptoms associated with urinary conditions and promote renal health.\[10\]

**Gastrointestinal Ailments:** In traditional medicine, *Bergenia ligulata* has been utilized to treat various gastrointestinal disorders such as dysentery, diarrhea, and gastritis. Its astringent and anti-diarrheal properties are believed to provide relief from abdominal discomfort and promote digestive health.\[11\]

**Anti-inflammatory and Analgesic Effects:** Extracts of *Bergenia ligulata* have demonstrated significant anti-inflammatory and analgesic activities in preclinical studies. These properties make it valuable in the management of inflammatory conditions such as arthritis, rheumatism, and musculoskeletal pain.\[12\]

**Antioxidant and Hepatoprotective Actions:** Bergenin, the principal bioactive compound in *Bergenia ligulata*, exhibits potent antioxidant
properties, scavenging free radicals and protecting cells from oxidative damage. Additionally, it has been shown to possess hepatoprotective effects, guarding against liver damage induced by toxins and oxidative stress.[7]

**Antidiabetic Activity:** Research suggests that *Bergenia ligulata* and bergenin may have potential in the management of diabetes mellitus. Studies have demonstrated their ability to lower blood glucose levels, improve insulin sensitivity, and protect pancreatic beta cells from damage, offering a promising avenue for the development of novel antidiabetic therapies.[13]

**Anti-urolithiasis and Nephroprotective Effects:** *Bergenia ligulata* extracts have shown promise in preventing and dissolving urinary calculi (stones) and protecting against nephrotoxicity. These effects are attributed to the herb's ability to inhibit crystal formation, enhance urinary excretion of calculi, and reduce renal oxidative stress.[14]

**Antimicrobial and Antifungal Properties:** Both *Bergenia ligulata* and bergenin exhibit antimicrobial activity against a wide spectrum of bacteria, fungi, and viruses. This antimicrobial action makes them valuable in the treatment of infectious diseases and in promoting overall immune function.[15]

**Cardioprotective and Neuroprotective Effects:** Preclinical studies have indicated that bergenin possesses cardioprotective properties, offering protection against ischemic heart injury and myocardial infarction. Furthermore, bergenin has shown neuroprotective effects, exerting a beneficial influence on neurological disorders such as Alzheimer's disease and cerebral ischemia.[16]

Bergenin has been investigated for its therapeutic potential in the management of inflammatory disorders (e.g., arthritis, colitis), liver diseases (e.g., hepatitis, cirrhosis), kidney diseases (e.g., nephritis, renal failure), metabolic disorders (e.g., diabetes, hyperlipidemia), hyperuricemia, microbial infections (e.g., bacterial, fungal), and certain types of cancer (e.g., breast cancer, lung cancer). Clinical studies and preclinical research support the use of bergenin-containing herbal preparations and bergenin-rich extracts in traditional medicine and modern pharmacotherapy.[17]

**Analytical Techniques and Extraction Methods**

**High-Performance Thin-Layer Chromatography (HPTLC):** High-performance thin-layer Chromatography (HPTLC) stands out as a powerful analytical technique for the qualitative and quantitative analysis of bergenin and other phytoconstituents present in *Bergenia ligulata* extracts.[18]

**Principle and Method Development**

HPTLC is a chromatographic technique extensively used for the separation and quantification of plant constituents, including bergenin. The developed and validated an HPTLC method for bergenin estimation in *Bergenia ligulata*. The method involved optimization of the mobile phase and stationary phase for optimal separation of bergenin from other components.[19] HPTLC has been widely employed in the quality control and standardization of herbal medicines containing *Bergenia ligulata*, ensuring the consistency and efficacy of these products. Moreover, HPTLC methods have been developed to detect adulterants and assess the authenticity of *Bergenia ligulata* raw materials and finished products in the herbal industry.[20]

**Solvent Selection**

The selection of an appropriate solvent system is critical in HPTLC for efficient solvation of bergenin. Various solvent systems with differing polarities have been evaluated for bergenin extraction and solvation.[21] The choice of solvent system depends on factors such as bergenin polarity, the presence of interfering compounds, and desired peak resolution. Common solvents used include methanol, ethanol, and their combinations with water or other organic solvents. HPTLC offers several advantages, including high sensitivity, rapid analysis, cost-effectiveness, and the ability to analyze multiple samples simultaneously.[21]

**Extraction Methods for Bergenin:** In HPTLC, a small volume of the sample extract or standard solution containing bergenin is applied as a spot onto a thin layer of adsorbent material, typically silica gel or cellulose, on a glass plate or aluminum
sheet. The plate is then developed in a solvent system, allowing the components of the sample to separate based on their differential partitioning between the stationary and mobile phases. After development, the plate is dried, and the separated bands are visualized using suitable detection methods, such as UV absorption or derivatization with specific reagents.\[22\]

Quantitative analysis of bergenin in *Bergenia ligulata* extracts by HPTLC involves the preparation of calibration curves using standard solutions of known concentrations. The peak areas or peak heights corresponding to bergenin spots on the chromatogram are measured and compared with those of the standard solutions to determine the concentration of bergenin in the sample extract.\[19\]

**Extraction Techniques**

Several extraction techniques are employed for the isolation of bergenin from *Bergenia ligulata* plant material, aiming to obtain high yields of pure bergenin for pharmaceutical and research purposes.\[23\] Some commonly used extraction methods include:

**Soxhlet Extraction:** Soxhlet extraction involves the repeated cycling of a solvent between a siphon reservoir and a sample chamber containing the plant material. This continuous extraction process allows for efficient extraction of bergenin and other constituents from *Bergenia ligulata*. Common solvents used in Soxhlet extraction include methanol, ethanol, and water.\[24\]

**Advantages:**

- **Efficient extraction:** The continuous cycling of solvent allows for thorough extraction of bergenin and other compounds from the plant material.\[25\]
- **High yield:** Soxhlet extraction typically yields a high quantity of extract, making it suitable for large-scale production.\[26\]

**Disadvantage:**

- **Time-consuming:** Soxhlet extraction requires extended extraction periods, which can prolong processing time.\[27\]

**Solvent consumption:** The process utilizes a significant amount of solvent, leading to increased environmental impact and operational costs.

**Maceration:** Maceration involves soaking the *Bergenia ligulata* plant material in a solvent for an extended period to allow the dissolution of bergenin and other active compounds. The macerate is then filtered, and the solvent is evaporated to obtain the crude extract, which can be further purified to isolate bergenin.\[23\]

**Advantages:**

1. **Simple technique:** Maceration is a straightforward extraction method that requires minimal equipment and expertise.
2. **Cost-effective:**

**Disadvantages:**

- **Longer extraction time:** Compared to other methods, maceration may require longer soaking periods to achieve optimal extraction.
- **Lower efficiency:** It may result in lower extraction efficiency compared to more advanced techniques like Soxhlet extraction or UAE.

**Ultrasound-Assisted Extraction (UAE):** UAE utilizes ultrasonic waves to enhance extraction efficiency by disrupting cell walls and promoting the release of bergenin from *Bergenia ligulata* tissues. This technique offers shorter extraction times and higher yields compared to conventional methods.\[28\]

**Supercritical Fluid Extraction (SFE):** SFE utilizes supercritical fluids, such as carbon dioxide (CO2), as solvents to extract bergenin from *Bergenia ligulata* under high pressure and temperature conditions. SFE offers advantages such as selective extraction, minimal solvent residues, and environmentally friendly operation.\[29\]

**Advantages:**

- **Selective extraction:** SFE allows for the selective extraction of bergenin while leaving behind unwanted compounds, resulting in a purer extract.
Minimal solvent residue: As supercritical fluids such as carbon dioxide are used, SFE produces extracts with minimal solvent residues, enhancing product purity.

Disadvantages:

High equipment cost: SFE equipment is expensive to purchase and maintain, making it less accessible for small-scale operations.

Complex operation: Operating under supercritical conditions requires specialized training and expertise, adding complexity to the extraction process.

The choice of extraction and analytical methods depends on several factors, including the desired purity of bergenin, the scale of extraction, cost considerations, and environmental impact. Soxhlet extraction, while efficient, is best suited for large-scale production due to its time-consuming nature and high solvent consumption. Maceration, being simple and cost-effective, is ideal for small-scale extractions but may not be as efficient. UAE and SFE represent advanced techniques that offer higher efficiency and selectivity but require significant investment in specialized equipment and expertise.[30] HPTLC remains a crucial tool for the analysis of bergenin, ensuring the quality control and standardization of extracts. The development of robust HPTLC methods facilitates the detection of adulterants and ensures the authenticity of raw materials and finished products, thereby maintaining the efficacy and safety of herbal medicines.[31]

Future Perspectives: Bergenia ligulata, has demonstrated significant potential as a medicinal plant due to its diverse phytochemical profile and the wide range of pharmacological activities exhibited by its constituents, particularly bergenin. The traditional uses of Bergenia ligulata, in treating urinary disorders, gastrointestinal ailments, and inflammatory conditions are well-supported by scientific research that highlights its diuretic, anti-inflammatory, and antimicrobial properties. The presence of other bioactive compounds, such as flavonoids, tannins, and saponins, further contributes to the plant's therapeutic efficacy. Modern analytical techniques, such as HPTLC, play a crucial role in the standardization and quality control of Bergenia ligulata, extracts, ensuring the consistency and reliability of herbal medicines. The development of efficient extraction methods, including Soxhlet extraction, maceration, UAE, and SFE, facilitates the isolation of bergenin and other phytoconstituents, enabling their use in pharmaceutical formulations and research.

CONCLUSION

Bergenia ligulata, with its rich phytochemical composition and diverse pharmacological activities, holds significant promise in both traditional and modern medicine. The primary bioactive compound, bergenin, along with other secondary metabolites, contributes to the plant's therapeutic potential. The application of advanced analytical techniques and optimized extraction methods ensures the effective utilization of Bergenia ligulata developing novel therapeutic agents. Continued research and sustainable cultivation practices will further enhance the understanding and utilization of this valuable medicinal plant, promoting health and economic development in regions where it is endemic.

Conflicts of Interest: The authors declare that there are no conflicts of interest.

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