

# The Protective Role of Silver Nanoparticles and Centella Asiatica Extract in Hypertension Management: A Literature Review

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## ABSTRACT

Hypertension remains a leading global health issue, affecting over 1.28 billion adults and necessitating innovative therapeutic strategies. This study explores the synergistic potential of silver nanoparticles (AgNPs) and Centella Asiatica extracts in hypertension management through a comprehensive systematic literature review. AgNPs offer precision and enhanced bioavailability in drug delivery, exhibiting antioxidative and anti-inflammatory properties essential for cardiovascular protection. Similarly, Centella Asiatica, a traditional herbal remedy, provides comparable efficacy to conventional antihypertensive drugs by targeting oxidative stress, modulating the renin-angiotensin system, and enhancing nitric oxide production. Despite their potential, challenges such as nanoparticle toxicity and the need for optimized herbal extraction methods remain critical. Experimental evidence supports the efficacy of these interventions in reducing blood pressure and protecting against hypertension-induced organ damage. The integration of nanotechnology and herbal medicine presents a promising, personalized therapeutic paradigm, addressing both the complexity and variability of hypertension pathophysiology. Future research must emphasize safety, precision, and sustainability in developing these innovative approaches. By incorporating advanced nanotechnological methods and traditional medicinal wisdom, this study paves the way for a more holistic and effective hypertension management framework.

**Keywords:** hypertension; silver nanoparticles; Centella Asiatica; nanotechnology; cardiovascular protection.

## INTRODUCTION

Hypertension represents a critical global health challenge characterized by persistent elevation of blood pressure within the cardiovascular system. The global epidemiological landscape reveals a significant increase in hypertension prevalence across both developed and developing regions. According to recent epidemiological assessments, approximately 1.28 billion adults aged 30-79 years are affected worldwide, with a disproportionate burden observed in low- and middle-income countries (Oparil & Schmieder, 2015).

The pathophysiological complexity of hypertension encompasses intricate biological mechanisms, including endothelial dysfunction, oxidative stress, systemic inflammation, and renin-angiotensin-aldosterone system activation. Traditional pharmacological interventions often encounter limitations such as substantial side effects and suboptimal patient compliance, motivating contemporary research to explore alternative and complementary therapeutic strategies that offer

targeted cardiovascular protection with minimal adverse consequences (Jones et al., 2021).

Emerging innovative approaches in hypertension management have increasingly focused on integrating nanotechnology and phytopharmaceutical interventions. Silver nanoparticles (AgNPs) and Centella Asiatica extract have demonstrated remarkable potential in providing multifunctional cardiovascular protection. Silver nanoparticles exhibit unique properties, including potent antimicrobial, anti-inflammatory, and antioxidant characteristics. Contemporary research substantiates their capacity to mitigate oxidative stress, suppress reactive oxygen species (ROS) production, and enhance endothelial function—critical mechanisms directly influencing blood pressure regulation (Preetha et al., 2023).

Centella Asiatica, a botanically rich herbal plant deeply rooted in traditional Ayurvedic and Southeast Asian medicinal practices, presents promising pharmacological potential for hypertension management.

Its bioactive constituents, including triterpenoids, flavonoids, and phenolic compounds, demonstrate significant antioxidant and anti-inflammatory properties. Recent scientific investigations have elucidated the compound's ability to modulate cellular signaling pathways associated with nitric oxide formation, vascular relaxation, and oxidative stress mitigation (Prasad et al., 2022).

The synergistic combination of silver nanoparticles and *Centella asiatica* extract represents an innovative therapeutic approach with comprehensive protective mechanisms. This integration offers potential advantages through multiple complementary pathways: AgNPs can enhance the stability and bioavailability of *Centella asiatica*'s active compounds, while the plant extract simultaneously reinforces the cardiovascular protective effects of silver nanoparticles (Z. Zhang et al., 2022). Molecular-level interactions involve sophisticated (Jones et al., 2021) cellular modulation mechanisms. Key potential mechanisms include suppressing proinflammatory cytokine expression (TNF- $\alpha$  and IL-6), stimulating antioxidant enzyme production (superoxide dismutase and catalase), and modulating the NF- $\kappa$ B signaling pathway integral to inflammatory responses. Experimental studies consistently demonstrate the combination's capacity to significantly reduce inflammatory markers and augment antioxidant capabilities (Li et al., 2021). The research confronts critical challenges, including nanoparticle formulation optimization, precise chemical-physical characterization, and rigorous clinical validation. A truly multidisciplinary approach integrating nanotechnology, herbal pharmacology, and cardiovascular physiology is imperative to comprehensively understand this innovative therapeutic potential (Kumar et al., 2023).

Genetic diversity and environmental factors significantly contribute to hypertension pathogenesis, rendering nanobiotechnology-based interventions particularly compelling. Emerging research highlights the critical role of epigenetic modifications in blood pressure-related gene expression. Silver nanoparticles and *Centella asiatica* extract demonstrate potential for complex epigenetic modulation, including histone modification regulation and microRNA expression associated with blood pressure control (W. Zhang et al., 2018). The molecular interaction mechanism suggests a sophisticated synergistic potential. Advanced pharmacokinetic studies reveal that this combination may enhance biodistribution and cellular penetration, enabling more targeted therapeutic interventions. Silver nanoparticles function as efficient carriers for *Centella asiatica*'s bioactive compounds, facilitating targeted molecular transport and enhancing compound stability during metabolic processes (Lee et al., 2023).

Immunological considerations remain paramount in hypertension management. The combination's ability to modulate systemic inflammatory responses offers promising strategies for minimizing endothelial dysfunction. By regulating

proinflammatory and anti-inflammatory cytokine production—suppressing TNF- $\alpha$  and IL-6 while increasing anti-inflammatory cytokines like IL-10—this approach presents a comprehensive therapeutic strategy (dos Passos et al., 2024). Beyond blood pressure reduction, clinical challenges encompass protecting critical target organs, including the kidneys, heart, and vascular system. The nanobioactive approach demonstrates significant potential for multiorgan protection through oxidative stress reduction, fibrosis prevention, and strategic modulation of cellular signaling pathways associated with chronic hypertension-induced organ damage.

The personalized medicine paradigm increasingly drives hypertension management, recognizing individual variability in pharmacological therapy responses. Silver nanoparticles and *Centella asiatica* extract offer unprecedented flexibility in therapeutic design, enabling precise adaptation to individual genetic and metabolic profiles. Clinical implications extend beyond primary hypertension management, potentially addressing associated comorbidities such as diabetes, obesity, and dyslipidemia. By integrating nanobiotechnology and phytopharmacology, this research aspires to develop a comprehensive, sustainable intervention strategy that addresses the multifaceted nature of cardiovascular health.

## METHOD

This study utilized a comprehensive systematic literature review (SLR) approach to explore the protective role of silver nanoparticles and *Centella asiatica* extract in hypertension management. The systematic literature review methodology was chosen to provide an in-depth and systematic synthesis of the current scientific evidence available in the international scientific literature. The literature search and selection process were conducted through several leading electronic databases, including PubMed, Scopus, Web of Science, and ScienceDirect. The search strategy was designed in a complex manner using a combination of specific keywords that included: "silver nanoparticles", '*Centella asiatica*', 'hypertension management', 'cardiovascular protection', 'oxidative stress', and 'nanomedical interventions'. The search was conducted using boolean operators such as AND, OR to ensure comprehensive coverage and precision of search results.

Literature inclusion and exclusion criteria were strictly set to ensure the quality and relevance of the articles analyzed. Inclusion criteria included: (1) English research articles, (2) publications from 2020 to 2024, (3) articles focusing on silver nanoparticles and/or *Centella asiatica* interventions in the context of hypertension, (4) articles from peer-reviewed accredited journals, and (5) articles with experimental, clinical, or systematic review research methods. The literature screening process was conducted through several systematic stages referring to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

protocol. The stages began with the elimination of duplicate articles, followed by title and abstract assessment, then full-text articles that fit the criteria were analyzed in depth. Each selected article was assessed for quality using comprehensive methodological assessment criteria.

Data extraction was conducted using a standardized extraction instrument, collecting specific information including study design, sample characteristics, interventions provided, main outcomes, and key findings from each article. Data analysis was conducted narratively and qualitatively, identifying patterns, themes, and research gaps in the literature. The methodological quality of the articles was assessed by considering several critical aspects, such as internal validity, rigor of the research design, statistical significance, and potential bias. Each article was given a quality score based on systematic assessment criteria that considered methodological aspects, reproducibility, and strength of scientific evidence.

Synthesis of research findings was conducted using a thematic approach, integrating results from various articles to produce a comprehensive picture of the role of silver nanoparticles and *Centella asiatica* extract in hypertension management. The analysis was conducted with attention to the molecular mechanisms, therapeutic potential, as well as the clinical implications of the interventions discussed.

## RESULT

Hypertension remains a critical global health challenge, demanding innovative and multifaceted approaches to management and treatment. Recent advancements in nanotechnology and herbal medicine have opened new frontiers in understanding and mitigating cardiovascular risks associated with this complex physiological condition. The convergence of cutting-edge nanoscientific techniques and traditional herbal interventions presents a promising paradigm for personalized hypertension management. Emerging research has demonstrated the potential of novel therapeutic strategies that extend beyond conventional pharmaceutical interventions. *Centella asiatica*, a well-studied herbal remedy, has garnered significant attention for its remarkable hypotensive properties. Studies by (Mohebbati, Hosseini, et al., 2020). provide compelling evidence of its ability to modulate the renin-angiotensin

system, effectively reducing blood pressure in experimental models. This is further corroborated by (Murhekar et al., 2021), who highlight the herb's cost-effective and safer profile compared to traditional pharmaceutical treatments.

Simultaneously, nanotechnology has emerged as a transformative approach in medical intervention (Roy et al., 2022). emphasize the potential of nanotechnology in delivering personalized healthcare, offering precision diagnostics and tailored therapeutic strategies. However, the application of silver nanoparticles (AgNPs) in hypertension management requires nuanced consideration. (Taslina et al., 2022). caution about the potential thrombotic effects and oxidative stress induced by PEG-coated silver nanoparticles in hypertensive models, underscoring the critical need for comprehensive safety evaluations. The protective mechanisms of *Centella asiatica* extend beyond its direct hypotensive effects. (Buranasudja et al., 2021). revealed the herb's significant antioxidant properties, demonstrating its capacity to enhance antioxidant enzyme expression and mitigate oxidative damage. This characteristic is particularly relevant in the context of hypertension-related oxidative stress, suggesting a multifaceted approach to cardiovascular health management.

Experimental studies, such as those conducted by (Bunaim et al., 2021), provide robust evidence of *Centella asiatica*'s efficacy. Their research on nitric oxide-deficient rat models demonstrated the extract's potential to prevent hypertension and cardiac damage, presenting performance comparable to established pharmaceutical interventions like captopril. The integration of technological innovations and natural remedies represents a promising frontier in hypertension management. (Nozato et al., 2023) emphasize the importance of incorporating digital solutions and lifestyle modifications, highlighting the need for comprehensive and adaptive treatment strategies.

These developments underscore the complex and multidimensional nature of hypertension management. The synergy between nanotechnology, herbal medicine, and advanced medical research offers unprecedented opportunities for developing more effective, personalized, and holistic approaches to cardiovascular health.

**TABLE 1:** Synthesis Table for Discussion.

Author(s) and Year	Focus of Study	Methodology	Key Findings	Relevance to Topic
(Haleem et al., 2023)	Applications of nanotechnology in medicine	Review of nanotechnology in diagnostics and therapeutics	Nanotechnology enhances targeted treatments with reduced toxicity; the potential for predictive healthcare.	Highlights the potential of nanotechnology (e.g., silver nanoparticles) in advanced medical treatments.
(Idris & Nadzir, 2021)	Extraction methods and bioactive compounds of <i>Centella Asiatica</i>	Comparison of conventional and modern extraction techniques	Modern methods yield better bioactive compounds, enhancing antimicrobial and therapeutic properties.	Explains the importance of effective extraction methods for harnessing <i>C. asiatica</i> benefits.

Author(s) and Year	Focus of Study	Methodology	Key Findings	Relevance to Topic
(Sharma et al., 2021)	Herbal remedies for hypertension	Review of medicinal plants in hypertension management	Herbs like <i>C. asiatica</i> are cost-effective and safer alternatives to pharmaceuticals for managing hypertension.	Supports the use of <i>C. asiatica</i> in hypertension therapy.
(Lauder et al., 2023)	Hypertension management with comorbidities	Review of lifestyle changes, drugs, and new therapies	Lifestyle and combined drugs reduce cardiovascular risks; innovative solutions like renal denervation are vital.	Provides insight into hypertension management complexities and integrated approaches.
(Barbato et al., 2023)	Renal denervation in hypertension management	Clinical consensus on catheter-based RDN	RDN is a viable alternative for resistant hypertension, emphasizing multidisciplinary treatment.	Suggests complementary treatment strategies for managing complex hypertension cases.
(Bunaim et al., 2021)	<i>C. asiatica</i> effects on hypertensive rat model	Experimental study on nitric oxide-deficient rats	<i>C. asiatica</i> extract prevents hypertension and cardiac damage, comparable to captopril.	Demonstrates <i>C. asiatica</i> 's efficacy in mitigating hypertension and its protective cardiovascular effects.
(Nemmar et al., 2023)	Cardiovascular effects of PEG-coated silver nanoparticles	Experimental study on hypertensive mice	Aggravated cardiotoxicity in hypertensive mice treated with AgNPs, including oxidative stress and inflammation.	Raises concerns about AgNPs' safety in hypertensive conditions, prompting a need for careful evaluation.
(Alghamdi et al., 2022)	Nanotechnology in personalized medicine	Review of nanotechnology's role in customized healthcare	Nanotechnology offers precision diagnostics and therapy tailored to individual genetic profiles.	Aligns with the personalized application of silver nanoparticles in hypertension therapy.
(Mahmoud et al., 2024)	Natural alternatives to ARBs in hypertension treatment	Molecular docking and simulations	Natural compounds (e.g., kaempferol) exhibit promising ARB inhibitory effects with fewer side effects.	Suggests synergy between natural products and pharmaceuticals for hypertension management.
(Mohebbati et al., 2020)	Hypotensive effect of <i>C. asiatica</i> on acute hypertension	Experimental study on rats injected with angiotensin II	<i>C. asiatica</i> reduces blood pressure by modulating the renin-angiotensin system.	Confirms the mechanistic role of <i>C. asiatica</i> in reducing hypertension.
(Malik et al., 2023)	Nanotechnology's industrial applications	Overview of nanotechnology in diverse industries	Highlights nanotechnology's versatility, including medical applications such as drug delivery and diagnostics.	Validates the potential of nanotechnology for broader medical interventions like hypertension treatment.
(Ferdous et al., 2022)	Thrombotic effects of AgNPs in hypertensive models	Experimental study on thrombotic responses in hypertensive mice	PEG-coated AgNPs exacerbate thrombosis and oxidative stress in hypertensive mice.	Warns of potential side effects of AgNPs, necessitating balanced therapeutic use.
(Halma & Saleeby, 2024)	Review of herbal medicine for hypertension	A systematic review of nutraceuticals in hypertension management	Natural products like <i>C. asiatica</i> demonstrate significant blood pressure reduction.	Reinforces the use of herbal approaches like <i>C. asiatica</i> in non-pharmaceutical hypertension management.
(Nozato et al., 2023)	Hypertension management adaptations during COVID-19	Analysis of telemedicine and home blood pressure monitoring	Emphasizes digital solutions and lifestyle changes for hypertension management.	Encourages integrating technology with traditional therapies for better hypertension control.
(Buranasudja et al., 2021)	Antioxidant properties of <i>C. asiatica</i> extract	Study on oxidative stress in dermal fibroblasts	<i>C. asiatica</i> enhances antioxidant enzyme expression, mitigating oxidative damage.	Highlights the antioxidative potential of <i>C. asiatica</i> relevant to hypertension-related oxidative stress.

## DISCUSSION

The management of hypertension, as one of the leading causes of global morbidity and mortality, demands a multidimensional approach that includes both conventional and innovative therapies. Two elements that are the focus of this study are the use of silver nanoparticles (AgNPs) and *Centella Asiatica* (*C. asiatica*) extract as potential solutions in hypertension management. An in-depth review of the existing literature suggests that these two interventions, both separately and together, provide promising prospects in the control of high blood pressure, despite certain challenges that must be overcome. AgNPs have long been recognized for their versatile properties, especially in medical applications. With their nano-size, these particles are capable of enhancing drug bioavailability and enabling more targeted drug delivery. However, in the context of hypertension, their therapeutic effects require careful evaluation. The study of (Nemmar et al., 2023) revealed that AgNPs coated with polyethylene glycol (PEG) exacerbated cardiovascular toxicity in hypertensive rats, triggering oxidative stress and inflammation. Something similar was also reported by (Ferdous et al., 2022), where the use of AgNPs increased the risk of thrombosis in a hypertensive rat model. These negative effects suggest that, although AgNPs have potential for medical applications, their use in patients with hypertensive conditions requires a cautious approach, especially to prevent adverse cardiovascular side effects.

Conversely, nanotechnology also offers great opportunities in the treatment of hypertension through personalized approaches. (Alghamdi et al., 2022) Emphasize that nanotechnology can be used to create therapies tailored to an individual's genetic profile. This enables the design of more effective and efficient treatments, including the more targeted utilization of AgNPs in treating hypertension that is resistant to conventional therapies. With this approach, the risk of side effects can be minimized, as emphasized by (Mahmoud et al., 2024), who proposed the combination of natural and pharmaceutical products to create therapeutic synergy. Besides AgNPs, natural approaches based on plant extracts such as *C. asiatica* have also shown significant potential in hypertension management. *C. Asiatica*, is known in traditional medicine as a plant that has broad therapeutic properties, including hypotensive and antioxidant effects. The study of (Mohebbati et al., 2020) showed that *C. asiatica* extract effectively lowers blood pressure by modulating the renin-angiotensin system, one of the key mechanisms in blood pressure regulation. In addition, research by (Bunaim et al., 2021) on a nitrogen oxide-deficient hypertensive rat model showed that this plant extract is able to prevent cardiovascular damage and hypertension, with efficacy equivalent to antihypertensive drugs such as captopril. The effectiveness of *C. asiatica* in reducing oxidative stress has also been revealed by (Buranasudja et al., 2021), who reported that this extract increased the expression of antioxidant enzymes in dermal fibroblasts.

These findings are relevant for hypertension, where oxidative stress is one of the main pathogenetic mechanisms. Therefore, the ability of *C. asiatica* to counteract oxidative stress not only supports cardiovascular health but may also improve the efficacy of other antihypertensive therapies. From the perspective of herbal medicine, (Sharma et al., 2021) highlighted that the use of medicinal plants, including *C. asiatica*, is a safer and cost-effective alternative to modern pharmaceuticals especially for populations in developing countries. *Asiatica* was able to significantly lower blood pressure through various biochemical mechanisms. These findings are in line with the increasing interest in natural therapies that are kinder to the human body than purely pharmacological approaches.

The combination of nanotechnology and natural extracts such as *C. asiatica* opens up great opportunities for creating a multidimensional therapeutic approach for hypertension. (Lauder et al., 2023) Emphasized the importance of an integrated approach in hypertension management, especially in patients with comorbidities. In this context, the integration of nanotechnology-based therapies with herbal approaches may provide a more holistic solution, which not only targets blood pressure but also addresses other cardiovascular complications. However, a major challenge in the development of these therapies is ensuring their safety and efficacy. The studies of (Ferdous et al., 2022) and (Nemmar et al., 2023) showed that although AgNPs are promising, their potential side effects cannot be ignored. Therefore, the development of methods to reduce the toxicity and increase the specificity of AgNPs is essential. In addition, the need for more effective extraction methods for plants such as *C. asiatica* was also expressed by (Idris & Nadzir, 2021), who found that modern methods are superior in obtaining bioactive compounds compared to conventional methods.

Technology can also play a role in improving accessibility and monitoring of hypertensive patients. (Nozato et al., 2023) Highlighted the importance of telemedicine and home blood pressure monitoring, especially during the COVID-19 pandemic. The integration of these technologies with nanotechnology and herbal-based therapies could create a more adaptive and effective hypertension management system. Ultimately, this study confirms that both AgNPs and *C. asiatica* extract have significant roles in hypertension management. Although both show great potential, their implementation requires a cautious approach to ensure that the benefits gained are not offset by the risk of adverse side effects. With a multidisciplinary approach that includes technology, pharmacology, and herbs, hypertension management can be significantly improved, providing new hope for millions of patients worldwide. The synergistic potential of silver nanoparticles (AgNPs) and *Centella Asiatica* extract represents a promising frontier in cardiovascular therapeutic strategies.

Recent investigations by (Sharifi-Rad et al., 2021) demonstrated the remarkable potential of functionalized AgNPs in targeted drug delivery, specifically highlighting their capability to enhance cellular penetration and reduce systemic toxicity. Their research underscores the importance of surface modification techniques in mitigating potential cardiovascular risks associated with nanoparticle interventions.

Moreover, a comprehensive study by Kumar et al. (2022) provides additional insights into the molecular mechanisms of *Centella asiatica*. Their findings revealed that specific triterpene compounds in *C. asiatica* extract significantly modulate endothelial function, reducing inflammatory markers and improving vascular elasticity. This mechanism offers a novel perspective on how herbal interventions can complement conventional hypertension management strategies.

The convergence of nanotechnology and botanical medicine presents an innovative approach to addressing the complex pathophysiology of hypertension. By integrating advanced nanoscale engineering with the holistic therapeutic properties of natural extracts, researchers can potentially develop more personalized and effective cardiovascular interventions. However, continued rigorous research is essential to fully understand the long-term implications and optimize these emerging therapeutic modalities.

Future investigations should focus on standardizing extraction protocols, defining precise nanoscale interactions, and conducting extensive clinical trials to validate the safety and efficacy of these integrated therapeutic approaches.

### CONCLUSION & SUGGESTION

The study underscores the significant potential of combining silver nanoparticles (AgNPs) and *Centella Asiatica* extract for hypertension management. Both interventions demonstrate multifaceted therapeutic benefits, including antioxidative, anti-inflammatory, and cardiovascular protective properties. However, challenges like AgNP toxicity and variability in *Centella asiatica*'s bioactive compound extraction require careful consideration. For future progress, research should prioritize:

1. Comprehensive safety evaluations of AgNPs in hypertensive models to mitigate potential adverse effects.
2. Optimization of *Centella Asiatica* extraction techniques for enhanced bioavailability and therapeutic efficacy.
3. Development of personalized therapeutic strategies that leverage nanomedicine and herbal pharmacology tailored to individual genetic profiles.

An interdisciplinary approach integrating nanotechnology, pharmacology, and digital health solutions is essential to advance safer, more effective

hypertension therapies while ensuring accessibility and adaptability to patient-specific needs.

### ACKNOWLEDGMENT

The authors would like to thank all the researchers and other contributors who have helped carry out this literature review.

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