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The Effectiveness of Combined Herbal Therapy and Conventional Therapy on Hypertension: A Literature Review of Clinical Trials and Methodological Limitations

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ABSTRACT

Hypertension is one of the leading causes of cardiovascular disease and global mortality. Many pharmacological therapies are effective, but the side effects they cause encourage the search for alternatives. Combination with herbal therapy is believed to increase effectiveness and reduce side effects compared to monotherapy. This study was a systematic literature review that analyzed studies in the last five years from PubMed, Google Scholar, and Connected Papers. The inclusion criteria focused on peer-reviewed articles published between 2018–2023, written in English, involving adult human subjects with hypertension, and specifically evaluating combined herbal and conventional therapies. Exclusion criteria included animal studies, non-English articles, and reviews without original data. After the screening process, the 4 main articles were selected and analyzed qualitatively and quantitatively. The combination of Cucumis sativus with Losartan, celery extract with Captopril as well as the combination of herbs such as garden cress, fenugreek, and black seed with metoprolol tartrate (MT) showed mixed results, some combinations providing better synergistic effects compared to the application of monotherapy. However, studies of Moringa oleifera with antihypertensive drugs showed no additional effects. The combination of herbal and pharmacological therapies has the potential to improve the effectiveness of hypertension treatment, but this review is limited by the small number of eligible studies, variability in sample sizes, heterogeneity of herbal preparations, and lack of standardized dosage across trials. Therefore, further large-scale clinical trials are required to confirm both safety and optimal efficacy.

INTRODUCTION

Hypertension is one of the global health problems with a prevalence that continues to increase every year. Based on data from the World Health Organization (WHO), in 2019 around 1.28 billion people in the world suffered from hypertension and more than two-thirds of them came from low- and middle-income countries (WHO, 2021). In Indonesia, the prevalence of hypertension also shows an increasing trend, from 34.1% in the population aged >18 years based on Riskesdas 2018 to 37.0% in the 2023 Indonesian Health Survey (Ministry of Health of the Republic of Indonesia, 2023). This trend is expected to rise further due to unhealthy lifestyles, obesity, and genetic as well as environmental factors. If not managed properly, hypertension can cause complications such as heart disease, stroke, kidney failure, and cognitive impairment (American Heart Association, 2022).

Pharmacological therapies such as diuretics, ACE inhibitors, calcium channel blockers, and beta-blockers remain the primary choice and have been proven effective in lowering blood pressure (JNC 8 Guidelines, 2019). However, side effects including dizziness, hyperkalemia, or kidney dysfunction often reduce treatment adherence (Gupta et al., 2022). This condition has driven increasing interest in complementary or alternative approaches such as herbal therapy. Several

medicinal plants, including Allium sativum (garlic), Hibiscus sabdariffa (rosella), Camellia sinensis (green tea), and Andrographis paniculata (sambiloto), have been investigated for their antihypertensive effects (Ried et al., 2020). The active compounds—such as allicin in garlic and flavonoids in green tea—exert vasodilatory and antioxidant effects.

Recent studies also indicate that combining herbal therapy with pharmacological drugs may provide synergistic benefits. For example, Bahar et al. (2021) demonstrated that garlic extract with amlodipine reduced blood pressure more effectively than amlodipine alone, while Ojulari et al. (2019) reported enhanced effects of rosella tea combined with lisinopril. However, these findings are still inconsistent and limited in scope, with some studies reporting no additional benefit or highlighting potential risks of herb–drug interactions (Al Disi et al., 2021).

Despite the growing body of research, a clear research gap remains: most studies are small-scale, short-term, and focused on a limited range of herbs. There is insufficient evidence synthesizing the effectiveness, mechanisms, and safety profiles of diverse herbal–pharmacological combinations in hypertension management. This review aims to address this gap by systematically analyzing recent studies (2018–2023) on combined herbal and conventional therapies, highlighting both their therapeutic potential and limitations, and providing directions for future clinical research.

RESEARCH METHODS

This study used a systematic literature review method to evaluate the effectiveness of a combination of herbal and pharmacological therapy in people with hypertension. This approach aims to analyze the latest scientific evidence regarding the effectiveness of the combination of herbal therapy and pharmacological treatment in hypertensive patients and evaluate the potential benefits and risks of the combination therapy.

A structured search strategy was developed to ensure comprehensive coverage. Searches were conducted in PubMed, Google Scholar, and Connected Papers between January 2018 and December 2023. The following Boolean string was applied: (“hypertension” OR “high blood pressure”) AND (“herbal therapy” OR “medicinal plants” OR “phytotherapy”) AND (“pharmacological therapy” OR “antihypertensive drugs”) AND (“combination” OR “adjunct” OR “herb–drug interaction”). To minimize bias, reference lists of included studies were also screened manually for additional relevant articles.

The inclusion criteria were: (1) peer-reviewed original research articles; (2) studies involving adult human subjects diagnosed with hypertension; (3) interventions assessing the combined use of herbal and pharmacological therapies compared to monotherapy; and (4) publications in English. The five-year limit (2018–2023) was applied to ensure up-to-date evidence reflecting current therapeutic practices. Exclusion criteria included: (1) animal or in vitro studies, (2) articles not in English, (3) studies evaluating only herbal–herbal or drug–drug combinations, (4) non-experimental designs (e.g., narrative reviews, commentaries), and (5) studies with incomplete or insufficient methodological data. These criteria were applied to ensure methodological rigor and relevance to clinical practice.

To critically appraise methodological quality, the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Randomized Controlled Trials and the Newcastle–Ottawa Scale (NOS) for observational studies were used. Each study was independently assessed by two reviewers, and discrepancies were resolved through discussion until consensus was reached. Studies were categorized into high, moderate, or low quality based on their appraisal scores, with only high- and moderate-quality studies retained for synthesis.

The initial search identified 62 articles from PubMed, 10 from Google Scholar, and 7 from Connected Papers. After removing duplicates and applying relevance filters, 15 articles were screened in full text. Following inclusion/exclusion criteria and critical appraisal, 4 main articles of sufficient quality were selected. The data extracted from these studies were analyzed using both qualitative synthesis (identifying recurring themes, mechanisms, and outcome measures) and quantitative comparisons (where applicable, effect size and blood pressure reduction values). This integrative

analysis was then synthesized to formulate evidence-based recommendations on the application of combined herbal and pharmacological therapy in the management of hypertension.

RESULTS AND DISCUSSION

The characteristics of the articles analyzed in this review show similarities and differences in aspects of the author, year of publication, research location, sample type, study design, and findings obtained. Most of the studies reviewed used experimental designs with a model of hypertensive mice as the subject of the study. These studies were conducted in two countries, namely Indonesia and Saudi Arabia, with a focus on the effectiveness of a combination of herbal and pharmacological therapies in lowering blood pressure.

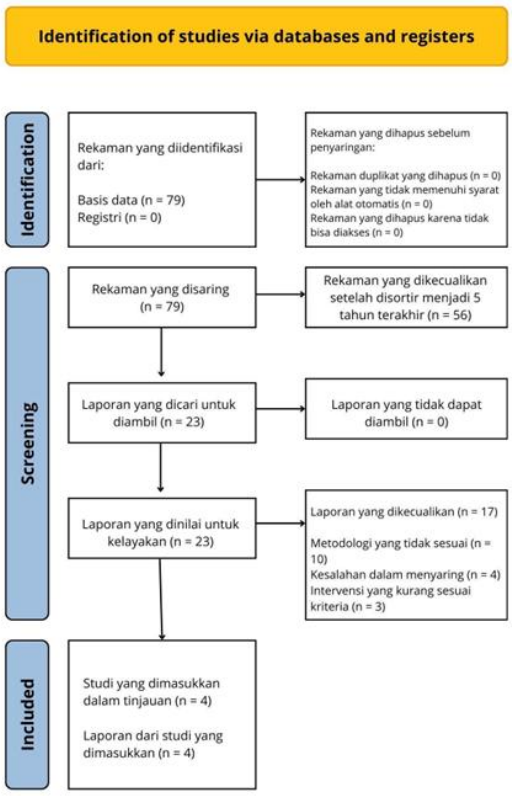

Figure 1. PRISM

All of the articles analyzed were published in 2023, so they have high relevance to the latest developments in the treatment of hypertension. The results showed that the combination of herbal therapy with pharmacological antihypertensive drugs, such as Losartan, Amlodipine, and Captopril, provided more effective results in lowering blood pressure compared to single therapy. In addition, several studies evaluated the pharmacokinetic activity of these drugs against herbal compounds, such as Cucumis sativus, Lepidium sativum, and Garden cress extract, which provides additional insight into the mechanism of action of the combination of therapies. The research examined in this review highlights the potential of combining herbal and pharmacological therapies as an alternative approach in hypertension management.

Results

Table 1. Matrix Articles

Article Title/Year	Writer	Coumtry	Sample	Research Design	Results

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Cucumber (Cucumis sativus L.) Fruit and Combination with Losartan Attenuate the Elevation of Blood Pressure in Hypertensive Rats Induced by Angiotensin II/ 2023	Tomi Hendrayana , et al.	Indonesia	Adult male Wistar rats weighing 220-250 g induced angiotensin II	Experimental	Cucumis sativus in preventing increased blood pressure showed that when given together with losartan, C. sativus had a blood pressure-lowering effect. It is likely that this is mediated by the active ingredient C. sativus in renin-angiotensin-aldosterone which still requires further study.
Article Title/Year	Writer	Coumtry	Sample	Research Design	Results
Drug-Herb Interactions: Selected Antihypertensive Drugs with Moringa oleifera Leaves Extract/ 2021	Endang Kumolosari, et al.	Malaysia	66 male rats were divided into 11 treatment groups.	Experimental	Single-administered M. oleifera extract significantly lowered systolic and diastolic blood pressure in hypertensive rats after 14 days. The ACE inhibiting activity of M. Oleifera extract is similar to that of enalapril. However, there were no additional effects when M. Oleifera extract was combined with enalapril indicating a possible drug-herbal interaction. The mechanism of interaction needs to be further researched to ensure the safety of using M. Oleifera extract in conjunction with antihypertensive drugs.
Effect of Administration of Combination of Captopril and Celery Extract on Blood Pressure and Electrolyte Levels of Hypertensive Rats/ 2020	Siska Siska, *et al.*	Indonesia	Male white rats of *the Sprague-Dawley* strain aged 3-4 months weighing 200-300 g and induced through oral administration of 4% NaC. Categorize	Experimental	The combination of captopril (5 mg/kgBB) and celery extract was more effective in lowering blood pressure than single use. This effect occurs through the mechanisms of diuresis, natriuresis, and relaxation vessels. Suggests that the combination of captopril and celery has the potential to be an adjunct therapy for hypertensive patients. However, further research in humans is needed to ensure the safety of its effectiveness.

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			d into 9 groups.		
ffects of garden cress, fenugreek and black seed on the pharmacodynamics of metoprolol: an herb-drug interaction study in rats with hypertension/ 2021	Yousef A Bin Jardan, et al.	Saudi Arabia	The mice were induced N-nitro L-arginine methil ester (L-NAME) and were divided into five groups.	Experimental	This study showed that garden cress, fenugreek, and black seed had antihypertensive effects in L-NAME-induced hypertensive *mice.* The combination of herbs with metoprolol tartrate (MT) gives more significant results in the effect of lowering blood pressure than the administration of herbs or MT alone.

Discussion

This study involved a model of hypertension mice as a test sample in observing the effectiveness of a combination of herbal therapy and pharmacology. Hypertensive mice were chosen as research subjects because they have physiological characteristics similar to hypertension in humans, so the results of the study can provide a preliminary picture of the potential effectiveness and safety of this combination of therapies before they are applied in clinical trials in humans.

The research of Tomi Hendrayana et al. (2023), used adult male Wistar mice weighing 220-250 grams induced hypertension through angiotensin II. The results showed that C. sativus (cucumber) combined with losartan had a significant effect on lowering blood pressure. This effect is likely mediated by the active ingredient C. sativus against the renin-angiotensin-aldosterone system which requires further study to understand its mechanism in depth. The study by Endang Kumolosari et al. (2021) used 66 male rats divided into 11 treatment groups to test the interaction between M. Oleifera extract and significant antihypertensive drugs on a single basis, in combination with pharmacological antihypertensive drugs did not show any additional effects, this indicates the possibility of interactions between the drugs and herbs that need to be investigated further.

The study conducted by Siska Siska et al. (2020) used male white rats of the Sprague-Dawley strain induced hypertension through oral administration of NaCl 4%. The study divided the mice into 9 treatment groups. The results showed that the combination of captopril and celery extract was more effective in lowering blood pressure than single use (monotherapy). These effects mainly occur through the mechanisms of diuresis, natriuresis, and vasorerelaxation which indicates that this combination has potential as an adjunct therapy for hypertensive patients. The study conducted by Yousef A Bin Jardan et al. (2021) used mice induced with N-nitro L-arginine methyl ester (L-NAME) and divided into five treatment groups. The results showed that the combination of herbs such as garden cress, fenugreek, and black seed with metoprolol tartrate (MT) could have a more significant blood-lowering effect compared to herbal or MT alone. This shows the synergistic potential between herbs and beta-blockers in hypertension therapy.

The results of these studies suggest that the combination of herbal and pharmacological therapies has the potential to improve the effectiveness of hypertension treatment compared to monotherapy, but further studies are needed to understand the mechanisms of pharmacokinetic and pharmacodynamic interactions in more depth, and to confirm these findings in human clinical trials

Main Results of the Study

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The reviewed study showed that the combination of Cucumis sativus with losartan provided a greater antihypertensive effect than with losartan therapy alone. This effect can be caused by bioactive activity in C. sativus that plays a role in modulating the renin-angiotensin system. However, the specification mechanism still requires further research. The combination of Moringa oleifera with antihypertensive drugs did not show an additional effect in lowering blood pressure compared to drug monotherapy. This indicates the possibility of pharmacokinetic interactions that can reduce the effectiveness of drugs, so its use needs to be considered and further reviewed.

In another study, the combination of celery extract with captopril showed results that this combination not only lowered blood pressure more significantly compared to captopril alone, but also improved the balance of electrolytes such as sodium and potassium. The main contributing mechanisms are increased diuresis and natriuresis which help to better control blood pressure, but more research is needed to ensure their safety in the long term. Combination therapy of garden cress, fenugreek, and black seed with metoprolol provides a better antihypertensive effect compared to metoprolol monotherapy. The study confirms that certain herbal combinations may work synergistically with beta-blockers to lower blood pressure more effectively, although their long-term effects and safety still need to be further studied through human clinical trials.

Based on research on the combination of herbal therapy and pharmacology, it was found that this method has the potential to be more effective in lowering blood pressure than monotherapy, although there is one study that said that the combination of M. oleifera therapy with antihypertensive drugs did not show any additional effects in mice. According to Damayanti (2024), the combination of Hibiscus sabdariffa and Allium sativum with conventional drugs can reduce blood pressure by 10-20 mmHg and improve sleep quality and reduce fatigue. This is in line with the reviewed studies on the effectiveness of Cucumis sativus (cucumber) and Apium graveolens (celery) in lowering blood pressure when combined with pharmacological therapy.

Interpretation of Results

This was reviewed by Suryaningsih & Septiari (2023), that Cucumis sativus (39%), Apium graveolens (30%), and Allium sativum (9%) are the most commonly used herbs in herbal therapy, with the main uses as vasodilators and diuretics. Other clinical studies have shown that the combination of herbs with pharmacological antihypertensives such as Losartan, Amlodipine, and Captopril results in a more significant reduction in blood pressure compared to single therapy. These results show that the combination of therapies, both herbal and pharmacological, has their respective effectiveness in their use. However, this study also highlights that there are challenges in providing combination therapy, namely related to patient compliance and the potential between herbs and pharmacology given.

In addition to its effectiveness combined with pharmacological therapy, herbal therapy alone is also able to lower blood pressure. Such as research conducted by Mahrunnisa Syahratudar and Arina Maliya in the Pajang Surakarta Health Center area by providing interventions to 15 participants. The participants were given cucumber juice 1 time a day in 50 ml cooked and the pulp filtered. This was done for 7 consecutive days until the participants' systolic and diastolic blood pressure values decreased. The results of this study are also in line with the study conducted by Hanifa Putri et al., who intervened in 11 participants by drinking 250 cc cucumber juice 2 times a day for 7 days had a significant effect on lowering blood pressure.

Research related to the effectiveness of celery leaves conducted by Febri S Yolanda shows that giving the decoction 2 times a day can lower blood pressure in hypertensive patients. This is also in line with a study by Hasria Simamora where the blood pressure of volunteers dropped from 158/96 mmHg to 118/82 mmHg after consuming celery. The results of statistical analysis showed significant differences before and after the administration of celery juice. In addition, another study that provided Garden Cress intervention as much as 150 cc a day for 7 days had a difference in blood pressure reduction which provides evidence that Garden Cress can be used as a therapy in the management of hypertension. The study conducted by Etri Yanti et al., also found that from 16 hypertensive patients observed before and after the administration of moringa leaf decoction, the average systolic blood

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pressure before administration was 153.50 mmHg while after administration became 129.56 mmHg. The average diastolic blood pressure also decreased from 94.38 mmHg to 86.25 mHg.

However, the study conducted by Lukmanul Khakim et al., in the administration of black cumin or Nigella sativa to SGPT (Serum Glutamic Pyruvic Transaminase) levels in hypertensive patients showed that the treatment group experienced an average decrease in SGPT levels by 0.65 U/L with a P-value 0.179 and the control group taking placebo had a decrease in the mean SGPT level of 0.60 U/L with a P-value of 0.179. The results of the independent T-test showed that there was no significant difference between the control and treatment groups in terms of decreased SGPT levels (P-value 0.6).

Implications for Society

The results of this study have important implications for the treatment of hypertension in the population. Given that the combination of herbal and pharmacological therapies can provide more effective results than monotherapy, this approach may be an alternative for patients who want to reduce their dependence on medications or suffer from the side effects of conventional antihypertensive medications. In addition, the study showed that many patients received information about herbal therapy from family or friends, rather than from medical professionals. This suggests that evidence-based health education needs to be improved, especially to avoid drug interactions that can reduce the effectiveness of treatment. In clinical practice, medical staff should be more active in providing proper information about these combination therapies and ensuring that their use complies with safe medical standards.

The findings that the majority of hypertensive patients use combination pharmacological therapy also suggest that the health care system needs to better support the use of combination therapy by monitoring its effectiveness and side effects. The development of public health policies that encourage further research on the standard dosage and safety of combining herbs with antihypertensive drugs is also an important step forward.

Research Limitations

The research conducted still has several limitations that need to be considered and further researched. The reviewed study used animals in its trials so the effectiveness and safety of herbal and pharmacological combination therapy still require further clinical trials in humans. Variations in the methods used as well as differences in formulation and dosage used can affect the results obtained. The available and studied studies have also not explored the pharmacokinetic and pharmacodynamic interactions between herbal therapy and pharmacological therapy in the form of antihypertensive drugs, so further research is needed to ensure their safety in long-term use in humans.

CONCLUSION

The results of this literature review showed that the combination of herbal and pharmacological therapy had better effectiveness in lowering blood pressure compared to monotherapy with some herbs such as cucumber, celery, and garlic that function as vasodilators and diuretics. Combinations of herbs and antihypertensive drugs such as Amlodipine and Losartan also give significant results. While single herbal therapies such as cucumber juice, celery stew, and moringa leaves have been proven to lower blood pressure. However, black cumin did not show a significant difference in lowering SGPT levels.

These findings have several important implications. From a policy perspective, integrating evidence-based herbal options into national hypertension management guidelines could expand affordable and culturally acceptable treatment strategies, particularly in low- and middle-income countries where access to medications may be limited. For clinical practice, healthcare providers should be encouraged to consider herbal–drug combinations as complementary options, while remaining cautious about potential herb–drug interactions and ensuring patient safety through proper monitoring. For future research, more large-scale randomized controlled trials with standardized dosages and longer follow-up periods are needed to establish efficacy, safety, and cost-effectiveness.

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Furthermore, pharmacokinetic studies are essential to clarify mechanisms of interaction between specific herbs and antihypertensive drugs. In summary, while combined herbal and pharmacological therapy shows promise in enhancing hypertension treatment outcomes, its translation into practice requires robust evidence, clear regulatory guidance, and interdisciplinary collaboration between clinicians, researchers, and policymakers.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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