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Efficacy of Angiotensin Receptor Blockers (Valsartan, Candesartan, Losartan) in Lowering Blood Pressure: A Systematic Review

Shafa S. Maharani, Dika P. Destiani

1Departement of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Padjadjaran, Sumedang, Indonesia

Abstract

Hypertension is a significant health issue that significantly increases the risk of cardiovascular disease. Angiotensin II receptor blockers (ARBs) are commonly used in Indonesia to treat hypertension, yet comprehensive comparative efficacy data within this drug class remain limited. This review seeks to evaluate the blood pressure-lowering efficacy of three particular angiotensin receptor blockers (ARBs) —Valsartan, Candesartan, and Losartan— in individuals diagnosed with all stage hypertension. This systematic review identified randomized controlled trials (RCT) obtained from PubMed and Google Scholar using several keyword combinations. Among 20 RCTs with 6.425 patients treated with three ARBs, all included studies demonstrated significant blood pressure reductions. The mean reductions in systolic blood pressure (SBP) and diastolic blood pressure (DBP) were the greatest for Candesartan (-18.69/-10.25 mmHg), followed by Losartan (-14.80/-7.8 mmHg), and Valsartan (-8.94/-7.58 mmHg). Candesartan achieved the largest reduction, decreasing baseline systolic blood pressure (SBP)/diastolic blood pressure (DBP) by 38.16/18.95 mmHg over 12 weeks. In contrast, Valsartan showed the smallest reduction, with SBP decreasing by 0.81/0.04 mmHg after 66 months. It can also be linked to the pharmacokinetic properties of the drugs, where Valsartan has a higher bioavailability, and Losartan has a lower bioavailability compared to the other ARBs. It can be concluded that ARBs, including Valsartan, Candesartan, and Losartan, are generally effective in reducing blood pressure in hypertensive patients, with Candesartan showing the greatest efficacy. Future research should involve direct comparative trials of Valsartan, Candesartan, and Losartan, along with studies on their molecular mechanisms, to increase effective hypertension treatments.

Keywords: Angiotensin Receptor Blocker, Blood Pressure, Hypertension, Systematic Review

Corresponding author: Shafa Shaomi Maharani. Departement of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Padjadjaran, Sumedang, Indonesia. Email: shafa21008@mail.unpad.ac.id.
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Introduction

One serious health problem that significantly increases the risk of getting cardiovascular disease is hypertension. It is the primary cause of mortality worldwide and is often indicated by systolic blood pressure (SBP) and diastolic blood pressure (DBP) of 140/90 mm Hg or greater. Normal blood pressure is defined as less than 120/80 mmHg, and the overall goal is to lower SBP/DBP to less than 140/90 mmHg[1]. The number of individuals worldwide who have hypertension is expected to rise from 918 million in 2000 to 1.56 billion by 2025[2].

According to data from the World Health Organization (WHO), in 2015, around 972 million people or 26.4%, suffered from hypertension, and it is expected to increase to 29.2% in 2025[3,4]. In Asia, this disease kills 1.5 million people every year[4]. The rise in prevalence highlights the urgency for optimizing current treatment to ensure better management and control of hypertension on a global scale[5].

Treatments for reducing blood pressure have been shown to be beneficial in preventing cardiovascular disease. A 10 mmHg reduction in systolic blood pressure correlates with decreased risks of heart failure (28%), coronary heart disease (17%), major cardiovascular events (20%), stroke (27%), and overall mortality (13%). Lowering diastolic blood pressure is linked to reduced risks of all-cause mortality ($p = 0.009$) and recurrent stroke ($p = 0.026$)[6].

These results emphasize the need to preserve stable blood pressure regulation, which is becoming more widely acknowledged as the most important treatment approach for successful secondary prevention of cardiovascular disorders. Therefore, appropriate pharmacological therapy is crucial as the first step to lowering the risk of cardiovascular events in hypertensive patients efficaciously[7].

Drugs targeting the renin-angiotensin-aldosterone system (RAAS) have shown particularly impressive efficacy and are recommended for hypertension management[1]. The majority of national hypertension treatment guidelines recommend angiotensin II receptor blockers (ARBs) as a first-line therapy[1,8]. ARBs function by inhibiting angiotensin II through specific binding to type 1 (AT1) receptors in vascular smooth muscle[9].

To help with better-informed treatment decisions, it is crucial to evaluate the effectiveness of antihypertensive medications that are part of the ARB drug class and that are accessible in Indonesia. This study aims to provide a complete and updated systematic review of the comparative efficacy of ARBs, specifically valsartan, candesartan, and losartan, in decreasing blood pressure in hypertensive patients in response to differences in SBP and DBP from baseline. This review compares these ARBs with placebo and other antihypertensive medications, assessing their efficacy through randomized controlled trials (RCTs).

Method

Literature Search Strategy

A systematic search was conducted in PubMed and Google Scholar in May 2024. Database searches were initially conducted using the keyword combinations using the boolean operators "AND" and "OR" and listing seven keywords for searching the eligible articles, namely, “efficacy”, “blood pressure”, “angiotensin receptor blockers”, “ARB”, “valsartan monotherapy”, “candesartan monotherapy”, “losartan monotherapy”. This review focused on the response to ARBs, so the chosen articles needed to include both

baseline data and evaluation results for the ARBs monotherapy groups.

The search was restricted to full-text papers, human participants, and randomized controlled trials (RCTs) published in the English language within the last 10 years. The review will exclude case series, observational studies, case reports, and narrative reviews. Additionally, publications older than 10 years, non-human studies, and studies that do not report any relevant outcome events will also be excluded.

Subject Characteristics

Eligibility was assessed by screening titles and abstracts using specified inclusion and exclusion criteria. Full-text screening was then applied to studies that might be relevant. Eligible studies have to meet the criteria in order to be considered for inclusion in this analysis. The criteria were the study that used a randomized control trial design and included adult patients (>18 years of age) with essential hypertension who met the JNC 8 criteria for systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg. Publications were required to include at least one treatment with candesartan, valsartan, and losartan. Patients with contraindications to ARB drugs were excluded from the studies.

Outcomes of interest included blood pressure of treatment. Studies involving concomitant antihypertensive medication, step-care, up-titration, or combination therapy were included. The selected study must also show a change in through and/or peak systolic and diastolic blood pressure from baseline when compared to other antihypertensive medicines and/or PBO.

Data Extraction and Risk of Bias

A structured form that was evaluated and approved by S.S.M. and D.P.D. was used to obtain data from each included trial. Information about the study population (e.g., age, settings), study design (e.g., timeframe, methods), and study results (e.g., blood pressure measurements) was acquired for this review. A systematic literature search was conducted using the Population, Intervention, Comparator, Outcomes, and Study Design (PICOS) paradigm.

The risk of bias was assessed using the Jadad score. The Jadad scale was used to rate the quality (validity) of individual trials based on five criteria (each worth one point): (i) proper randomization, (ii) description of randomization, (iii) double-blind method (iv) double-blind method adequately described, (v) withdrawals/drop-out documented. One point is deducted if the methods for randomization or blinding are inappropriate. A study with a score of 0–2 is considered low quality, a score of 3–4 is considered moderate quality, and a score of 5 is considered good quality[10,11]. After data extraction, efficacy estimates were obtained by comparing changes from baseline data or before receiving the intervention with data after the intervention in each group.

Result and Discussion

Study Selection

After retrieving 457 results in total and eliminating duplicates, 443 publications were found. Out of these, 418 were eliminated after title and abstract screening. These articles still included reviews, animal studies, and non-randomized controlled trials. In total, 25 studies were identified. Then, a total of 20 articles were examined for this review's inclusion after the methodologies and findings were screened. These 20 trials were with valsartan (n=11), candesartan (n=4), and losartan (n=5). The doses of ARBs were 80 mg, 160 mg, and 320 mg for valsartan; 8 mg, 16 mg, and 32 mg for candesartan; and 50 mg

for losartan.

Study Characteristics

Twenty studies with RCTs enrolling 6.425 patients fulfilled the inclusion criteria and are included in the analysis. The mean age of participants are 56 years old with the mean duration of 22 weeks. The most duration used in the study was 8 weeks with 10 articles, followed by 12 weeks duration in 3 articles. The least time of observation was 1 week, while the longest was 66 months.

The studies included participants from a wide range of medical conditions including hypertension, diabetes, hypercholesterolemia, and post-dialysis. Every study that was included involved individuals with mild to moderate hypertension. The studies' blood pressure goals differed considerably, with diastolic blood pressure goals ranging between <80 and <95 mmHg and systolic blood pressure goals between <130 and <160 mmHg.

Quality assessment

The risk of bias evaluation for the selected studies is shown in Table 1. Among the RCTs that were included, nine (45%) had a Jadad score of 5, two (10%) had a score of four, three (15%) had a standard score of three, and five (25%) had a score of less than three. The greater the Jadad total score, the better the quality of the study[10].

Antihypertensive Efficacy Of Angiotensin Receptor Blockers

Angiotensin Receptor Blocker (ARB) is an antihypertensive agent that is the first line of choice because of its essential mechanism of action in maintaining the renin-angiotensin-aldosterone system (RAAS). ARB works by substituting angiotensin II from the AT1 receptor and increasing stimulation of the AT2 receptor, resulting in increased excretion of uric acid in the urine and activated peroxisome proliferator-activated receptor (PPAR)-β. ARB agents such as valsartan, candesartan, and losartan are ARBs with a tetrazolo-biphenyl structure. The different structures of each ARB will create pharmacological and pharmacokinetic characteristics in each agent. With differences in structure, the oral bioavailability, absorption rate, metabolism, and elimination rate of each agent also have differences[32].

Valsartan has a pharmacokinetic profile in the form of a T-max of 2.0 hours, a bioavailability of 23%, and a t/12 of 7. 32,33 Valsartan can be used either as monotherapy or in combination with other antihypertensive agents. Valsartan as monotherapy can be used at doses of 80, 160, and 320 mg, with the effectiveness of lowering blood pressure at a dose of 80 mg reaching -23.6 ± 14.2 mmHg in SBP and -15.5 ± 9.2 mmHg in DBP[21]. At a dose of 160 mg, valsartan can lower blood pressure to maximum results of up to -19.19 ± 5.76 mmHg in SBP15 and -10.8 mmHg in DBP[17]. At a dose of 320 mg, valsartan can lower blood pressure to maximum results of up to -14.8 mmHg in SBP and -11.2 mmHg in DBP[17]. As observed from the results of the study, the dose of valsartan does not have a clear linear relationship with its effectiveness. Valsartan is also known to be combined with other antihypertensive agents such as amlodipine, hydrochlorothiazide, lercanidipine, aliskiren, and benazepril. However, based on the results of the study, valsartan is most effective in combination with aliskiren agents, with a valsartan dose of 160 mg and aliskiren doses of 150–300 mg, resulting in a significant decrease in systolic and diastolic blood pressure of -13/5 mmHg[13]. Candesartan has a T-max of 3.0-5.0 hours, a bioavailability of 42%, and a t1/2 of 9–13[32]. Based on the systematic review conducted, candesartan can also be given as monotherapy at doses of 8, 16, and 32 mg or in combination

with other antihypertensive agents. Candesartan at a dose of 8 mg can effectively lower blood pressure to -16.7 mmHg in SBP and -11.2 mmHg in DBP.24 Candesartan at a dose of 16 mg can effectively lower blood pressure to -26 mmHg in SBP26 and -12.1 mmHg in DBP[24]. While candesartan at a dose of 32 mg can effectively lower blood pressure to -15.9 mmHg in SBP and -7.7 mmHg in DBP[23]. As in the results of the systematic review of valsartan, the dose of candesartan does not have a clear linear relationship with the effectiveness of lowering blood pressure. Candesartan in the study was combined with amlodipine, which is an angiotensin-converting enzyme inhibitor (ACEi) agent with the effectiveness of lowering blood pressure, reaching -39 mmHg in PSBP and -23 mmHg in CSBP[25].

Losartan has a pharmacokinetic profile in the form of a T-max of 3.0-4.0 hours, bioavailability of 33%, and t1/2 reaching 4-6[32]. Based on the results of a systematic review conducted, losartan was given at a dose of 50 mg and produced the greatest effectiveness in lowering blood pressure up to -27 ± 14.2 mmHg in SBP30 and -10.6 ± 10.3 mmHg in DBP[27]. Losartan has also been studied for its effectiveness against valsartan, which resulted in losartan having a higher effectiveness in lowering blood pressure compared to valsartan.

Three ARB agents have been studied, all of which have beneficial blood pressure-lowering effectiveness and can be applied to hypertension therapy. The blood pressure control was significantly improved in all of the trials that were included in the systematic review. The goal of blood pressure control is to reduce blood pressure at both the systolic and diastolic levels. However, some studies focus only on reporting the results of systolic blood pressure (SBP) rather than diastolic blood pressure (DBP)[12,18,25,29,30].

One study reported the largest reduction in baseline systolic blood pressure among the 20 studies and three types of ARBs were Candesartan. Candesartan showed a decrease of 38.16 ± 2.41 mmHg, with baseline systolic blood pressure dropping from 165.02 ± 12.60 mmHg to 126.86 ± 10.19 mmHg after 12 weeks. Additionally, diastolic blood pressure decreased by 18.95 ± 0.8 mmHg, with baseline dropping from 101.09 ± 11.67 mmHg to 82.14 ± 10.87 over the same duration[25].

The smallest reduction was observed with Valsartan 160 mg, showing a decrease of 0.81 mmHg in baseline systolic blood pressure and a decrease of 0.04 mmHg in diastolic blood pressure after 66 months[22]. The mean reduction in systolic blood pressure (SBP) was -8.94 mmHg for valsartan, -18.69 mmHg for candesartan, and -14.80 mmHg for losartan. The mean reduction in diastolic blood pressure (DBP) was -7.58 mmHg for valsartan, -10.25 mmHg for candesartan, and -7.8 mmHg for losartan. Candesartan shows the most significant average decrease in systolic blood pressure and diastolic blood pressure among the three drugs. In contrast, valsartan shows the least significant reduction. The results are shown in Table 2.

Although all ARBs inhibit angiotensin II receptors, pharmacokinetic differences may explain the variations in antihypertensive efficacy. Moreover, the greatest blood pressure-lowering effectiveness was obtained in the candesartan compound, which is thought to have a higher binding ability to the AT1 receptor compared to other compounds with the highest bioavailability profile of 42%. The smallest blood pressure-lowering effectiveness was obtained with valsartan because its bioavailability profile is also low, namely only 23%. However, the blood

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pressure-lowering effectiveness of valsartan can be increased by a combination strategy of ARB agents with other antihypertensive compounds, such as the ACEi group[32].

Treatment duration also played an important role in the observed outcomes. Studies in this review ranged from short-term (1 week) to long-term (66 months) trials. In short-term studies, such as the 1-week crossover trial, ARBs like losartan showed a significant reduction in systolic blood pressure. However, these studies only capture the immediate effects of treatment and may not show the long-term benefits or delayed side effects[28]. On the other hand, longer-duration studies provide more reliable data on how ARBs perform over time. For example, in a 66-month study found that valsartan not only helped reduce blood pressure but also slowed the progression of kidney failure in patients with type 2 diabetes. Such outcomes need longer periods to become clear and are not captured in short-duration trials[18].

Several studies included in this review involved hypertensive patients with comorbidities such as type 2 diabetes, hypercholesterolemia, and chronic kidney disease (CKD). Evidence showed that angiotensin receptor blockers (ARBs) such as losartan, valsartan, and candesartan provide various benefits beyond just lowering blood pressure. In patients with type 2 diabetes, losartan and valsartan were both effective in lowering blood pressure, with additional beneficial effects. Valsartan at a dose of 320 mg/day significantly delayed the onset of end-stage renal disease (ESRD) and reduced microalbuminuria progression by 31.8%[18]. Losartan has been shown to lower blood pressure more effectively when combined with SGLT2 inhibitors, compared to using either drug alone. Losartan also helps to reduce sympathetic nervous system activity and arterial stiffness, which supports better vascular health in comorbid conditions[28].

For patients with CKD-related hypertension, losartan showed high efficacy of post-dialysis patients. Losartan significantly reduced post-dialysis systolic blood pressure, achieving the target <140 mmHg compared to those receiving standard (non-RAAS) therapy. Furthermore, losartan was associated with a lower mortality rate (2 vs. 6 deaths) and better 1-year survival (95% vs. 84%) in this high-risk group, with only mild adverse effects such as hyperkalemia and dizziness[29].

In patients with primary hypercholesterolemia and hypertension, Candesartan when combined with rosuvastatin, the fixed-dose therapy not only improved blood pressure control but also resulted in a significant reduction in low-density lipoprotein cholesterol (LDL-C) levels by 49.8%, along with improvements in high-density lipoprotein (HDL-C), triglyceride levels, and insulin sensitivity in non-diabetic patients, compared to rosuvastatin monotherapy[23]. Candesartan also has shown antioxidant effects by significant improvements in oxidative stress markers, including increased levels of glutathione (GSH) and total antioxidant status (TAS), and decreased malondialdehyde (MDA)[26].

Cost and availability are additional factors influencing ARB selection in clinical practice, especially in low- and middle-income countries like Indonesia. Losartan is usually more affordable and most widely accessible, making it a common first-line option in Indonesia's public healthcare system (JKN). Valsartan is also available as a generic but may be slightly more expensive. Candesartan, although showing the highest efficacy, is more expensive and harder to find.

The systematic review conducted has the strength of proving the effectiveness of

lowering blood pressure with three ARB agents, namely valsartan, candesartan, and losartan, with parameters of systolic blood pressure and diastolic blood pressure. However, the systematic review conducted has limitations, including the lack of a specific comparison between the three agents with the same clinical trial procedure, so the comparison results are only compared based on the decrease in blood pressure from each different trial procedure.

Conclusion

Our findings indicate that ARBs, including Valsartan, Candesartan, and Losartan, are effective in lowering blood pressure among hypertensive patients. Candesartan showed the most significant blood pressure reduction, likely due to its higher binding affinity to the AT1 receptor and better bioavailability. Valsartan showed the least effectiveness, but its antihypertensive effect can be enhanced when combined with other antihypertensive agents. Further research should include direct comparative clinical trials of Valsartan, Candesartan, and Losartan to better assess their relative efficacies in lowering blood pressure. Furthermore, future research is needed to assess the studies focused on the molecular mechanisms behind the varying efficacies of these ARBs that could lead to more effective treatments for hypertension.

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Conflict of Interest

None

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Table 1. Quality assessment by Jadad scale

Author	Randomization	Description of randomization	Double-blind method	Description of the blinding method	Description of withdrawal/ drop-out	Total Score
Ahn et al., 2018[12]	1	1	1	1	1	5
Serebruany et al., 2014[13]	1	1	1	1	1	5
Na et al., 2015[14]	1	1	1	1	1	5
Shi et al., 2017[15]	1	1	0	0	1	3
Park et al., 2014[16]	1	1	0	0	1	3
Giles et al., 2014[17]	1	0	1	1	1	4
Ruggenenti et al., 2019[18]	1	0	0	0	1	2
Park et al., 2016[19]	1	0	0	0	1	2
Wang et al., 2020[20]	1	1	1	1	1	5
Mancia et al., 2015[21]	1	1	1	1	1	5
Ruggenenti et al., 2021[22]	1	1	0	1	1	4

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Author	Randomization	Description of randomization	Double-blind method	Description of the blinding method	Description of withdrawal/ drop-out	Total Score
Cho et al., 2019[23]	1	1	1	1	1	5
Sohn et al., 2017[24]	1	0	1	1	1	4
Hanna et al., 2024[25]	1	0	0	0	1	2
Tamuli et al., 2015[26]	1	0	0	0	0	1
Lai et al., 2022[27]	1	1	1	1	1	5
Scholtes et al., 2023[28]	1	1	1	1	1	5
Aftab et al., 2017[29]	1	1	0	0	1	3
Boonbaichai-yapruck et al., 2015[30]	1	0	0	0	1	2
Mujeeb et al., 2016[31]	1	1	1	1	1	5

Information about the studies characteristics in 20 studies can be seen in the following table.

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Table 2. Studies Characteristics

No.	Author, year	Study duration	Study design	Patients	Intervention dose	Comparator	Outcome
1	Ahn et al., 2018[12]	8 weeks	RCT, parallel-group	Population: mild to moderate HTN msDBP ≥90mmHg. Mean age: 56.14 years Patients: 184 Setting: Republic of Korea.	Amlodipine/Valsartan 5/160mg (AML/VAL) group	Valsartan/hydrochlorothiazide (VAL/HCTZ) 160/12.5mg	AML/VAL group: msDBP was decreased by 9.44±0.69 mmHg with a BP control rate of 71.3%; VAL/HCTZ group: msDBP from baseline -7.47±0.71 mmHg with a BP control rate of 84.3%.
2	Serebruany et al., 2014[13]	4 weeks	RCT	Population: mild-to-moderate hypertensive diabetics Mean age: 53.6 years Patients: 52 Setting: Northern Baltimore area	Aliskiren (150–300 mg/d) and Valsartan (160 mg/d)	Aliskiren 150–300 mg/day monotherapy	SBP/DBP from baseline were decreased to -13/ 5 mmHg for aliskiren and valsartan combination.
3	Na et al., 2015[14]	8 weeks	RCT, parallel-group	Population: hypertensive patients with diastolic blood pressure, (DBP) >90 mmHg Mean age range: 55 Patients: 315 Setting: Korea	Lercanidipine 10mg/ valsartan 80 mg (L10/ V80),	Lercanidipine 10mg/valsartan 160 mg (L10/ V160)	The L10/V80 group had a mean difference of -4.6 mm Hg, while the L10/V160 group had a mean difference of -5.9 mm Hg.

4	Shi et al., 2017[15]	10 weeks	RCT, parallel-group	Population: Newly diagnosed mild to moderate hypertension Mean age: 64.68 years Patients: 139 Setting: Chengdu, China.	Valsartan 160mg	Amlodipine 10 mg and Amlodipine 5 mg + Valsartan 80 mg	Reduction SBP from baseline for valsartan 160mg was -19.19 ± 5.76 mm Hg, and DBP -8.34 ±6.56 mm Hg. Valsartan 160mg showed greatest reduction in PWV (−228.87 ± 60.41 cm/s).
5	Park et al., 2014[16]	8 weeks	RCT	Population: mild to moderate hypertension Mean age range: 20-70 years Patients: 391 Setting: Korea	Valsartan 160 mg (V160)	Nifedipine 60 mg or Nifedipine 30 mg + Valsartan 80 mg	Valsartan 160 mg significantly reduced central SBP by −14.4 ± 16.6 mmHg.
6	Giles et al., 2014[17]	8 weeks	RCT, placebo-controlled, parallel-group	Population: stage 1 or 2 hypertension Mean age: 51.1 years Patients: (G1= 555, G2=554) Setting: US sites	G1: Valsartan 160 mg G2: Valsartan 320 mg	Placebo	Mean decrease in mDBP/mSBP were 10.8/14.2 mmHg for valsartan 160 mg/day; 11.2/14.8 mmHg for valsartan 320 mg/day.
7	Ruggenenti et al., 2019[18]	4.5 years	RCT, parallel-group	Population: mild to moderate hypertension with type 2 diabetes Mean age: 63.9 years Patients: 77 Setting: 11 sites in Italy and Slovenia	Valsartan 160-320 mg	Benazepril 10 mg-20 mg	mSBP/mDBP were decreased by −0.81/−0.04 mmHg. In people with type 2 diabetes with nephropathy, valsartan (320 mg) ESRD were decreased to 13.9%, more effective than benazepril

8	Park et al., 2016[19]	8 weeks	RCT	Population: Patient with stage II or higher hypertension Mean age range: 48,2-49,4 years Patients: 181 Setting: 17 study centers in South Korea	Valsartan 80 to 160 mg/ day	Nifedipine 30 mg to 60 mg	SBP/DBP from baseline were decreased to -18.7 (15.9)/–10.5 (9.9) mm Hg for Valsartan 80mg to 160 mg.
9	Wang et al., 2020[20]	8 weeks	RCT, parallel-group	Population: mild to moderate hypertension Mean age: 57.3 years Patients: 60 Setting: Taipei Veterans General Hospital	Valsartan 160 mg monotherapy	Amlodipine/valsartan 5/80mg	SBP changes from baseline for Valsartan 160mg were –6.9 ± 11.4 mmHg while in DBP were –2.5 ± 6.6 mmHg; less effective than combination therapy.
10	Mancia et al., 2015[21]	6 months	RCT, parallel-group	Population: mild to moderate hypertension Mean age: 55.5 years Patients: 2740 Setting: 194 centers in 18 countries	Valsartan 80 mg/ Amlodipine 5 mg	Perindopril/ Amlodipine 3.5/2.5 mg	Reductions from baseline for Valsartan/Amlodipine combination in SBP were - 23.6 ± 14.2 mmHg while in DBP -15.5 ± 9.2 mmHg; less effective than comparator.
11	Ruggenenti et al., 2021[22]	66 months	RCT, parallel	Population: mild to moderate hypertension with type 2 diabetes Mean: 64.3 years Patients: 202 Setting: Italy	Valsartan (320 mg/day)	Benazepril (10 mg/day) and valsartan (160 mg/day)	mSBP/mDBP were reduced to −0.81/-0.04 mmHg for valsartan versus combination therapy.

12	Cho et al., 2019[23]	12 weeks	RCT, placebo-controlled	Population: mild to moderate hypertension with primary hypercholesterolemia Mean age: 63 years Patients: 219 Setting: Korea	Candesartan 32 mg	Placebo	mSBP were reduced to −15.9 mmHg while mDBP −7.7 mmHg on candesartan 32 mg
13	Sohn et al., 2017[24]	8 weeks	RCT	Population: moderate hypertension Mean age range: 56.8-58.9 years Patients: 57 Setting: 23 sites in South Korea.	G1: Candesartan 8 mg G2: Candesartan 16 mg	Placebo	mSBP/mDBP were reduced to -16.7/-11.2 mmHg on candesartan 8 mg and -15.9/-12.1 mmHg on candesartan 16 mg.
14	Hanna et al., 2024[25]	12 weeks	RCT	Population: hypertension stages II or III Mean age: 55.70 years Patients: 86 patients Setting: BeniSuef University Hospital.	Candesartan 16 mg + Amlodipine 10 mg	Valsartan 160 mg + Amlodipine 10 mg	Amlodipine/Candesartan reduced PSBP by −39 mmHg and CSBP by −23 mmHg. Amlodipine/Valsartan reduced PSBP by −38.7 mmHg and CSBP by −23.3 mmHg.
15	Tamuli et al., 2015[26]	8 weeks	RCT	Population: untreated essential hypertensive patient Mean age range: 46-47 years Patients: 40 Setting: North Eastern part of India.	Candesartan (8-16mg)	Atenolol 50–100 mg	Both drugs have the same significant effect on decreasing blood pressure. SBP/DBP were reduced to -26/−10 mmHg for Candesartan monotheraphy.

16	Lai et al., 2022[27]	8 weeks	RCT	Population: mild (grade 1) essential hypertension Mean age: 52.5 years Patients: 302 Setting: China	Losartan 50 mg	Placebo	SiDBP was reduced to −8.1±7.9 mmHg and SiDBP was reduced to −10.6±10.3 mmHg
17	Scholtes et al., 2023[28]	1 week	RCT	Population: essential hypertension with type 2 diabetes Mean age: 66 years Patients: 24 Setting: Amsterdam	Losartan 50 mg	Placebo	SBP/ DBP were reduced to -12 mmHg/-6 mmHg.
18	Aftab et al., 2017[29]	12 months	RCT	Population: patients with systolic blood pressure >140 mmHg post-dialysis Mean age: 54 years Patients: 88 Setting: Malaysia	Losartan 50mg	Standard antihypertensive (non-RAAS drugs)	Losartan reduced blood pressure more effectively than standard therapy, with SBP dropping -10.23 mmHg pre-dialysis, -6.6 mmHg post-dialysis, and DBP -7.6 mmHg during dialysis.
19	Boonbaichaiyapruck et al., 2015[30]	12 weeks	RCT	Population: mild to moderate hypertension Mean age: 54 years Patients: 22 patients Setting: Thailand	Losartan 50 mg	Original vs. Generic Losartan	Both original and generic Losartan 50 mg reduced BP equally. Office BP was reduced to 28±15.1 mmHg, Home BP was reduced to 18±9 mmHg

20	Mujeeb et al., 2016[31]	8 weeks	RCT, parallel-group	Population: with an average diastolic blood pressure between 100-115 mmHg and a mean daytime diastolic blood pressure between 90-120 mmHg Mean age: 52 years Patients: 200 Setting: Mumbai	G1: Losartan 50 mg G2: Valsartan 80 mg	Placebo	Losartan reduced the mean 24-hour SBP by 12.5 mmHg, similar to valsartan's reduction of 11.3 mmHg. Mean night-time DBP decreased by 6.8 mmHg on losartan and 7.4 mmHg on valsartan. The reduction in nighttime SBP was 10.3 mmHg with losartan and 8.8 mmHg with valsartan.