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Review Article

Formulation and Evaluation of a Polyherbal Antihypertensive Tablet Containing *Rauwolfia serpentina* and *Terminalia arjuna*: A Comprehensive Review

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ABSTRACT

Hypertension is a widespread chronic disorder and a major contributor to cardiovascular morbidity and mortality worldwide. Despite the availability of several synthetic antihypertensive drugs, long-term therapy is often associated with adverse effects, poor patient compliance, and high treatment costs. These limitations have increased interest in plant-based therapies that are considered safer, cost-effective, and suitable for prolonged use. Among the various medicinal plants, Rauwolfia serpentina and Terminalia arjuna have gained significant attention due to their well-documented antihypertensive and cardioprotective properties. Rauwolfia serpentina contains the alkaloid reserpine, which exerts its effect by depleting catecholamines and reducing sympathetic activity, thereby lowering blood pressure. In contrast, Terminalia arjuna acts through multiple mechanisms, including vasodilation, antioxidant activity, and improvement of myocardial function. The combination of these plants in a polyherbal formulation is expected to produce a synergistic effect, targeting multiple pathways involved in hypertension. The present review aims to summarize the pharmacological mechanisms, therapeutic efficacy, and formulation aspects of polyherbal antihypertensive preparations containing these two plants. Available literature indicates that such combinations offer enhanced antihypertensive activity with improved safety profiles compared to single-drug therapy. In conclusion, polyherbal formulations based on Rauwolfia serpentina and Terminalia arjuna represent a promising and effective approach for the management of hypertension, warranting further clinical investigation and standardization for wider therapeutic application.

INTRODUCTION

1.1 Definition and Prevalence of Hypertension

Hypertension, commonly referred to as high blood pressure, is a chronic cardiovascular disorder characterized by a sustained elevation in arterial

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blood pressure. ^[1] Clinically, it is defined as a systolic blood pressure (SBP) of ≥ 140 mmHg and/or a diastolic blood pressure (DBP) of ≥ 90 mmHg measured on repeated occasions. It is often termed a “silent killer” because it may remain asymptomatic for long periods while gradually causing damage to vital organs. ^[2]

Hypertension is one of the most prevalent non-communicable diseases globally and represents a major public health challenge. The incidence of hypertension is steadily increasing due to rapid urbanization, sedentary lifestyle, unhealthy dietary habits (especially high salt intake), obesity, stress, and aging population. ^[3] It significantly contributes to morbidity and mortality by increasing the risk of cardiovascular diseases such as myocardial infarction, stroke, heart failure, and renal disorders. Early detection and effective management are therefore essential to reduce its long-term complications. ^[4]

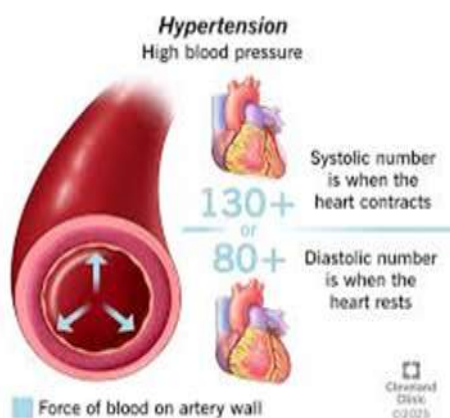


Figure 1: Hypertension

1.2 Limitations of Synthetic Antihypertensive Drugs

Modern pharmacotherapy offers a variety of antihypertensive agents, including diuretics, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and calcium channel blockers. ^[5] Although these drugs are effective in lowering blood pressure,

their long-term use is often associated with several limitations. ^[6]

Common adverse effects include dizziness, fatigue, headache, electrolyte imbalance, dry cough (with ACE inhibitors), and sexual dysfunction. In addition, prolonged therapy may lead to drug tolerance, dependence on medication, and increased risk of drug interactions, especially in elderly patients receiving multiple medications. ^[7] Another major concern is poor patient compliance due to the need for lifelong therapy and the high cost of treatment. These limitations highlight the need for safer and more acceptable therapeutic alternatives. ^[8]

1.3 Need for Herbal Alternatives

In recent years, there has been a growing interest in herbal medicines as alternative or complementary therapies for hypertension. ^[9] Medicinal plants have been used in traditional systems of medicine such as Ayurveda for centuries and are known for their therapeutic potential and safety profile. ^[10]

Herbal drugs possess multiple pharmacological properties, including antihypertensive, antioxidant, anti-inflammatory, and cardioprotective activities. Unlike synthetic drugs, they often act on multiple targets and pathways involved in the disease process. ^[11] Furthermore, herbal medicines are generally well-tolerated, cost-effective, and suitable for long-term use, making them an attractive option for chronic conditions like hypertension. ^[12]

1.4 Importance of Polyherbal Approach

The polyherbal approach involves the use of a combination of two or more medicinal plants in a single formulation to achieve enhanced therapeutic effects. ^[13] This concept is well-

established in traditional medicine and is based on the principle of synergism, where the combined effect of multiple herbs is greater than the sum of their individual effects.^[14]

In the context of hypertension, a polyherbal formulation can target various mechanisms such as vascular resistance, oxidative stress, sympathetic overactivity, and fluid balance simultaneously.^[15] This multi-target action not only improves efficacy but also reduces the required dose of individual components, thereby minimizing potential side effects.^[16]

Additionally, polyherbal formulations may improve patient compliance by providing comprehensive therapeutic benefits in a single dosage form. Hence, the development of

polyherbal antihypertensive formulations, such as those containing *Rauwolfia serpentina* and *Terminalia arjuna*, represents a promising strategy for effective and holistic management of hypertension.^[17]

2. Pathophysiology of Hypertension

Hypertension is a multifactorial disorder that develops due to complex interactions between neural, hormonal, vascular, and renal mechanisms. The sustained elevation of blood pressure results primarily from increased peripheral vascular resistance and, in some cases, increased cardiac output. Several key pathophysiological mechanisms are involved in the development and progression of hypertension.^[18]

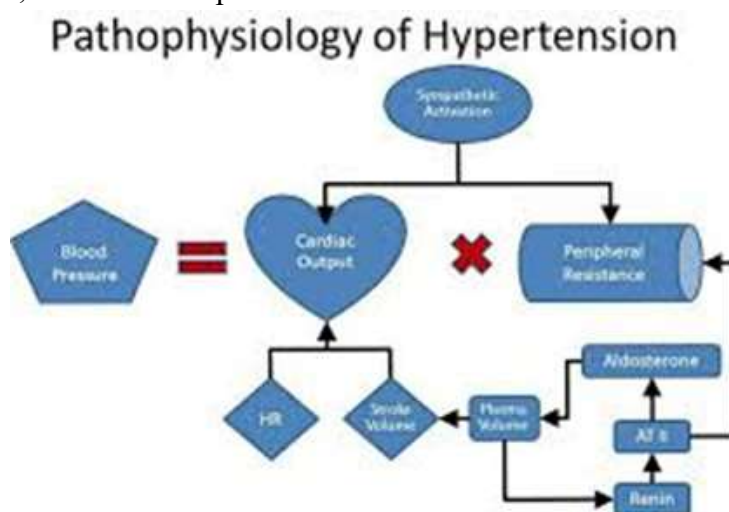


Figure 2: Pathophysiology of Hypertension

2.1 Renin–Angiotensin–Aldosterone System (RAAS)

The renin–angiotensin–aldosterone system plays a central role in the regulation of blood pressure and fluid balance. In response to decreased renal perfusion or sodium levels, renin is released from the juxtaglomerular cells of the kidney. Renin converts angiotensinogen into angiotensin I, which is further converted into angiotensin II by angiotensin-converting enzyme (ACE).^[19]

Angiotensin II is a potent vasoconstrictor that increases peripheral vascular resistance, leading to elevated blood pressure. It also stimulates the secretion of aldosterone from the adrenal cortex, promoting sodium and water retention, which further increases blood volume and blood pressure. Overactivation of the RAAS is a major contributing factor in the development of hypertension.^[20]

2.2 Sympathetic Nervous System Overactivity

The sympathetic nervous system (SNS) plays a vital role in cardiovascular regulation. In hypertension, there is often chronic overactivation of the SNS, leading to increased heart rate, enhanced cardiac output, and vasoconstriction of blood vessels. [21]

This overactivity also stimulates renin release, thereby indirectly activating the RAAS pathway. Persistent sympathetic stimulation contributes to vascular remodeling and increased arterial stiffness, both of which sustain elevated blood pressure over time. [22]

2.3 Endothelial Dysfunction

The endothelium, which lines the inner surface of blood vessels, plays a critical role in maintaining vascular tone by releasing vasoactive substances. [23] In healthy conditions, the endothelium produces nitric oxide (NO), a potent vasodilator that helps maintain normal blood pressure. [24]

In hypertension, endothelial dysfunction occurs due to reduced production or availability of nitric oxide and increased production of vasoconstrictors such as endothelin. This imbalance leads to impaired vasodilation, increased vascular resistance, and ultimately sustained elevation of blood pressure. [25]

2.4 Oxidative Stress

Oxidative stress is characterized by an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defense mechanisms. [26] Excessive ROS can damage vascular cells, reduce nitric oxide bioavailability, and promote inflammation. [27]

In hypertension, oxidative stress contributes to endothelial dysfunction, vascular inflammation, and structural changes in blood vessels. [28] These effects further increase peripheral resistance and

worsen the hypertensive state. Antioxidant mechanisms are therefore crucial in protecting against hypertension-related vascular damage. [29]

3 Role of Herbal Medicine in Hypertension

Herbal medicine has gained increasing attention in the management of hypertension due to its holistic approach and long-standing use in traditional systems like Ayurveda. [30] Medicinal plants contain a wide range of bioactive constituents that exert antihypertensive effects through diverse mechanisms. Unlike conventional drugs that often target a single pathway, herbal therapies can act on multiple physiological systems simultaneously, making them particularly useful in complex disorders such as hypertension. [31]

3.1 Advantages of Herbal Drugs

Herbal drugs offer several benefits over synthetic medications, especially in chronic conditions requiring long-term treatment. [32]

- They are generally natural and well-tolerated, with a lower incidence of adverse effects
- Provide cost-effective therapy, making them accessible to a larger population
- Possess multiple pharmacological activities such as antihypertensive, antioxidant, anti-inflammatory, and cardioprotective effects
- Improve patient compliance due to better tolerability and fewer side effects
- Suitable for long-term management of chronic diseases

These advantages make herbal medicines a promising alternative or adjunct to conventional antihypertensive therapy. [33]

3.2 Multi-Target Mechanism



One of the key strengths of herbal medicine lies in its ability to act on multiple targets simultaneously. Hypertension involves several interconnected pathways such as RAAS activation, sympathetic overactivity, endothelial dysfunction, and oxidative stress.^[34]

Herbal drugs contain a combination of phytoconstituents that can:

- Promote vasodilation by enhancing nitric oxide availability
- Reduce oxidative stress through antioxidant activity
- Modulate neurotransmitter levels, thereby reducing sympathetic activity
- Exhibit diuretic effects, helping in the elimination of excess fluid
- Improve endothelial function and vascular health^[35]

This multi-target action helps in achieving better control of blood pressure and reduces the likelihood of resistance or treatment failure.^[36]

3.3 Safety and Long-Term Use

Herbal medicines are generally considered safe for prolonged use, especially when used in appropriate doses.^[37] Their natural origin and balanced composition reduce the risk of severe side effects commonly associated with synthetic drugs.^[38]

In hypertension, which often requires lifelong therapy, safety is a major concern. Herbal formulations:^[39]

- Show lower toxicity and fewer adverse effects
- Are less likely to cause drug dependency

- Can be used as adjunct therapy along with conventional drugs
- Support overall health by improving cardiovascular function and metabolic balance

However, proper standardization, quality control, and clinical validation are essential to ensure consistent safety and efficacy.^[40]

4. Plant Profile and Pharmacology

4.1 *Rauwolfia serpentina*

4.1.1 Botanical Description

Rauwolfia serpentina is a perennial, evergreen undershrub belonging to the family Apocynaceae. It is widely distributed in India, Bangladesh, Sri Lanka, and other tropical regions of Southeast Asia, particularly in moist and shaded forest areas. The plant typically grows to a height of 60–90 cm with a simple, erect stem.^[41]

The leaves are arranged in characteristic whorls of three to four, are lanceolate in shape, and measure about 7–10 cm in length. They are dark green, smooth, and glossy in appearance. The flowers are small, tubular, and range from pink to violet in color, usually appearing in terminal or axillary clusters. The fruit is a small, ovoid drupe that turns purple to black upon ripening.

The root is the most important medicinal part of the plant. It is long, cylindrical, tapering, and brownish-gray externally with a pale interior. The root possesses a bitter taste and characteristic odor, and it contains the highest concentration of pharmacologically active alkaloids.^[42]





Figure 3: *Rauwolfia serpentina*

4.1.2 Phytoconstituents

Rauwolfia serpentina is rich in more than 50 indole alkaloids, which are responsible for its wide range of pharmacological activities. The most important constituents include:

- Reserpine – Major active alkaloid responsible for antihypertensive and sedative effects
- Ajmaline – Antiarrhythmic alkaloid
- Ajmalicine (Raubasine) – Improves cerebral blood flow
- Serpentine – Mild sedative and hypotensive effect
- Yohimbine – Affects adrenergic receptors
- Deserpidine – Similar activity to reserpine but milder

Apart from alkaloids, the plant also contains flavonoids, glycosides, tannins, and sterols, which contribute to its antioxidant and supportive therapeutic properties. ^[43]

4.1.3 Mechanism of Action (Sympatholytic Action)

The antihypertensive effect of *Rauwolfia serpentina* is mainly due to reserpine, which acts

as a centrally and peripherally acting sympatholytic agent.

Reserpine works by:

- Irreversibly blocking the storage of catecholamines (norepinephrine, dopamine, serotonin) in synaptic vesicles
- Causing gradual depletion of these neurotransmitters from nerve endings
- Reducing sympathetic nervous system activity

As a result:

- Peripheral vasoconstriction decreases, leading to reduced vascular resistance
- Heart rate and cardiac output decline
- Blood pressure is lowered gradually and sustained over time

Additionally, depletion of serotonin in the brain produces a sedative and tranquilizing effect, which may indirectly help in reducing stress-related hypertension. ^[44]

4.1.4 Pharmacological Activities ^[45] ^[46]

Rauwolfia serpentina exhibits a wide range of pharmacological effects:

- Antihypertensive – Reduces blood pressure through depletion of catecholamines and decreased sympathetic tone
- Sedative and tranquilizer – Calms the central nervous system and reduces anxiety
- Antipsychotic – Historically used in the management of schizophrenia and mental disorders

- Antiarrhythmic – Ajmaline helps in stabilizing cardiac rhythm
- Antioxidant – Protects against oxidative stress and vascular damage

4.2 *Terminalia arjuna*

4.2.1 Botanical Description

Terminalia arjuna is a large, deciduous tree belonging to the family Combretaceae and is widely distributed throughout India, particularly along riverbanks and in tropical and subtropical regions. The tree can attain a height of 20–25 meters, with a strong trunk and spreading crown. [47]

The leaves are simple, opposite, oblong, and measure about 6–15 cm in length. They are smooth and dark green on the upper surface. The bark is thick, smooth, and pinkish to reddish-brown, and it peels off in large, flat flakes. This bark is the primary medicinal part used in traditional medicine.

The flowers are small, pale yellow, and arranged in spikes, while the fruits are fibrous, woody drupes with five distinct wings, which aid in their dispersal. [48]



Figure 4: *Terminalia arjuna*

4.2.2 Phytoconstituents

The bark of *Terminalia arjuna* is rich in bioactive compounds that contribute to its cardioprotective and antihypertensive properties. Major constituents include:

- Triterpenoids – Arjunolic acid, arjunic acid, arjungenin, arjunetin
- Flavonoids – Quercetin, kaempferol, arjunone
- Saponins – Arjunosides I–IV
- Tannins – Provide astringent and antioxidant properties
- Phenolic compounds – Gallic acid, ellagic acid
- Minerals – Calcium, magnesium, zinc, copper

Among these, arjunolic acid and arjunosides are considered key contributors to its cardiotonic and antihypertensive activity. [49]

4.2.3 Mechanism of Action [50] [51]

Terminalia arjuna exerts its therapeutic effects through multiple mechanisms that target different aspects of cardiovascular function:

- Vasodilation – Enhances endothelial function and increases nitric oxide (NO) availability, leading to relaxation of blood vessels and reduced vascular resistance
- Antioxidant action – Neutralizes free radicals and reduces oxidative stress, thereby protecting vascular endothelium
- Cardiotonic effect – Improves myocardial contractility and strengthens heart muscles
- Anti-ischemic action – Enhances oxygen supply to cardiac tissues and reduces ischemic damage

- Diuretic effect – Promotes excretion of excess sodium and water, reducing blood volume and pressure

These combined effects contribute to overall cardiovascular protection and effective blood pressure regulation.

4.2.4 Pharmacological Activities

Terminalia arjuna exhibits diverse pharmacological properties:

- Cardioprotective – Protects heart tissue from damage and improves cardiac efficiency
- Antihypertensive – Lowers blood pressure through vasodilation and diuretic effects
- Anti-ischemic – Reduces the risk of ischemic heart disease
- Hypolipidemic – Decreases total cholesterol, LDL, and triglycerides
- Antioxidant – Prevents oxidative damage to cardiovascular tissues
- Anti-inflammatory – Reduces inflammation associated with cardiovascular disorders
- Hepatoprotective – Supports liver function ^[52]

Table 1: Phytochemical Constituents and Mechanism

Plant	Major Constituents	Mechanism of Action	Therapeutic Effect
<i>Rauwolfia serpentina</i>	Reserpine, Ajmaline, Serpentine	Depletion of catecholamines (↓ SNS activity)	Antihypertensive, Sedative
<i>Terminalia arjuna</i>	Arjunolic acid, Arjunosides, Flavonoids	Vasodilation, Antioxidant, Cardiotonic	Cardioprotective, Antihypertensive

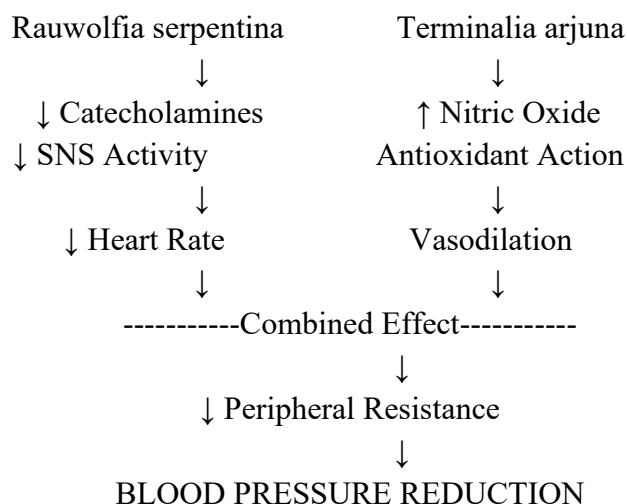


Figure 5: Mechanism of Action of Polyherbal Combination

5. Synergistic Potential of Polyherbal Combination

5.1 Concept of Synergy

The concept of synergy refers to a phenomenon in which the combined effect of two or more drugs or herbal components is greater than the sum of their individual effects. ^[53] principle is widely recognized in traditional systems of medicine, particularly in Ayurveda, where multiple herbs are combined to enhance therapeutic efficacy and reduce unwanted effects. ^[54]

In polyherbal formulations, different plant constituents interact in a complementary manner, targeting various pathways involved in disease progression. This leads to improved therapeutic outcomes, better efficacy at lower doses, and reduced toxicity. ^[55] Synergy can occur through pharmacodynamic interactions (acting on different receptors or pathways) or pharmacokinetic interactions (enhancing absorption, distribution, or bioavailability). ^[56]

5.2 Combined Mechanism

In the case of *Rauwolfia serpentina* and *Terminalia arjuna*, the synergistic effect arises from their distinct yet complementary mechanisms of action:

- *Rauwolfia serpentina* acts primarily as a sympatholytic agent, reducing blood pressure by depleting catecholamines such as norepinephrine and decreasing sympathetic nervous system activity. This results in reduced heart rate, cardiac output, and peripheral vascular resistance. [57]
- *Terminalia arjuna* exerts cardioprotective and vasodilatory effects, improves endothelial function, enhances nitric oxide availability, and reduces oxidative stress. It also strengthens myocardial function and promotes diuresis. [58]

When combined:

- There is simultaneous modulation of neural, vascular, and cardiac pathways
- Blood pressure is reduced through both central and peripheral mechanisms
- Oxidative stress and vascular damage are minimized
- Overall cardiovascular function is improved

Thus, the combination provides a multi-target therapeutic approach, which is more effective than using a single agent. [59]

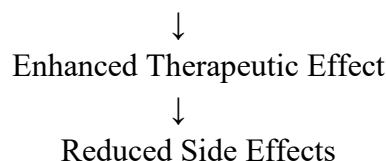
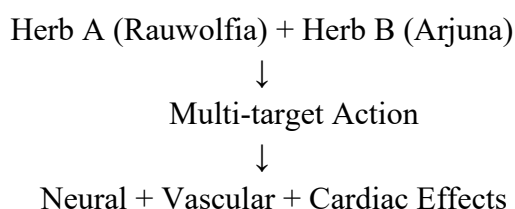


Figure 7: Synergistic Effect of Polyherbal Formulation

5.3 Advantages over Single Drug Therapy

Polyherbal formulations offer several advantages compared to single-drug therapy:

- Enhanced efficacy due to synergistic interaction of multiple active constituents
- Multi-target action, addressing different mechanisms involved in hypertension
- Reduced dose requirement of individual components, minimizing toxicity
- Lower incidence of side effects compared to synthetic drugs or high-dose single herbs
- Improved patient compliance due to better therapeutic outcomes
- Broader therapeutic benefits, including antioxidant, cardioprotective, and anti-inflammatory effects

Additionally, polyherbal formulations may help overcome the limitations of monotherapy, such as incomplete response or development of resistance. [60]

Table 2: Comparison of Individual vs Polyherbal Therapy

Parameter	Single Herbal Drug	Polyherbal Formulation
Mechanism	Single target	Multi-target
Efficacy	Moderate	Enhanced (Synergistic)
Dose	Higher	Lower
Side Effects	Possible	Reduced



Therapeutic Benefit	Limited	Broad spectrum
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6. Formulation Aspects of Polyherbal Tablets

Polyherbal tablet formulation involves the integration of multiple herbal extracts into a stable, effective, and patient-acceptable oral dosage form. [61] Unlike synthetic drugs, herbal materials present unique formulation challenges such as variability, poor flow properties, and complex chemical composition. Therefore, careful selection of excipients, appropriate manufacturing methods, and strict standardization are essential to ensure quality and therapeutic efficacy. [62]

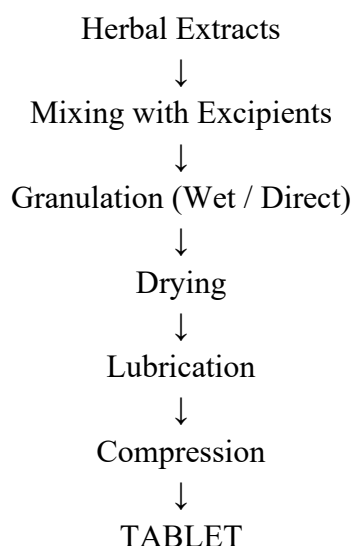


Figure 8: Tablet Formulation Process

6.1 Selection of Excipients

Excipients are inactive ingredients that support the formulation and performance of tablets. In polyherbal formulations, excipients play a critical role in overcoming the limitations of herbal powders, such as poor compressibility and flowability. [63]

- **Diluents (Fillers):**

Substances like microcrystalline cellulose (MCC) and lactose are used to increase the bulk of the

tablet, ensuring uniform weight and content distribution. MCC also enhances compressibility. [64]

- **Binders:**

Binders such as polyvinylpyrrolidone (PVP K-30), starch paste, or gum acacia help in holding the particles together and provide sufficient mechanical strength to the tablet.

- **Disintegrants:**

Superdisintegrants like crosscarmellose sodium and sodium starch glycolate facilitate rapid disintegration of the tablet in the gastrointestinal tract, ensuring faster drug release. [65]

- **Lubricants:**

Magnesium stearate is commonly used to reduce friction between the tablet and die wall during compression and ejection, preventing sticking and picking. [67]

- **Glidants:**

Talc improves the flow properties of the powder blend, ensuring uniform die filling during tablet compression. [68]

- **Flavoring and Coloring Agents (optional):**

These may be added to mask the unpleasant taste and odor of herbal extracts and improve patient acceptability.

All excipients should be non-toxic, pharmacologically inert, and compatible with the herbal ingredients to avoid any interaction that may affect stability or efficacy.

Table 3: Excipients and Their Role

Excipient	Category	Function
Microcrystalline Cellulose	Diluent	Improves compressibility



Lactose	Filler	Adds bulk
PVP K-30	Binder	Provides tablet strength
Crosscarmellose Sodium	Disintegrant	Rapid disintegration
Magnesium Stearate	Lubricant	Reduces friction
Talc	Glidant	Improves flow

6.2 Methods of Preparation

6.2.1 Wet Granulation Method

Wet granulation is commonly employed when herbal powders exhibit poor flowability and compressibility.^[69]

Procedure:^[70]

- The herbal extracts are mixed uniformly with excipients
- A suitable binding solution (e.g., PVP in water or alcohol) is added to form a damp mass
- The mass is passed through a sieve to form granules
- Granules are dried at controlled temperature
- Dried granules are lubricated and compressed into tablets

Advantages:^[71]

- Improves flow and compressibility of powders
- Ensures uniform distribution of active constituents
- Produces tablets with good hardness and low friability

Limitations:

- Not suitable for heat- or moisture-sensitive compounds
- Time-consuming and involves multiple steps

6.2.2 Direct Compression Method^[72]

Direct compression is a simpler method where the powder blend is directly compressed into tablets without granulation.

Procedure:

- Herbal extracts are blended with directly compressible excipients
- Lubricants and glidants are added
- The mixture is compressed into tablets

Advantages:

- Fewer processing steps
- Cost-effective and less time-consuming
- Suitable for thermolabile and moisture-sensitive constituents

Limitations:

- Requires excellent flow and compressibility
- Risk of poor content uniformity if mixing is inadequate

6.3 Challenges in Herbal Formulation^[73]

Formulating polyherbal tablets is more complex compared to synthetic drugs due to the inherent variability and complexity of plant materials.

- **Variability of Raw Materials:**

Differences in climate, soil, harvesting time, and processing methods can lead to variations in phytochemical content.

- **Poor Flow and Compressibility:**

Herbal powders are often fibrous, hygroscopic, and irregular in shape, leading to poor flow properties.

- **Taste and Odor Issues:**

Many herbal extracts have a bitter taste and strong odor, affecting patient compliance.

- **Stability Problems:**

Herbal constituents may degrade due to exposure to light, heat, moisture, and oxygen.

- **Complex Composition:**

Presence of multiple phytoconstituents makes it difficult to identify and control active components.

- **Drug–Excipient Interactions:**

Possible interactions between herbal constituents and excipients may affect stability and efficacy.

- **Dose Uniformity Issues:**

Ensuring uniform distribution of active compounds in each tablet is challenging.

6.4 Standardization ^[74]

Standardization is essential to ensure quality, safety, and reproducibility of polyherbal formulations. It involves a series of tests and procedures at different stages of formulation.

- **Authentication of Raw Materials:**

Proper identification of plant species using botanical and pharmacognostic methods.

- **Phytochemical Screening:**

Qualitative and quantitative analysis of active constituents such as reserpine and arjunolic acid.

- **Physicochemical Evaluation:**

Determination of parameters like moisture content, ash value, extractive value, and pH.

- **Preformulation Studies:**

Evaluation of flow properties, particle size, and compatibility studies (e.g., FTIR).

- **Evaluation of Tablets:**

- Hardness
- Friability
- Weight variation
- Disintegration time
- Dissolution profile

- **Stability Studies:**

Conducted under different temperature and humidity conditions to assess shelf-life.

- **Quality Control:**

Ensures batch-to-batch consistency and compliance with pharmacopeial standards.

7. Evaluation Parameters

Evaluation of polyherbal tablets is essential to ensure their quality, efficacy, safety, and stability. It includes preformulation studies, tablet evaluation tests, and stability studies, which collectively confirm the suitability of the developed formulation. ^[75]



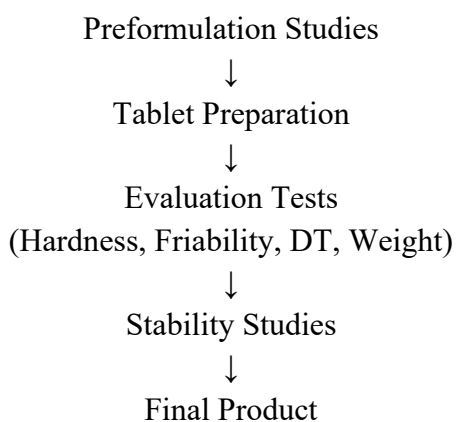


Figure 9: Evaluation Flowchart

7.1 Preformulation Studies

Preformulation studies are carried out before tablet formulation to evaluate the physical and chemical properties of the herbal extracts and excipients. ^[76]

These include:

- Organoleptic properties – color, odor, taste
- Particle size and shape – affects flow and compressibility
- Bulk density and tapped density – used to determine packing ability
- Angle of repose – indicates flow properties of powder
- Carr's index and Hausner ratio – evaluate compressibility and flowability
- Compatibility studies – interaction between drug and excipients (e.g., FTIR analysis)

These studies help in selecting suitable excipients and formulation method. ^[77]

7.2 Tablet Evaluation

After formulation, tablets are evaluated using standard quality control parameters:

7.2.1 Hardness ^[78]

Hardness indicates the mechanical strength of tablets and their ability to withstand handling, packaging, and transportation.

- Measured using a hardness tester
- Ensures tablets are not too soft (break easily) or too hard (delay disintegration)

7.2.2 Friability ^[79]

Friability measures the resistance of tablets to abrasion and shock.

- Determined using a friabilator
- Acceptable limit is generally less than 1% weight loss
- Indicates durability of tablets during handling

7.2.3 Disintegration Time ^[80]

Disintegration test determines the time required for a tablet to break down into smaller particles in a specified medium.

- Important for drug release and absorption
- For uncoated tablets, it is usually within 15 minutes
- Faster disintegration ensures better therapeutic effect

7.2.4 Weight Variation ^[81]

This test ensures uniformity of weight among tablets.

- Random tablets are selected and weighed individually

- Deviation should be within pharmacopeial limits
- Ensures consistent dose of active ingredients

7.3 Stability Studies^[82]

Stability studies are conducted to determine the shelf life and storage conditions of the formulation.

- Performed under different conditions of temperature and humidity (e.g., 25°C/60% RH, 40°C/75% RH)
- Parameters evaluated include:
 - Physical appearance
 - Hardness
 - Disintegration time
 - Drug content
 - Helps in identifying any degradation or loss of efficacy over time

Table 4: Evaluation Parameters of Tablets

Parameter	Purpose	Ideal Result
Hardness	Mechanical strength	4–8 kg/cm ²
Friability	Resistance to breakage	<1%
Disintegration Time	Drug release	<15 min
Weight Variation	Dose uniformity	Within limits
Stability	Shelf life	No significant change

8. Safety and Toxicological Aspects

8.1 Side Effects of Reserpine

Reserpine, the principal alkaloid of *Rauwolfia serpentina*, is effective in lowering blood pressure

but is associated with certain adverse effects, especially with prolonged or high-dose use.

- Central nervous system effects: sedation, drowsiness, depression
- Gastrointestinal effects: increased gastric acid secretion, which may lead to ulcers
- Cardiovascular effects: bradycardia and hypotension in some cases
- Nasal congestion and fatigue

Due to these effects, careful dose optimization and monitoring are necessary. In polyherbal formulations, the dose of reserpine is usually minimized, which helps reduce the risk of such side effects.

8.2 Safety of *Terminalia arjuna*

Terminalia arjuna is generally considered safe and well-tolerated, especially when used in recommended doses.

- Exhibits low toxicity in both experimental and clinical studies
- Provides cardioprotective benefits without significant adverse effects
- May occasionally cause mild gastrointestinal discomfort in some individuals
- Suitable for long-term use in chronic cardiovascular conditions

Its strong safety profile makes it an ideal component in polyherbal antihypertensive formulations.

8.3 Toxicity Considerations



Although herbal medicines are considered safer, certain precautions are necessary:

- Dose standardization is essential to avoid toxicity
- Quality control of raw materials to prevent contamination (heavy metals, pesticides)
- Herb–drug interactions should be evaluated when used with conventional medicines
- Long-term safety studies are required to confirm chronic toxicity profile

Proper formulation, standardization, and clinical validation are necessary to ensure safety and efficacy.

9. Future Perspectives

9.1 Need for Clinical Trials

Most studies on polyherbal antihypertensive formulations are limited to preclinical or small-scale clinical investigations.

- There is a need for large-scale, randomized controlled trials
- Clinical validation is required to confirm efficacy and safety in humans
- Long-term studies are essential to evaluate chronic use and outcomes

Such studies will help in establishing the scientific credibility of herbal formulations.

9.2 Standardization of Herbal Drugs

Standardization remains a major challenge in herbal medicine.

- Requires identification and quantification of active constituents (e.g., reserpine, arjunolic acid)
- Ensures batch-to-batch consistency
- Improves quality, safety, and reproducibility
- Development of validated analytical methods is essential

Proper standardization is critical for acceptance in modern healthcare systems.

9.3 Scope of Novel Drug Delivery Systems

Advancements in pharmaceutical technology provide opportunities to improve herbal drug delivery.

- Development of controlled-release and sustained-release formulations
- Use of nanotechnology-based delivery systems to enhance bioavailability
- Formulation of herbal nanoparticles, liposomes, and phytosomes
- Improvement in targeted delivery and therapeutic efficacy

These approaches can overcome limitations of conventional herbal dosage forms.

10. CONCLUSION

10.1 Summary of Findings

Hypertension is a major global health concern requiring long-term management. Herbal medicines, particularly *Rauwolfia serpentina* and *Terminalia arjuna*, have demonstrated significant antihypertensive and cardioprotective effects through various mechanisms such as



sympatholytic action, vasodilation, antioxidant activity, and improvement of cardiac function.

10.2 Justification of Polyherbal Formulation

The combination of these two medicinal plants provides a synergistic effect, targeting multiple pathways involved in hypertension. This polyherbal approach enhances therapeutic efficacy while reducing the required dose of individual components, thereby minimizing adverse effects. It also offers a holistic treatment strategy compared to single-drug therapy.

10.3 Therapeutic Potential

Polyherbal antihypertensive formulations represent a promising, safe, and cost-effective alternative to conventional therapy. With proper standardization, clinical validation, and advanced formulation strategies, such preparations have strong potential for future use in the management of hypertension and related cardiovascular disorders.

REFERENCES

1. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, et al. Global disparities of hypertension prevalence and control: a systematic analysis. *Circulation*. 2016;134(6):441-450.
2. World Health Organization. Hypertension fact sheet. WHO Report. 2023.
3. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, et al. 2017 guideline for the prevention, detection, evaluation, and management of high blood pressure. *Hypertension*. 2018;71(6):e13-e115.
4. Forouzanfar MH, Liu P, Roth GA, Ng M, Biryukov S, Marczak L, et al. Global burden of hypertension and systolic blood pressure. *Lancet*. 2017;389(10064):37-55.
5. Burnier M, Egan BM. Adherence in hypertension: a review of prevalence, risk factors, and management. *Circ Res*. 2019;124(7):1124-1140.
6. Gupta AK, Arshad S, Poulter NR. Compliance, safety, and effectiveness of fixed-dose combinations in hypertension. *Hypertension*. 2010;55(2):399-407.
7. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence. *J Hypertens*. 2014;32(12):2285-2295.
8. Elliott WJ. Drug interactions and adverse effects of antihypertensive agents. *J Clin Hypertens*. 2011;13(9):687-693.
9. World Health Organization. WHO traditional medicine strategy 2014–2023. WHO Press. 2014.
10. Ekor M. The growing use of herbal medicines: issues relating to adverse reactions. *Front Pharmacol*. 2014;4:177.
11. Firenzuoli F, Gori L. Herbal medicine today: clinical and research issues. *Evid Based Complement Alternat Med*. 2007;4(S1):37-40.
12. Pan SY, Litscher G, Gao SH, Zhou SF, Yu ZL, Chen HQ, et al. Historical perspective of traditional medicine. *Evid Based Complement Alternat Med*. 2014;2014:525340.
13. Wagner H. Synergy research: approaching a new generation of phytopharmaceuticals. *Fitoterapia*. 2011;82(1):34-37.
14. Williamson EM. Synergy and other interactions in phytomedicines. *Phytomedicine*. 2001;8(5):401-409.
15. Parasuraman S, Thing GS, Dhanaraj SA. Polyherbal formulation: concept of Ayurveda. *Pharmacogn Rev*. 2014;8(16):73-80.

16. Kong DX, Li XJ, Zhang HY. Where is the hope for drug discovery? *Drug Discov Today*. 2009;14(3-4):115-119.
17. Choudhary N, Singh V. A census of plants used in herbal medicine. *J Ethnopharmacol*. 2018;213:34-45.
18. Fyhrquist F, Saijonmaa O. Renin-angiotensin system revisited. *J Intern Med*. 2008;264(3):224-236.
19. Atlas SA. The renin-angiotensin aldosterone system: pathophysiological role and pharmacologic inhibition. *J Manag Care Pharm*. 2007;13(8 Suppl B):9-20.
20. Paul M, Poyan Mehr A, Kreutz R. Physiology of local renin-angiotensin systems. *Physiol Rev*. 2006;86(3):747-803.
21. Esler M, Lambert E, Schlaich M. Point: chronic activation of the sympathetic nervous system is the dominant contributor to systemic hypertension. *J Appl Physiol*. 2010;109(6):1996-1998.
22. Grassi G, Mark A, Esler M. The sympathetic nervous system alterations in human hypertension. *Circ Res*. 2015;116(6):976-990.
23. Fisher JP, Paton JFR. The sympathetic nervous system and blood pressure in humans: implications for hypertension. *J Hum Hypertens*. 2012;26(8):463-475.
24. Vanhoutte PM, Shimokawa H, Tang EHC, Feletou M. Endothelial dysfunction and vascular disease. *Acta Physiol*. 2009;196(2):193-222.
25. Förstermann U, Sessa WC. Nitric oxide synthases: regulation and function. *Eur Heart J*. 2012;33(7):829-837.
26. Ghiadoni L, Taddei S, Virdis A. Hypertension and endothelial dysfunction: therapeutic approach. *Curr Vasc Pharmacol*. 2012;10(1):42-60.
27. Harrison DG, Gongora MC. Oxidative stress and hypertension. *Med Clin North Am*. 2009;93(3):621-635.
28. Touyz RM. Reactive oxygen species in vascular biology: role in arterial hypertension. *Expert Rev Cardiovasc Ther*. 2003;1(1):91-106.
29. Montezano AC, Touyz RM. Molecular mechanisms of hypertension—reactive oxygen species and antioxidants. *Nat Rev Cardiol*. 2012;9(3):162-175.
30. Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Front Pharmacol*. 2014;4:177.
31. Calixto JB. Twenty-five years of research on medicinal plants in Latin America: a personal view. *J Ethnopharmacol*. 2005;100(1-2):131-134.
32. Gurib-Fakim A. Medicinal plants: traditions of yesterday and drugs of tomorrow. *Mol Aspects Med*. 2006;27(1):1-93.
33. Fabricant DS, Farnsworth NR. The value of plants used in traditional medicine for drug discovery. *Environ Health Perspect*. 2001;109(Suppl 1):69-75.
34. Wagner H. Multitarget therapy—the future of treatment for more than just functional dyspepsia. *Phytomedicine*. 2006;13(Suppl 5):122-129.
35. Hopkins AL. Network pharmacology: the next paradigm in drug discovery. *Nat Chem Biol*. 2008;4(11):682-690.
36. Li S, Zhang B. Traditional Chinese medicine network pharmacology: theory, methodology and application. *Chin J Nat Med*. 2013;11(2):110-120.
37. Rasoanaivo P, Wright CW, Willcox ML, Gilbert B. Whole plant extracts versus single compounds for the treatment of malaria. *Phytomedicine*. 2011;18(5):417-423.
38. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs. *Drugs*. 2009;69(13):1777-1798.



39. Tilburt JC, Kaptchuk TJ. Herbal medicine research and global health: an ethical analysis. *Bull World Health Organ.* 2008;86(8):594-599.
40. Posadzki P, Watson LK, Ernst E. Herb–drug interactions: an overview of systematic reviews. *Br J Clin Pharmacol.* 2013;75(3):603-618.
41. Vakil RJ. A clinical trial of Rauwolfia serpentina in essential hypertension. *Br Heart J.* 1949;11(4):350-355.
42. Shamon SD, Perez MI. Blood pressure-lowering efficacy of reserpine for primary hypertension. *Cochrane Database Syst Rev.* 2016;12:CD007655.
43. Lobay D. Rauwolfia serpentina for the treatment of hypertension. *Integr Med (Encinitas).* 2015;14(3):40-46.
44. Bhatia BB, Singh H. Pharmacognosy of Rauwolfia serpentina—a review. *Int J Pharm Sci Res.* 2010;1(10):1-8.
45. Klohs MW. Pharmacology and toxicology of Rauwolfia alkaloids. *J Pharm Sci.* 1956;45(1):1-18.
46. Gupta R, Gupta VP. Indigenous herbs for cardiovascular disorders: focus on Rauwolfia serpentina. *J Assoc Physicians India.* 1997;45(8):669-671.
47. Dwivedi S, Udupa N. Terminalia arjuna: pharmacological, phytochemical and clinical studies. *Fitoterapia.* 1989;60(5):413-420.
48. Kapoor D, Vijayvergiya R, Dhawan V. Terminalia arjuna in cardiovascular diseases: a review. *J Ethnopharmacol.* 2014;155(2):1029-1045.
49. Maulik SK, Talwar KK. Therapeutic potential of Terminalia arjuna in cardiovascular disorders. *Am J Cardiovasc Drugs.* 2012;12(3):157-163.
50. Parveen A, Baboota S, Ali J, Ahuja A, Ahmad S. Effects of Terminalia arjuna on cardiovascular system. *J Ethnopharmacol.* 2011;136(1):1-8.
51. Singh RB, Niaz MA, Ghosh S, Beegom R, Rastogi SS. Clinical effects of Terminalia arjuna in chronic stable angina. *Int J Cardiol.* 1992;35(3):373-379.
52. Ram A, Lauria P, Gupta R, Kumar P, Sharma VN. Hypcholesterolaemic effects of Terminalia arjuna in rats. *J Ethnopharmacol.* 1997;57(3):197-201.
53. Khan MS, Ahmad I. Herbal medicine: current trends and future prospects. *New Look to Phytomedicine.* 2019;1:3-13.
54. Parasuraman S, Thing GS, Dhanaraj SA. Polyherbal formulation: concept of Ayurveda. *Pharmacogn Rev.* 2014;8(16):73-80.
55. Joshi H, Mehta P. Evaluation of polyherbal formulation containing Rauwolfia serpentina and Terminalia arjuna in hypertension. *J Herb Med.* 2023;35:100582.
56. Verma S, Singh SP. Current and future status of herbal medicines. *Vet World.* 2008;1(11):347-350.
57. Wagner H. Synergy research: approaching a new generation of phytopharmaceuticals. *Fitoterapia.* 2011;82(1):34-37.
58. Williamson EM. Synergy and other interactions in phytomedicines. *Phytomedicine.* 2001;8(5):401-409.
59. Spinella M. The importance of pharmacological synergy in psychoactive herbal medicines. *Altern Med Rev.* 2002;7(2):130-137.
60. Hemaiswarya S, Kruthiventi AK, Doble M. Synergism between natural products and antibiotics. *Phytomedicine.* 2008;15(8):639-652.
61. Aulton ME, Taylor K. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 5th ed. London: Elsevier; 2018.
62. Allen LV, Popovich NG, Ansel HC. Ansel's Pharmaceutical Dosage Forms and Drug

- Delivery Systems. 10th ed. Philadelphia: Lippincott Williams & Wilkins; 2014.
63. Banker GS, Anderson NR. Tablets. In: Lachman L, Lieberman HA, Kanig JL, editors. *The Theory and Practice of Industrial Pharmacy*. 3rd ed. Mumbai: Varghese Publishing; 2009. p. 293-345.
 64. Patel RP, Patel MM. Formulation and evaluation of herbal tablets: a review. *Int J Pharm Sci Rev Res*. 2012;15(1):1-8.
 65. Rowe RC, Sheskey PJ, Quinn ME. *Handbook of Pharmaceutical Excipients*. 7th ed. London: Pharmaceutical Press; 2012.
 66. Wade A, Weller PJ. *Handbook of Pharmaceutical Excipients*. 2nd ed. Washington: American Pharmaceutical Association; 1994.
 67. Jivraj M, Martini LG, Thomson CM. An overview of different excipients useful for direct compression of tablets. *Pharm Sci Technol Today*. 2000;3(2):58-63.
 68. Shangraw RF. Compressed tablets by direct compression. *Pharm Technol*. 1989;13(4):56-64.
 69. Aulton ME. Granulation. In: *Pharmaceutics: The Science of Dosage Form Design*. 2nd ed. Churchill Livingstone; 2002. p. 397-440.
 70. Parikh DM. *Handbook of Pharmaceutical Granulation Technology*. 2nd ed. New York: Informa Healthcare; 2009.
 71. Augsburger LL, Hoag SW. Pharmaceutical dosage forms: tablets. *Pharm Dev Technol*. 2008;13(2):123-125.
 72. Kunle OF, Egharevba HO, Ahmadu PO. Standardization of herbal medicines. *Int J Biodivers Conserv*. 2012;4(3):101-112.
 73. Pandey MM, Rastogi S, Rawat AKS. Standardization of herbal drugs. *Evid Based Complement Alternat Med*. 2013;2013:376327.
 74. Aulton ME. Preformulation studies. In: *Aulton's Pharmaceutics*. Elsevier; 2018. p. 137-167.
 75. Sinko PJ. *Martin's Physical Pharmacy and Pharmaceutical Sciences*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2011.
 76. Wells JL. Pharmaceutical preformulation: the physicochemical properties of drug substances. *J Pharm Pharmacol*. 1988;40(1):1-7.
 77. United States Pharmacopeia (USP). USP 43–NF 38. Rockville: USP Convention; 2020.
 78. Indian Pharmacopoeia Commission. *Indian Pharmacopoeia*. Ghaziabad: IPC; 2018.
 79. British Pharmacopoeia Commission. *British Pharmacopoeia*. London: TSO; 2019.
 80. Fell JT, Newton JM. Determination of tablet strength by diametral compression test. *J Pharm Sci*. 1970;59(5):688-691.
 81. Banker GS. Tablets. In: Lachman L, Lieberman HA, Kanig JL, editors. *Industrial Pharmacy*. 3rd ed. p. 293-345.
 82. United States Pharmacopeia Convention. Disintegration test for tablets. USP. 2020.
 83. British Pharmacopoeia. Uniformity of weight. BP. 2019.
 84. ICH. Stability testing of new drug substances and products Q1A(R2). ICH Guidelines. 2003.
 85. Blessy M, Patel RD, Prajapati PN, Agrawal YK. Stability indicating methods: a review. *J Pharm Anal*. 2014;4(3):159-165.

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