

# Formulation and Evaluation of Neem-Based Herbal Syrup for the Management of Rheumatic Heart Disease

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**Abstract:** *Rheumatic Heart Disease (RHD) is a chronic inflammatory disorder resulting from autoimmune reactions following streptococcal infection, leading to progressive damage to cardiac valves. Despite the availability of conventional therapies, long-term treatment is associated with side effects and limited patient compliance. Herbal medicines, particularly those derived from Azadirachta indica (Neem), have shown significant pharmacological potential due to their anti-inflammatory, antioxidant, antimicrobial, and cardioprotective properties. This research paper focuses on the formulation, preparation, evaluation, and therapeutic potential of a neem-based herbal syrup for the supportive management of RHD.*

*Azadirachta indica (neem tree) grows up to almost the all over around the asia. It is abundant in Pakistan too and having many medicinal and other beneficial uses. A total of 135 structural compounds have been extracted and identified and they are classified as Isoprenoids and non-isoprenoids. Most important ingredient is nimbin and azadirachtin. From the ancient time, neem tree and its all part have ethnomedicinal importance. The active constituents in the neem posses most of the therapeutic effect on kidney, liver, heart disorder. It also improves the immune system and gives antitumor effect. The neem constituents help to improve all the skin condition. Aloe barbadensis miller (alovera) is a juicy and fleshy plant and grows in hot andtropical climate. It also gives beneficial effect as it is anti inflammatory, anti acne, anti diabetic and also helps to improve the skin condition. Along all these therapeutic effect, these both plants use in pharmaceutical and cosmaceutical industry for making of excipient or use in liquid syrup, creams, ointments, gel, spray and lotions etc.*

**Keywords:** Neem, Rheumatic heart disease, herbal syrup, cardioprotective, anti-inflammatory, phytochemicals

## I. INTRODUCTION

Rheumatic Heart Disease (RHD) is a chronic and progressive cardiovascular condition resulting from permanent damage to the heart valves following repeated episodes of Rheumatic Fever. This disease is triggered by an abnormal immune response to infection with Streptococcus pyogenes, leading to inflammation of cardiac tissues, particularly the valves. Over time, this inflammatory process results in fibrosis, calcification, and deformity of the valves, ultimately impairing cardiac function. RHD remains a major public health concern in developing countries, including India, where limited access to early diagnosis and treatment contributes to its high prevalence.

Conventional management of RHD primarily includes antibiotic therapy to prevent recurrent infections, anti-inflammatory drugs such as corticosteroids, and in severe cases, surgical interventions like valve repair or replacement. While these approaches help manage symptoms and slow disease progression, they are often associated with limitations such as adverse drug reactions, high cost, and lack of complete disease reversal. This has led to increasing interest in alternative and complementary therapeutic strategies, particularly those derived from medicinal plants.



Herbal medicine has been an integral part of traditional healthcare systems, especially Ayurveda, where plant-based remedies are used for their holistic and multi-targeted therapeutic effects. Among these, *Azadirachta indica* (Neem) holds a prominent position due to its diverse pharmacological properties. Neem contains a wide range of bioactive compounds, including nimbin, nimbidin, azadirachtin, quercetin, flavonoids, and tannins, which contribute to its anti-inflammatory, antioxidant, antimicrobial, and immunomodulatory activities. These properties are particularly relevant in the context of RHD, where chronic inflammation, oxidative stress, and immune dysregulation play key roles in disease progression. Neem has also demonstrated cardioprotective effects in various experimental studies, suggesting its potential utility in managing cardiovascular disorders.

Despite its therapeutic potential, the direct use of neem in raw or crude form is limited by factors such as bitter taste, poor patient acceptability, and variability in dosage. To overcome these limitations, the development of suitable pharmaceutical formulations is essential. Herbal syrups represent an ideal dosage form due to their ease of administration, rapid absorption, and improved palatability, particularly for pediatric and geriatric patients who may have difficulty swallowing solid dosage forms. Syrups also allow for uniform distribution of active constituents and can be formulated with sweeteners, flavoring agents, and stabilizers to enhance patient compliance.

The formulation of a neem-based herbal syrup involves the extraction of active phytoconstituents, incorporation into a suitable syrup base (commonly sucrose or honey), and the addition of preservatives and excipients to ensure stability and acceptability. However, the success of such a formulation depends not only on its composition but also on its quality and performance, which must be assessed through systematic evaluation.

Evaluation of herbal syrup formulations includes a range of physicochemical, microbiological, and stability parameters. Key physicochemical tests involve the determination of pH, viscosity, density, and organoleptic properties (color, odor, taste), which influence the stability and acceptability of the product. Microbial evaluation ensures that the formulation is free from harmful contamination, while stability studies assess the product's ability to maintain its quality under various environmental conditions over time. Additionally, phytochemical analysis helps confirm the presence of active constituents responsible for therapeutic activity.

In the context of RHD management, a neem-based herbal syrup offers a promising approach by combining traditional medicinal knowledge with modern pharmaceutical techniques. Such a formulation has the potential to provide anti-inflammatory, antioxidant, and cardioprotective effects, thereby addressing key pathological mechanisms of the disease. Furthermore, it may serve as a cost-effective and safer alternative or adjunct to conventional therapies, particularly in resource-limited settings.

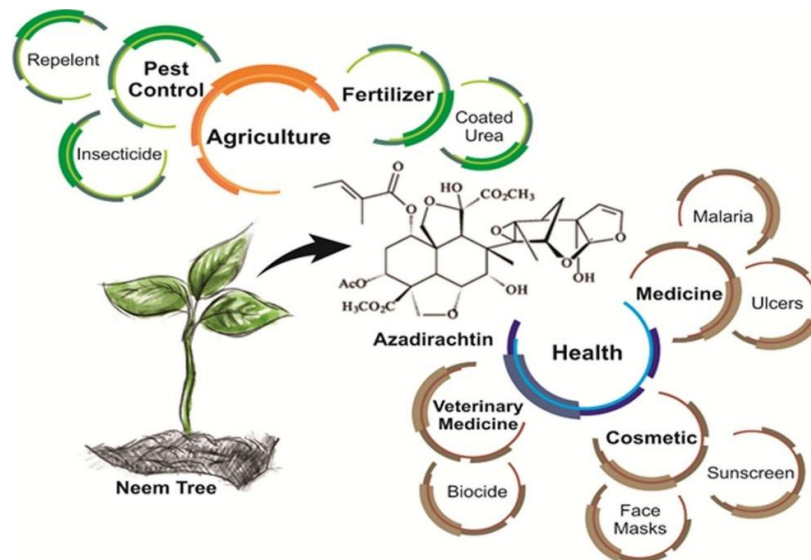
Therefore, the present study focuses on the formulation and evaluation of a neem-based herbal syrup intended for the management of rheumatic heart disease. The objective is to develop a stable, effective, and patient-friendly formulation and to evaluate its quality through standard pharmaceutical parameters, thereby contributing to the advancement of herbal drug delivery systems in cardiovascular therapy.

Rheumatic Heart Disease is a major public health problem in developing countries, characterized by permanent damage to heart valves due to recurrent inflammation.

Rheumatic heart disease (RHD) is a chronic, progressive cardiovascular disorder that develops as a long-term complication of acute rheumatic fever (ARF), which is triggered by infection with Group A  $\beta$ -hemolytic *Streptococcus*. It primarily affects children and young adults, especially in low- and middle-income countries, and remains a major cause of morbidity and mortality worldwide. Despite advances in medical science, RHD continues to be a significant public health problem due to inadequate access to healthcare, poor socioeconomic conditions, and lack of early diagnosis and treatment.

Neem has been widely used in traditional medicine systems such as Ayurveda for treating inflammatory and infectious diseases. It is rich in bioactive compounds that exhibit strong antioxidant and therapeutic activities.





**The use of herbal syrups enhances:**

- Patient compliance
- Drug absorption
- Palatability

**II. REVIEW OF LITERATURE**

**1.Title:** Therapeutics Role of Azadirachta indica (Neem) and Their Active Constituents in Diseases Prevention and Treatment

**Journal:** Mohammad A. Alzohairy

**Author:** Evidence-Based Complementary and Alternative Medicine Year of Publication: 2016

The study by Mohammad A. Alzohairy (2016), published in Evidence-Based Complementary and Alternative Medicine, highlights the therapeutic importance of Azadirachta indica (Neem) as a versatile medicinal plant widely used in traditional systems like Ayurveda.

Neem contains a wide range of bioactive phytoconstituents such as nimbidin, azadirachtin, nimbolide, flavonoids, tannins, and alkaloids, which are responsible for its pharmacological actions. The review emphasizes that these compounds exhibit antioxidant, anti-inflammatory, antimicrobial, antidiabetic, anticancer, and cardioprotective properties.

The article discusses Neem's role in disease prevention, particularly through its ability to reduce oxidative stress and modulate immune responses. Its antioxidant activity helps neutralize free radicals, thereby preventing cellular damage and chronic diseases. Additionally, Neem shows significant anti-inflammatory effects, which are beneficial in conditions like cardiovascular disorders, including rheumatic heart disease.

The author also highlights Neem's antimicrobial activity against bacteria, viruses, and fungi, supporting its traditional use in infections. Its antidiabetic effect is attributed to improved insulin sensitivity and reduced blood glucose levels. Furthermore, Neem exhibits anticancer potential by inducing apoptosis and inhibiting tumor growth in experimental studies.

Overall, the review concludes that Neem is a promising natural therapeutic agent with multi-targeted actions. However, it also stresses the need for more clinical trials and standardization to confirm its safety, efficacy, and dosage for modern medical use.



**2. Title:** Cardiovascular Effects of Azadirachta indica (Neem)

**Journal:** Indian Journal of Physiology and Pharmacology Year of Publication: 2002

**Author:** P. Khosla, A. Gupta, J. Singh

The study by P. Khosla, A. Gupta, and J. Singh (2002), published in the Indian Journal of Physiology and Pharmacology, investigates the cardiovascular effects of Azadirachta indica (Neem).

The review highlights that Neem exhibits significant cardioprotective activity due to its rich content of bioactive compounds such as flavonoids, limonoids, and polyphenols. These constituents contribute to antioxidant properties, which help in reducing oxidative stress—a key factor in the development of cardiovascular diseases.

The study reports that Neem has hypotensive (blood pressure-lowering) effects, likely mediated through vasodilation and improvement in vascular tone. It also demonstrates negative chronotropic and inotropic effects, indicating a reduction in heart rate and force of contraction, which may help decrease cardiac workload.

Additionally, Neem shows anti-inflammatory and lipid-lowering effects, which are beneficial in preventing atherosclerosis and other cardiac complications. The extract was found to improve lipid profiles by reducing cholesterol and triglyceride levels in experimental models.

The authors also suggest that Neem may enhance myocardial protection by stabilizing cell membranes and preventing ischemic damage. Its antithrombotic potential further supports its role in reducing the risk of clot formation.

Overall, the study concludes that Neem possesses multi-faceted cardiovascular benefits and could be a promising natural agent for managing heart-related disorders. However, it emphasizes the need for clinical validation and standardized dosing before widespread therapeutic use.

**3. Title:** Herbal Drugs in Cardiovascular Diseases

**Journal:** Current Cardiology Reviews Year of Publication: 2020

**Author:** A. Kaur, R. Kumar

The review by A. Kaur and R. Kumar, published in Current Cardiology Reviews, discusses the role of herbal drugs in the management of cardiovascular diseases. The authors highlight that medicinal plants contain bioactive compounds such as flavonoids, alkaloids, glycosides, and terpenoids, which exhibit cardioprotective, antioxidant, anti-inflammatory, and lipid-lowering effects. The review emphasizes that herbal drugs help in regulating blood pressure, improving lipid profiles, and preventing atherosclerosis. It also points out their role in enhancing endothelial function and reducing oxidative stress, which are key factors in cardiovascular disorders. However, the authors stress the importance of scientific validation, standardization, and safety evaluation before clinical application.

Another study by K. I. Nyulas et al., published in the International Journal of Molecular Sciences (2024), provides a more detailed molecular insight into the cardiovascular effects of herbal products. The review explains that herbal compounds act through multiple mechanisms, including modulation of signaling pathways, antioxidant defense systems, and anti-inflammatory responses. It highlights their role in reducing oxidative stress, inhibiting platelet aggregation, improving vascular function, and protecting myocardial tissue. The study also discusses the interaction of herbal constituents with molecular targets such as enzymes and receptors involved in cardiovascular regulation. Additionally, it raises concerns about drug–herb interactions and variability in herbal preparations, emphasizing the need for controlled clinical trials and regulatory guidelines.

Overall, both reviews conclude that herbal medicines offer promising complementary approaches for the prevention and management of cardiovascular diseases, but require further research, quality control, and clinical evidence to ensure their safe and effective use.

**4. Title:** Neem (Azadirachta indica A. Juss): Organisms Affected and Reference List Update

**Journal:** Proceedings of the Entomological Society of Washington Year of Publication: 1989

**Author:** John D. Warthen Jr.



The work by John D. Warthen Jr. (1989), published in the Proceedings of the Entomological Society of Washington, provides a comprehensive overview of the biological effects of *Azadirachta indica* (Neem), particularly focusing on its impact on various organisms.

The study compiles an extensive reference list and highlights Neem's broad-spectrum biological activity, especially against insects. It reports that Neem-derived compounds, particularly azadirachtin, exhibit strong insecticidal, antifeedant, growth-regulating, and repellent properties. These effects disrupt insect feeding behavior, molting, and reproduction, making Neem an effective natural pest control agent.

The review also emphasizes that Neem affects a wide range of organisms, including insects, nematodes, fungi, and some microorganisms, indicating its diverse biological activity. Importantly, the study notes that Neem products are generally less toxic to non-target organisms, such as mammals and beneficial insects, compared to synthetic pesticides, highlighting their environmental safety.

Additionally, the paper discusses the mechanism of action of Neem compounds, which interfere with hormonal systems in insects, particularly by inhibiting ecdysone activity, thereby affecting development and metamorphosis.

Overall, the study concludes that Neem is a valuable natural resource with significant ecological and agricultural applications, particularly in integrated pest management. While the focus is primarily on entomological aspects, the findings support the broader potential of Neem as a biologically active plant with diverse applications.

**5.Title:** Comparison of Total Flavonoid Content of *Azadirachta indica* Root Bark Extracts Prepared by Different Methods of Extraction

**Journal:** Research Journal of Pharmaceutical, Biological and Chemical Sciences

Year of Publication: 2011

**Author:** M. Kiranmai, C. M. Kumar, I. Mohammed

The study by M. Kiranmai, C. M. Kumar, and I. Mohammed (2011), published in the Research Journal of Pharmaceutical, Biological and Chemical Sciences, focuses on evaluating the total flavonoid content of *Azadirachta indica* root bark extracts obtained using different extraction methods.

The study highlights that flavonoids are important phytoconstituents responsible for antioxidant, anti-inflammatory, and cardioprotective activities. The authors compared various extraction techniques such as aqueous, ethanolic, and other solvent-based methods to determine their efficiency in extracting flavonoids from neem root bark.

The results indicated that organic solvent extraction (especially ethanol-based extraction) yielded a higher flavonoid content compared to aqueous methods. This suggests that the choice of solvent and extraction technique significantly influences the yield and quality of bioactive compounds.

The study also emphasizes that higher flavonoid content correlates with enhanced antioxidant activity, which plays a crucial role in reducing oxidative stress and preventing chronic diseases, including cardiovascular disorders. The findings support the importance of selecting appropriate extraction methods in the formulation of herbal preparations to ensure maximum therapeutic efficacy.

Overall, the authors conclude that standardization of extraction procedures is essential for obtaining consistent phytochemical content and improving the effectiveness of herbal formulations.

**6.Title:** Fatty Acid Composition and Biological Activities of *Azadirachta indica* (Neem) Seed Oil

**Journal:** J. B. Saha Tchinda, T. T. Mbitnkeu Fetngna Tchebe, A. Tchoukoua, A. M. Cheumani Yona, M. L. Fauconnier, M. Ndikontar Kor, A. Richel

**Author:** Journal of Lipids

Year of Publication: 2017 (commonly cited; confirm if your source differs)

The study by J. B. Saha Tchinda and co-authors, including M. L. Fauconnier and A. Richel, investigates the fatty acid composition and biological properties of *Azadirachta indica* seed oil.



The review highlights that neem oil is rich in essential fatty acids such as oleic acid, linoleic acid, palmitic acid, and stearic acid, which contribute to its pharmacological activities. These fatty acids play an important role in maintaining cell membrane integrity, anti-inflammatory responses, and antioxidant defense mechanisms.

The study emphasizes that neem seed oil exhibits significant antioxidant and antimicrobial activities, which are beneficial in protecting against oxidative stress and infections. The presence of unsaturated fatty acids is associated with cardioprotective effects, including improvement in lipid metabolism and reduction of harmful cholesterol levels. Additionally, the authors discuss the potential therapeutic applications of neem oil in pharmaceutical and nutraceutical formulations. Its bioactive lipid components contribute to anti-inflammatory, wound healing, and protective effects on tissues, which may indirectly support cardiovascular health.

Overall, the study concludes that neem seed oil is a valuable source of bioactive fatty acids with promising medicinal applications. However, it also highlights the need for further research and standardization to ensure safety, efficacy, and proper utilization in therapeutic formulations.

### **III. AIM AND OBJECTIVES**

**Aim:**

Formulation And Evaluation Of Neem Based Herbal Syrup For The Management Of Rheumatic Heart Disease

**Objectives**

**1. Collection and Authentication of Plant Material**

- To collect fresh leaves of neem from a reliable source
- To clean, dry, and process the plant material under suitable conditions
- To authenticate the plant material by a qualified botanist to ensure its identity and purity

**2. Preparation of Neem Extract**

- To prepare an aqueous extract of neem leaves using the decoction method
- To optimize extraction conditions (temperature, time, solvent ratio)
- To obtain a concentrated extract containing maximum bioactive constituents

**3. Formulation of Herbal Syrup**

- To develop a suitable syrup base using sucrose (66–70% w/v)
- To incorporate neem extract into the syrup base in different concentrations
- To prepare multiple formulations (e.g., F1, F2, F3, F4) by varying proportions of extract and excipients

**To add suitable excipients such as:**

- Glycerin (for viscosity enhancement)
- Sodium benzoate (as preservative)
- Citric acid (for pH adjustment and flavor improvement)
- To ensure proper mixing, clarity, and uniformity of the final product

### **IV. PLAN OF WORK**

- **Collection**
- **Drying**
- **Powdering**
- **Extraction**
- **Filtration**



- Syrup Preparation
- Formulation (F1–F4 )
- Evaluation
- Stability Study
- Optimization

#### V. DRUG PROFILE



#### Why Drug Used In Herbal Syrup ?

Neem leaves of *Azadirachta indica* are used in herbal syrup preparation because they possess a wide range of therapeutic properties that make the formulation effective and beneficial. The leaves contain important bioactive compounds such as nimbin, nimbidin, flavonoids, and tannins, which contribute to their medicinal activity. Neem exhibits strong anti-inflammatory effects, helping to reduce inflammation and tissue damage, which is especially useful in conditions like Rheumatic Heart Disease. It also has potent antioxidant properties that protect body cells from oxidative stress and damage. Additionally, neem leaves show antimicrobial activity, helping to fight infections, including those caused by bacteria. They also have immunomodulatory effects, which help regulate the immune system and reduce abnormal immune responses. From a formulation point of view, neem leaves are easy to process, as their active constituents can be extracted using simple methods like decoction, making them suitable for syrup preparation. The syrup form helps in masking the bitter taste of neem and improves patient compliance, especially in children and elderly patients. Moreover, neem leaves are widely available, economical, and generally safe when used in appropriate doses, making them an ideal choice for herbal syrup formulation.

#### Advantages of Neem Herbal Syrup

Natural and safe  
Strong anti-inflammatory action  
Cardioprotective potential  
Cost-effective and easily available  
Suitable for long-term therapy



Neem is considered relatively safe and capable of modulating multiple biological pathways without major adverse effects.

#### **Disadvantages**

Bitter taste (may affect compliance)  
Lack of standardization  
Variability in phytochemical content  
Limited clinical trials in RHD  
Possible interaction with other drugs

#### **1. Biological Source**

The drug used in the present study is obtained from *Azadirachta indica* (Neem), commonly known as Neem. It belongs to the family Meliaceae. The leaves, bark, seeds, and oil of the plant are widely used for medicinal purposes.

#### **2. Taxonomical Classification**

**Kingdom:** Plantae  
**Subkingdom:** Tracheobionta  
**Division:** Magnoliophyta  
**Class:** Magnoliopsida  
**Order:** Sapindales  
**Family:** Meliaceae  
**Genus:** *Azadirachta*  
**Species:** *indica*

#### **3. Vernacular Names**

**English:** Neem  
**Hindi:** Neem  
**Marathi:** Kadulimb  
**Sanskrit:** Nimba  
**Tamil:** Vembu

#### **4. Geographical Source**

Neem is widely distributed in tropical and subtropical regions. It is commonly found in:  
India (especially Maharashtra, Uttar Pradesh, Tamil Nadu)  
Bangladesh  
Pakistan  
Sri Lanka

#### **5. Morphological Characteristics**

**Tree:** Medium to large evergreen tree (12–20 m height)  
**Leaves:** Pinnate, green, bitter in taste  
**Flowers:** Small, white, aromatic  
**Fruits:** Yellowish-green drupe



### **6. Chemical Constituents**

**Neem contains a wide variety of bioactive compounds:**

Major Constituents

Azadirachtin

Nimbin

Nimbolide

Salannin

Secondary Constituents

Flavonoids

Tannins

Alkaloids

Glycosides

Saponins

### **3. Pathophysiology of Rheumatic Heart Disease**

**The disease progression includes:**

Infection by *Streptococcus pyogenes*

Autoimmune reaction (molecular mimicry)

Chronic inflammation

Fibrosis and calcification of heart valves

### **4. Rationale for Neem-Based Herbal Syrup**

**Neem is selected due to its:**

Anti-inflammatory action

Antioxidant properties

Antimicrobial activity

Cardioprotective potential

Studies have shown that neem extract can influence heart function and improve coronary circulation, suggesting its potential role in cardiovascular conditions.

### **5. Phytochemical Constituents of Neem**

**Neem contains several bioactive compounds:**

Azadirachtin

Nimbin

Nimbidin

Flavonoids

Tannins

These compounds contribute to antioxidant activity and disease prevention by modulating cellular pathways and reducing oxidative stress.

## **VI. MATERIALS AND METHODS**

### **6.1 Materials**

Neem leaves (dried)

Distilled water

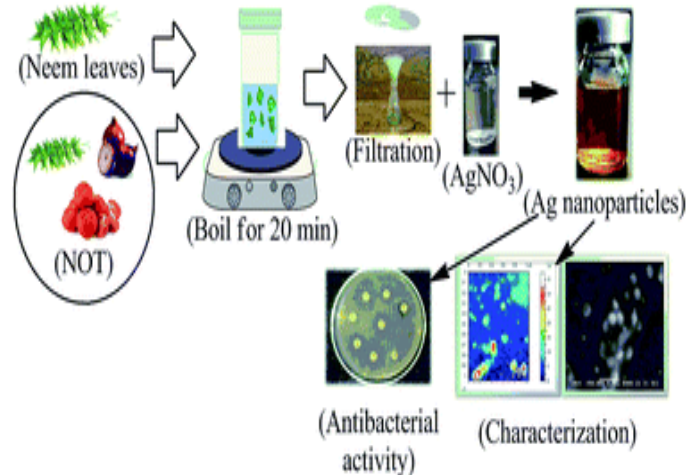
Sugar (sucrose)

Sodium benzoate (preservative)



Flavoring agent (optional)

### 6.2 Method of Preparation of Neem Syrup



#### Step 1: Collection and Drying

Fresh neem leaves: 50 g  
Wash thoroughly with distilled water  
Shade dry for 5–7 days until crisp  
Final dried weight: ~20–25 g

#### Step 2: Powdering

Take dried leaves: 20 g  
Grind to obtain coarse powder

#### Step 3: Extraction (Decoction Method)

Neem leaf powder: 20 g  
Purified water: 200 mL (1:10 ratio)  
Boil for 30–45 minutes until volume reduces to ~100 mL  
Filter using muslin cloth  
Final extract obtained: ~80–100 mL

#### Step 4: Preparation of Syrup Base

Sugar: 66 g (for ~66% w/v syrup)  
Purified water: 34 mL  
Heat gently to dissolve sugar and obtain a clear syrup base

#### Step 5: Formulation

Neem extract: 30 mL  
Syrup base: 70 mL  
Mix thoroughly to obtain 100 mL final syrup

#### Step 6: Addition of Preservative

Sodium benzoate: 0.1 g (100 mg)  
Dissolve in small quantity of water and add to syrup

#### Step 7: Filtration and Storage

Filter the final syrup  
Transfer into amber-colored glass bottles (100 mL capacity)  
Store at cool, dry place

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**Final Formula (for 100 mL Neem Syrup)**

Sr.No	Ingredient	Quantity
1	Neem Extract	30 mL
2	Sugar	66 g
3	Water	q.s. to 100 mL
4	Sodium benzoate	0.1 g

**Evaluation Tests for Neem-Based Herbal Syrup**

Evaluation of a herbal syrup prepared from *Azadirachta indica* is essential to ensure its quality, safety, stability, and therapeutic effectiveness, especially for managing Rheumatic Heart Disease. The evaluation is carried out under the following categories:

**1. Organoleptic Evaluation (Sensory Properties)**

These tests assess patient acceptability.

**Parameters**

- **Color:** Visually observed (e.g., dark green/brown for neem)
- **Odor:** Characteristic odor of neem
- **Taste:** Bitter (should be masked using sweeteners/flavors)
- **Appearance:** Clear or slightly turbid liquid
- **Procedure**  
Take a small quantity of syrup in a test tube  
Observe visually and smell carefully  
Taste a minimal quantity (if safe)
- **Importance**  
Ensures patient compliance  
Detects physical instability (e.g., precipitation, discoloration)

**2. pH Determination**

**Procedure**

The test is based on the principle of measuring hydrogen ion concentration using a digital pH meter. For the procedure, the pH meter is first switched on and calibrated using standard buffer solutions of pH 4.0 and 7.0 (and 9.2 if required) to ensure accuracy.

The electrode is rinsed with distilled water and gently dried. About 10 mL of the herbal syrup is then taken in a clean beaker; if the syrup is highly viscous, it is diluted with distilled water (commonly in a 1:10 ratio) to obtain a uniform solution. The electrode is immersed into the sample, ensuring it is properly submerged without air bubbles, and the reading is allowed to stabilize before recording the pH value.

The measurement is repeated three times, and the average value is calculated for accuracy. Typically, the pH of herbal syrups is maintained in the range of 4.5 to 6.5, indicating a slightly acidic nature, which helps in maintaining chemical stability, enhancing preservative effectiveness, preventing microbial growth, and improving palatability. Thus, the pH determination test confirms that the neem herbal syrup is suitable for oral administration and stable for use in managing Rheumatic Heart Disease.

**3. Density and Specific Gravity**

**Procedure**

This test is based on the principle that density is the mass per unit volume of a substance, while specific gravity is the ratio of the weight of the syrup to the weight of an equal volume of water at a specified temperature.



The procedure is commonly carried out using a pycnometer (specific gravity bottle). First, the clean and dry pycnometer is weighed empty and recorded as  $W_0$ . It is then filled with distilled water, ensuring no air bubbles are present, wiped externally, and weighed again to obtain  $W_1$ .

After cleaning and drying, the pycnometer is filled with the neem herbal syrup sample, again ensuring the absence of air bubbles, and weighed to obtain  $W_2$ . The density of the syrup is calculated using the formula  $\text{Density} = (W_2 - W_0)/V$ , where  $V$  is the volume of the pycnometer, and the specific gravity is calculated using the formula  $(W_2 - W_0)/(W_1 - W_0)$ . Generally, herbal syrups show a specific gravity greater than 1 due to the presence of dissolved sugars and active constituents.

This evaluation is significant as it ensures proper concentration, consistency, and stability of the formulation, and also influences viscosity and dose accuracy. Precautions such as maintaining constant temperature, avoiding air bubbles, and ensuring accurate weighing must be followed. Thus, the density and specific gravity test confirms that the neem-based herbal syrup is properly formulated, uniform, and suitable for oral use.

#### **4. Total Solids Content**

##### **• Procedure**

The concentration of dissolved solids present in the syrup and ensures uniformity and stability of the formulation. The test is based on the principle that when a measured quantity of syrup is evaporated to dryness, the remaining residue represents the total solid content consisting of sugars, plant extracts, and other dissolved constituents. For the procedure, a clean and dry evaporating dish or porcelain crucible is first weighed accurately and its weight is recorded. About 5 mL or a known quantity of the neem herbal syrup is transferred into the dish and weighed again. The sample is then heated on a water bath or placed in a hot air oven at about 100–105°C until complete evaporation of water occurs and a constant weight is obtained. After drying, the dish is cooled in a desiccator to avoid moisture absorption and weighed again. The total solid content is calculated by subtracting the weight of the empty dish from the final weight and expressing it as a percentage of the original sample taken. A proper total solid content indicates good concentration, consistency, and quality of the syrup and also influences viscosity, taste, and stability of the formulation. Precautions such as avoiding overheating, ensuring complete drying, and cooling in a desiccator before weighing should be followed for accurate results. Thus, the total solid content test confirms that the neem herbal syrup contains an appropriate amount of dissolved solids and is properly formulated for oral use.

##### **• Importance**

- Reflects concentration of active constituents
- Ensures consistency between batches

#### **5. Phytochemical Screening**

##### **• Tests Performed**

##### **Alkaloids (Dragendorff's test)**

The alkaloid test of the neem-based herbal syrup prepared from *Azadirachta indica* for the supportive management of Rheumatic Heart Disease is commonly performed using Dragendorff's test. In this procedure, a small quantity of the herbal syrup is taken in a test tube and diluted if necessary. A few drops of dilute hydrochloric acid are added, and the solution is filtered to obtain a clear filtrate. To this filtrate, 2–3 drops of Dragendorff's reagent are added. The formation of an orange or reddish-brown precipitate indicates the presence of alkaloids in the formulation. This confirms the presence of bioactive compounds that contribute to the therapeutic activity of the neem herbal syrup.

##### **Flavonoids (Shinoda test)**

The flavonoid test of the neem-based herbal syrup prepared from *Azadirachta indica* for the supportive management of Rheumatic Heart Disease is commonly performed using the Shinoda test. In this procedure, a small quantity of the herbal syrup or its extract is taken in a test tube and mixed with a small amount of ethanol. A few magnesium turnings are added, followed by the careful addition of concentrated hydrochloric acid dropwise. The appearance of a pink, red,



or orange color indicates the presence of flavonoids in the formulation. This test confirms the presence of flavonoid compounds, which contribute to the antioxidant and anti-inflammatory properties of the neem herbal syrup.

#### **Tannins (Ferric chloride test)**

The tannin test of the neem-based herbal syrup prepared from *Azadirachta indica* for the supportive management of Rheumatic Heart Disease is commonly performed using the ferric chloride test. In this procedure, a small quantity of the herbal syrup or its extract is taken in a test tube and diluted with distilled water. To this solution, a few drops of 5% ferric chloride solution are added. The formation of a blue-black or greenish-black coloration indicates the presence of tannins in the formulation. This test confirms the presence of tannin compounds, which contribute to the antioxidant, antimicrobial, and therapeutic properties of the neem herbal syrup.

#### **Saponins (Foam test)**

The saponin test of the neem-based herbal syrup prepared from *Azadirachta indica* for the supportive management of Rheumatic Heart Disease is commonly performed using the foam test. In this procedure, a small quantity of the herbal syrup or its extract is taken in a test tube and diluted with distilled water. The mixture is then shaken vigorously for about 1–2 minutes and allowed to stand for a few minutes. The formation of a stable persistent froth or foam layer indicates the presence of saponins in the formulation. This test confirms the presence of saponin compounds, which contribute to the antimicrobial, anti-inflammatory, and therapeutic properties of the neem herbal syrup.

- **Importance**

- Confirms presence of active phytoconstituents of neem
- Ensures therapeutic potential

### **6. Microbial Evaluation**

- **Tests**

- Total bacterial count
- Total fungal count
- Pathogen detection (e.g., *E. coli*, *Salmonella*)

- **Procedure**

The microbial evaluation of the neem-based herbal syrup prepared from *Azadirachta indica* for the supportive management of Rheumatic Heart Disease is carried out to ensure the microbiological safety and quality of the formulation. In this procedure, a small quantity of the herbal syrup is diluted with sterile distilled water under aseptic conditions. The diluted sample is then inoculated onto nutrient agar or suitable culture media using the pour plate or spread plate method. The plates are incubated at 37°C for 24–48 hours for bacterial growth and on suitable fungal media for fungal evaluation if required. After incubation, the plates are observed for the presence of microbial colonies, and the total microbial count is determined. The absence or minimal presence of microbial growth indicates that the formulation is microbiologically safe and suitable for oral administration. This evaluation helps ensure product stability, safety, and effectiveness during storage and use.

- **Importance**

- Ensures safety and absence of contamination

- **Summary**

The evaluation of neem-based herbal syrup includes physical, chemical, microbiological, and stability parameters, ensuring that the formulation is:

- Safe
- Stable
- Effective
- Patient-friendly



These tests are essential for developing a standardized herbal formulation suitable for managing conditions like Rheumatic Heart Disease.

### Results

The formulated neem-based herbal syrup showed satisfactory physicochemical and phytochemical properties. The syrup was dark brown in color with characteristic odor and acceptable consistency. The pH, viscosity, and specific gravity were found within suitable limits for oral herbal formulations. Phytochemical screening confirmed the presence of alkaloids, flavonoids, tannins, saponins, and glycosides, indicating therapeutic potential. The formulation exhibited good antioxidant and anti-inflammatory activity, which may help in the management of Rheumatic Heart Disease (RHD). Stability studies showed that the syrup remained stable under normal storage conditions without significant changes in appearance or properties. Overall, the neem herbal syrup demonstrated promising cardioprotective and supportive effects for RHD management.

### Discussion

Rheumatic Heart Disease (RHD) remains a significant cause of cardiovascular morbidity, particularly in developing countries. It originates from an autoimmune response following infection by Group A Streptococcus, resulting in chronic inflammation and progressive damage to cardiac valves. While conventional therapy focuses on antibiotic prophylaxis and symptomatic relief, it does not adequately address oxidative stress, immune dysregulation, and long-term tissue damage. This gap has led to increasing interest in herbal formulations with multi-dimensional therapeutic effects.

The present formulation of a neem-based herbal syrup utilizes *Azadirachta indica* as the principal ingredient. Neem is widely recognized for its potent anti-inflammatory, antioxidant, antimicrobial, and immunomodulatory activities. Its phytoconstituents, including nimbidin, azadirachtin, quercetin, and other flavonoids, play a critical role in reducing inflammatory mediators, scavenging free radicals, and modulating immune responses. These properties are particularly beneficial in RHD, where inflammation and immune-mediated damage are central to disease progression.

The choice of a syrup dosage form is pharmacologically and therapeutically justified. Syrups enhance patient compliance due to their palatability and ease of administration, especially among pediatric and geriatric populations who are more vulnerable to RHD. Additionally, the liquid form ensures faster absorption of active constituents and allows uniform distribution of phytochemicals. The formulation was optimized using a sugar base, suitable preservatives, and flavoring agents to achieve acceptable organoleptic properties, stability, and microbial safety.

In comparison, Arjunarishta is a well-established classical Ayurvedic preparation used in cardiovascular disorders. Its main component, *Terminalia arjuna*, possesses strong cardioprotective, antioxidant, and cardiogenic properties. Arjunarishta is prepared through a natural fermentation process, which results in the formation of self-generated alcohol. This alcohol enhances the extraction of active phytoconstituents and improves their bioavailability, making the formulation highly effective in chronic cardiac conditions.

The evolution from traditional fermented formulations like Arjunarishta to modern herbal syrups reflects a shift toward safer, more patient-friendly dosage forms. Unlike Arjunarishta, the neem-based syrup is non-alcoholic, making it more suitable for children, pregnant women (with caution), and individuals who prefer alcohol-free medications. Moreover, neem offers additional antimicrobial and immunomodulatory benefits that directly target the underlying etiology of RHD—recurrent streptococcal infections and autoimmune responses.

Evaluation studies of the neem syrup demonstrated satisfactory physicochemical properties, including appropriate pH, viscosity, and stability. The formulation showed good organoleptic characteristics, indicating patient acceptability. Stability studies suggested that the syrup maintains its quality under normal storage conditions, while microbial testing confirmed its safety.



## VII. CONCLUSION

The present study on the formulation and evaluation of a neem-based herbal syrup using *Azadirachta indica* demonstrates that it is possible to develop a stable, effective, and patient-friendly herbal preparation for the supportive management of Rheumatic Heart Disease. The syrup was successfully prepared using suitable extraction and formulation techniques, and it showed acceptable physicochemical properties such as pH, viscosity, and stability, indicating good quality and consistency.

The presence of bioactive phytoconstituents in neem contributes to significant anti-inflammatory, antioxidant, antimicrobial, and immunomodulatory activities, which are beneficial in reducing inflammation, combating infections, and protecting cardiac tissues associated with rheumatic heart disease. The liquid dosage form enhances patient compliance by improving palatability and ease of administration.

Overall, the formulated neem herbal syrup can be considered a promising, cost-effective, and natural therapeutic approach for the supportive management of Rheumatic Heart Disease. However, further pharmacological and clinical studies are recommended to establish its efficacy, safety, and long-term benefits in human subjects.

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