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Preparation and Evaluation of Polyherbal Syrup for Prognosis of Rheumatic Heart Disease

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ABSTRACT -

Rheumatic heart disease (RHD) is a serious and preventable condition caused by acute rheumatic fever (ARF). ARF happens when your immune system gets confused and starts attacking your own body after an infection with Streptococcus Pyogen (Strep A). This can lead to RHD, which is a heart problem. RHD can be avoided, but it still causes around 320,000 deaths each year. Most of these happen in poorer countries and among Indigenous people in developed countries like Australia. In Australia, some cases of ARF come from different kind of streptococcus infection called streptococcal pyoderma. Also, there are issues with RHD in remote Indigenous communities. The government has programs to check for the disease and provide medicine to prevent it, but these programs don't always work well. Scientists are also working on a vaccine to protect against Strep A, which could help prevent ARF and RHD.

Acute rheumatic fever (ARF) happens when your body's immune system reacts to a throat infection caused by certain bacteria. This can lead to long-term damage to your heart valves, called rheumatic heart disease (RHD). RHD can result from a severe ARF episode or repeated ones. It's a big health problem, especially in poor areas worldwide. Even though we've learned more about the disease, diagnosing it and treating it hasn't improved much. Penicillin has been the main treatment for a long time, and there's no other proven way to prevent or reduce RHD after ARF. But there's hope for the future with better diagnostic tools, vaccines, and a focus on improving the lives of people with RHD.

Keywords - Autoimmune, Fever, Heart, Infection, Rheumatism.

Introduction –

Acute Rheumatic Fever (ARF) is a condition that happens when your immune system mistakenly attacks your body after an infection caused by a bacterium called Streptococcus pyogenes, often linked to a throat infection. ARF can cause various problems like joint pain, heart valve issues, unusual movements (chorea), skin problems, and fever. It can be very severe, leading to painful joints, heart problems, high fevers, and difficulty moving. Usually, ARF is treated in the hospital for a few weeks to confirm the diagnosis and manage the symptoms.

However, even after the acute phase, heart valve damage may persist, known as rheumatic heart disease (RHD), which can be very harmful. ARF can come back if you get infected with Streptococcus again, and each time it returns, it can make RHD worse. So, the main focus in managing ARF is to prevent it from coming back by taking long-term penicillin treatment, called secondary prophylaxis. This helps protect your heart and health in the long run.

Rheumatic Heart Disease (RHD) is a severe cardiac condition that arises when untreated streptococcal infections, like strep throat or scarlet fever, wreak havoc on the heart.

When you catch a streptococcal infection, your body goes into battle mode, deploying its immune system to fend off the intruders. But if these infections don't receive proper antibiotic treatment, they can cause RHD. Leaky or narrowed valves disrupt the normal flow of blood through your heart, placing immense strain on this vital organ. Left untreated, RHD can lead to heart failure, which is often life-threatening.

Etiology of Rheumatic Heart Disease -

Rheumatic heart disease (RHD) happens when you get sick with rheumatic fever, which is an inflammation in your body. This can cause problems in your heart, especially with the parts that control the flow of blood. These problems can make your heart valves stiff, cause them to stick together, or make certain strings in your heart get shorter and join together. It's a serious condition, so it's important to get medical help and take steps to prevent it if you're at risk.

In rheumatic heart disease, the heart valves can get damaged. Most often, it's the valve between the left atrium and left ventricle (mitral valve) that gets affected, happening in about 50% to 60% of cases. Sometimes, both the valve between the aorta and left ventricle (the aortic valve) and the mitral valve can be damaged together, which occurs in about 20% of cases. The valve on the right side of the heart (tricuspid valve) is less commonly affected, happening in only about 10% of cases. Interestingly, tricuspid valve issues tend to occur when there have been repeated infections and are more likely to develop alongside problems in the mitral or aortic valves. The good news is that the valve controlling blood flow to the lungs (pulmonary valve) is rarely harmed in Rheumatic heart disease.

This damage can make it hard for blood to flow through the heart, especially the mitral valve. People who've had rheumatic fever need to see a doctor regularly to check and manage any valve problems to keep their heart healthy.

Epidemiology of Rheumatic Heart Disease –

Rheumatic heart disease (RHD) is a serious heart problem that mainly affects children and young adults in poorer countries. It is caused by untreated throat infections with a bacteria called group A streptococcus. In these places, RHD is a major cause of heart failure, which is when the heart can't pump blood effectively.

In 2015, a study counted about 33.4 million people with RHD worldwide. It also found that RHD caused 10.5 million years of healthy life lost and about 319,400 deaths that year. RHD is most common in certain areas, like Oceania, central sub-Saharan Africa, and South Asia.

What's troubling is that many cases of RHD don't show any symptoms at first. This makes it hard to detect and treat early. In fact, for every person with obvious symptoms of RHD, there are about seven to eight people with hidden or "silent" RHD.

RHD becomes more common as children grow older, especially between the ages of 5 and 16. If things don't change, the number of people with RHD could double in the future, especially in places like sub-Saharan Africa.To tackle this problem, we need better healthcare access, early treatment of strep throat, and more awareness about RHD in these regions so we can help millions of people live healthier lives.

Physiology of Heart –

The human heart is a very important organ in the human body and serves as central pump of the circulatory system. It's job is to move oxygenated blood throughout the body and collect deoxygenated blood from different parts of body for oxygenation.

At first, blood that has low oxygen levels comes to the heart from different parts of the body through superior vena cava and inferior vena cava. These veins deposit the deoxygenated blood into right atrium of the heart. The right atrium chamber squeezes and pushes the received deoxygenated blood into right ventricle through a valve called as tricuspid valve.

As the right ventricle contracts, it exerts force on blood which flows through the pulmonary valve in the pulmonary artery. The pulmonary artery carries deoxygenated blood to the lungs for the exchange of gases. In the lungs, carbon dioxide is removed from the blood and fresh oxygen is absorbed converting the deoxygenated blood into oxygenated blood.

From the lungs, oxygenated blood enters the heart through pulmonary veins. The oxygenated blood is deposited in the left atrium which contracts and pushes the blood into left ventricle through the bicuspid (mitral) valve. The left ventricle is the most powerful chamber of the heart because it contracts strongly so as to pass the blood into the aorta through the aortic valve.

The aorta is the largest artery in the body which carries oxygenated blood to different parts of the body. The aorta further branches into smaller arteries and arterioles and then it reaches every cell, tissue and organ of the body. This network of arteries and arterioles deliver oxygen and nutrients and collects carbon dioxide and other waste products for their removal.

Pathophysiology of Rheumatic Heart Disease –

Rheumatic heart disease happens when your heart valves get damaged due to a strange immune reaction to an infection caused by Streptococcus pyogenes, which is a type of bacteria known as group A streptococcus. This bacteria can lead to a sickness called Acute rheumatic fever, which usually shows up about three weeks after you've had a sore throat caused by the same bacteria. This fever can affect various parts of your body like your joints, skin, brain, and heart.

When someone gets rheumatic fever multiple times, it can harm their heart valves over time. This harm can result in rheumatic valvular heart disease. If this heart valve problem isn't treated, it can lead to heart failure or even death.

The exact reasons why all of this happens aren't completely understood. However, doctors can see some signs in the heart and its valves. The doctors may find the Aschoff nodules in the heart when rheumatic fever is present. These nodules form because of inflammation in the heart muscle. Additionally, there are MacCallum plaques on the valves and the inner part of the left atrium. These plaques are also linked to the disease.

Causes of Rheumatic Heart Disease –

1)Streptococcal Infections :-

Streptococcal infections, specifically those caused by the group A Streptococcus bacteria, can lead to a condition called Rheumatic Heart Disease (RHD). RHD is a complex autoimmune disease that primarily affects the heart, particularly the heart valves.

It starts with an infection caused by group A Streptococcus bacteria, commonly known as strep throat or other streptococcal infections like impetigo.

When someone contracts such an infection, the body's immune system responds by producing antibodies to fight off the bacteria.

In some cases, the antibodies produced to combat the streptococcal infection can mistakenly target certain proteins found on the heart valves. These proteins are similar in structure to those on the streptococcus bacteria. This phenomenon is known as molecular mimicry, where the body's immune system confuses its own tissues with the pathogen it's trying to fight.

Once the antibodies target these heart valve proteins, the immune system initiates an autoimmune response. This means that the immune system starts attacking the body's own heart valves, believing them to be infected by the streptococcal bacteria.

2) Autoimmune Response :-

In susceptible individuals, the immune system's response to the streptococcal infection can result in the formation of antibodies called antistreptolysin O (ASO) and anti-DNase B. These antibodies can cross-react with proteins found in heart valve tissues, causing inflammation and damage. The autoimmune response triggers an inflammatory process within the heart. Chronic inflammation, over time, can cause damage to the heart valves, leading to scarring and thickening of the valve tissue.

Symptoms of Rheumatic Heart Disease -

The symptoms of RHD can vary widely in severity and may not become apparent until many years after the initial streptococcal infection. The most common symptoms and complications associated with RHD include:

1)Heart Murmurs : A heart murmur, which is an abnormal sound heard during a heartbeat, may be an early sign of RHD.

2) Erythema marginatam :It's a distinctive, non-itchy rash characterized by pink or light red rings or snake-like (serpiginous) patterns with a clear or slightly pale center and a slightly raised, red border. It typically appears on the trunk and the upper parts of the arms and legs, but rarely on the face, palms, or soles of the feet.

3) Painful joints : Rheumatic fever typically causes inflammation of the joints (arthritis), leading to pain, tenderness, redness, and swelling. Sometimes, there might just be joint pain without visible inflammation (arthralgia).

4)Fatigue : Individuals with RHD often experience fatigue and weakness, as the damaged heart valves make it harder for the heart to pump blood effectively.

5)Shortness of Breath : As RHD progresses, it can lead to shortness of breath, especially during physical activity or when lying down.

6) Chest Pain : Some people with RHD may experience chest pain or discomfort, which can be a result of the heart's increased workload.

7)Irregular Heartbeat : RHD can cause irregular heart rhythms (arrhythmias) due to the strain on the heart.

8) Swelling : Fluid retention can occur, leading to swelling in the ankles, feet, or abdomen.

9) Stroke : RHD can increase the risk of blood clots forming in the heart, which can potentially lead to a stroke.

Diagnosis of Rheumatic Heart Disease -

1. Medical History and Physical Examination :

The initial step in diagnosing RHD involves a thorough medical history and physical examination by a healthcare provider. The doctor or the health provider may ask about symptoms, previous illnesses, and assess for signs of heart problems, like heart murmurs or abnormal heart sounds.

2. Echocardiogram :

An echocardiogram is a crucial diagnostic tool for RHD. It uses sound waves to create images of the heart's structure and function. This test can show if there are any abnormalities in the heart valves, such as thickening, scarring, or regurgitation (leakage).

3. Electrocardiogram (ECG or EKG) :

An ECG measures the electrical activity of the heart. It can help identify abnormal heart rhythms or other electrical issues that may be associated with RHD.

4. Chest X-ray :

A chest X-ray can provide images of the heart and lungs. It may show if the heart is enlarged or if there are signs of heart failure, which can occur in advanced RHD cases.

5. Blood Tests :

Blood tests may be done to check for markers of inflammation (e.g., C-reactive protein) and to detect streptococcal antibodies.

Elevated levels of certain antibodies can suggest a previous strep infection, which is often a precursor to RHD.

6. Cardiac MRI (Magnetic Resonance Imaging) :

In some cases, a cardiac MRI may be used to get more detailed images of the heart and its structures. This can provide additional information about the extent and severity of valve damage.

7. Transesophageal Echocardiogram (TEE) :

TEE is a specialized type of echocardiogram where a probe is inserted through the oesophagus to get a close-up view of the heart valves. It is often used when a regular echocardiogram doesn't provide clear images.

8. Doppler Ultrasound :

Doppler ultrasound measures blood flow through the heart and can help assess the severity of valve regurgitation or stenosis.

9. Cardiac Catheterization :

This invasive procedure involves threading a thin tube (catheter) through a blood vessel to the heart. It can provide detailed information about the heart's anatomy and pressures within the heart chambers.

10. Clinical Criteria :

In some cases, RHD may be diagnosed based on clinical criteria, which include a combination of symptoms, physical exam findings, and echocardiogram results, especially in areas with limited access to advanced diagnostic tools.

Procedure -

1)Collection of crude drugs –

Taxonomically identified and authenticated roots of Withania somnifera, Curcuma longa, Glycyrrhiza glabra ; leaves of Ocimum basilicum; bark of Terminalia arjuna, Cinnamomum zeylanicum; bulbs of Allium sativum and whole plant of Centella asiatica were subjected to shade drying.

After sufficient drying they were powdered with help of various milling techniques and ensured proper milling of each crude drug .

a]Terminalia arjuna :

Synonym – Dhananjay, Indravriksha

Biological source – Arjuna consists of dried stem bark of the plant known as Terminalia arjuna ,belonging to family Combretaceae.

Uses – It is used as cardiotonic in heart failure, ischemic, cardiomyopathy.

In RHD, Arjuna is used for its cardioprotective, anti-inflammatory properties and improve cardiovascular health.

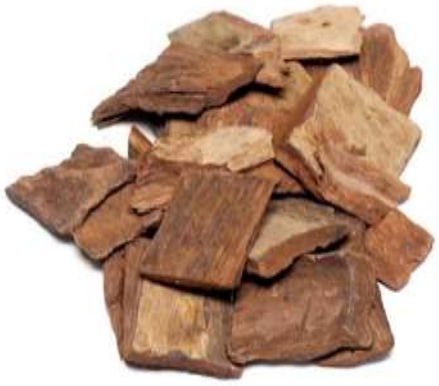

Fig 1– Terminalia arjuna

b] Centella asiatica:

Synonym – Kapotvadka , Somvalli , Saraswati

Biological source – Brahmi is the fresh or dried herb of Centella asiatica , belonging to family Umbelliferae.

Uses – Brahmi helps to reduce the symptoms of mental illness like anxiety and depression. Brahmi helps in controlling the symptoms of mental illness.

In RHD, Brahmi is used for its cardiotonic, antioxidant properties and improve brain and nerve functions.

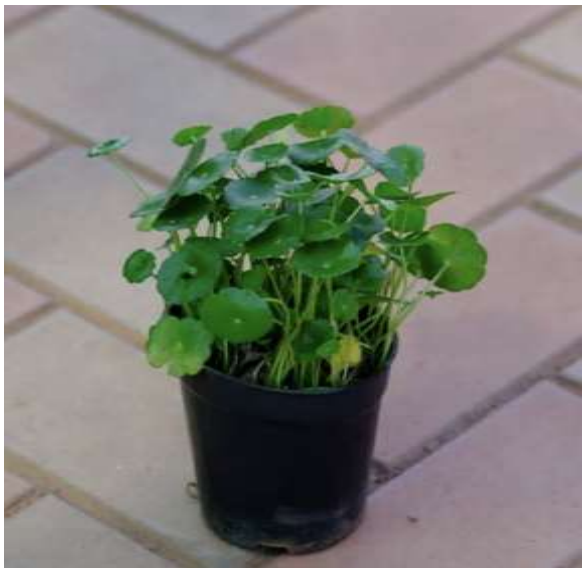

Fig 2 – Centella asiatica

c] Withania somnifera:

Synonym – Indian ginseng, Winter cherry, Ashwagandha

Biological source – Ashwagandha is derived from the root of the Withania somnifera plant belonging to family Solanaceae.

Uses – Reduces Anxiety ,Boosts cognitive abilities, Enhances exercise performance. Increases sperm health and testosterone levels.

In RHD, it is used for pain relief, stress reduction, immunomodulatory effects, anti-inflammatory properties and improved joint health.

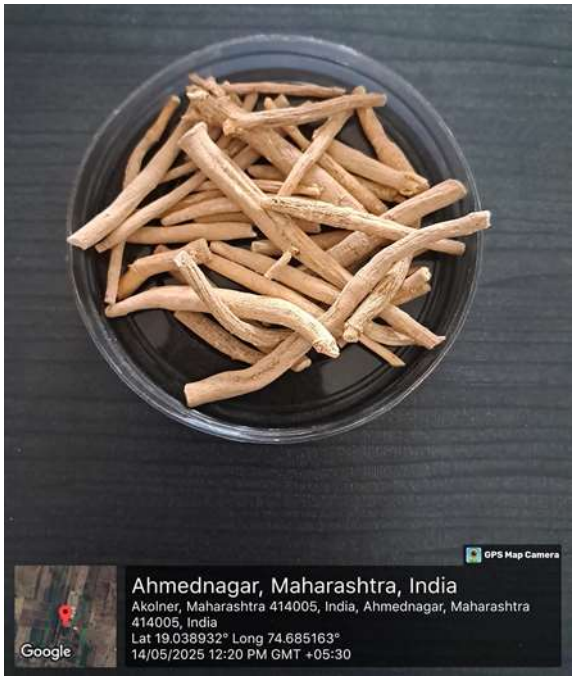

Fig 3 – Withania somnifera

d] Curcuma longa :

Synonyms – Haldi, Indian saffron, Yellow root

Biological source – The biological source of turmeric is the dried or fresh rhizome (underground stem) of the plant Curcuma longa Linn. belonging to the family Zingiberaceae.

Uses – Immune system support, improve brain health, enhance heart health.

In RHD, turmeric is used for its pain relief, antioxidant and anti-inflammatory properties.

Fig 4 – Curcuma longa

e] Ocimum basilicum :

Synonym – Gauri, bahumanjari, pavani, gramya, surasa

Biological source –Tulsi consists of the fresh and dried leaves of Ocimum species like Ocimum sanctum L. and Ocimum basilicum L. etc.

Uses- Lowers Stress and Anxiety Stimulates and Vitalises Your Body Easing Inflammation and Joint Aches Lowers Cholesterol.

In RHD, tulsi is used for its antioxidant, anti-inflammatory and stress relieving properties.

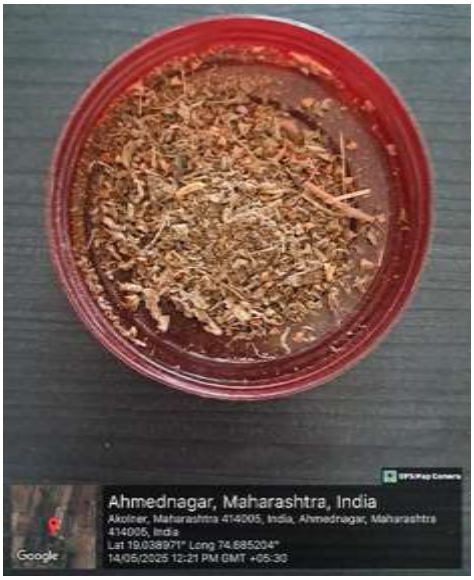

Fig 5 – Ocimum basilicum

f] Cinnamomum zeylanicum :

Synonym – Ceylon cinnamon, Ceylon cinnamon tree , Dalchini

Biological source – Cinnamon is the dried inner bark of the coppiced shoots of Cinnamomum zeylanicum Nees, belonging to family Lauraceae. Cinnamon contains about 10% of volatile oil, tannin, mucilage, calcium oxalate and sugar.

Uses – It is used as both a spice and a traditional medicine, Lower Blood Sugar, boost metabolism, help treat cancer, Lower blood pressure, Reduce inflammation.

In RHD, Cinnamon is used for its cholesterol and lipid management, regulation of blood pressure and antioxidant properties.

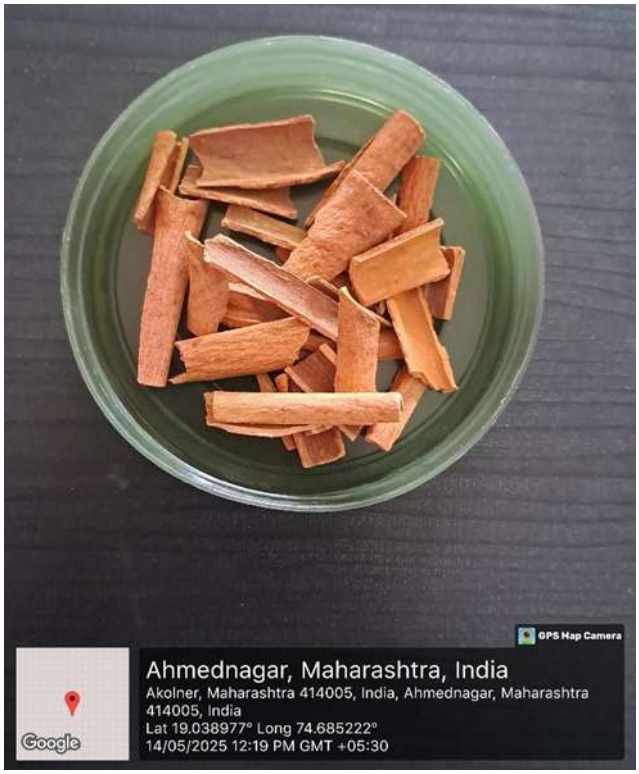

Fig 6 – Cinnamomum zeylanicum

g] Glycyrrhiza glabra :

Synonym – Mulethi , Sweetwood

Biological source – Liquorice consists of dried peeled or unpeeled roots of Glycyrrhiza glabra belonging to family Leguminosae

Uses –It is used for treating a variety of conditions, like lung, liver, circulatory, and kidney diseases.

It is used as a dietary supplement for conditions such as digestive problem, cough,bacterial and viral infections.

In RHD, liquorice is used for its immunomodulatory effects.

Fig 7 – Glycyrrhiza glabra

h] Allium sativum :

Synonyms – Garlic, Lasun

Biological source – The biological source of garlic is the fresh bulb of Allium sativum Linn. It belongs to the family Liliaceae .

Uses – Improve Cardiovascular health, Enhance Immune Support, Detoxification, Antioxidant.

In RHD, garlic is used to improve the blood circulation.

Fig 8 – Allium sativum

2]Preparation of Extracts :

a)5g of each powdered ingredient were mixed in 250ml beakers separately.

b)They were subjected to heating mantle for boiling.

c)Heating was discontinued once the total volume became $1/2^{th}$ of initial volume.

d)The decoction preparation was then filtered through muslin cloth followed by filtration with filter paper and stored until its use.

Active Pharmaceutical Ingredients	**Uses**
Terminalia arjuna	Cardioprotective, Anti-inflammatory
Centella asiatica	Cardiotonic, Antioxidant
Withania somnifera	Immunomodulatory, Anti-inflammatory, Pain relief
Curcuma longa	Pain relief, Antioxidant
Ocimum basilicum	Stress relief, Antioxidant
Cinnamomum zeylanicum	Regulation of blood pressure
Glycyrrhiza glabra	Immunomodulatory
Allium sativum	Improve blood circulation

Table 1: Useful Pharmacological properties of the drugs in RHD

Excipients	**Uses**
Sucrose	Sweetening Agent
Menthol	Flavouring agent
Sodium Benzoate	Preservative
Distilled water	Vehicle

Table 2 – Excipients used in the syrup

3]Preparation of polyherbal solution :

Finally polyherbal solution was formulated by mixing individual decoctions as per formula table.

Drug	**F 1 [Cardioprotective Focus]**	**F 2 [Anti-inflammatory Target]**	**F 3 (F1 + F2)**
Terminalia arjuna	7.5	3.0	6.0
Centella asiatica	3.0	4.5	3.75
Withania somnifera	3.0	3.0	3.0
Curcuma longa	3.0	6.0	3.5
Ocimum basilicum	1.5	3.0	2.25
Cinnamomum zeylanicum	1.5	1.5	1.5
Glycyrrhiza glabra	1.5	1.5	1.5
Allium sativum	2.5	2.5	2.0
Sodium Benzoate	0.03	0.03	0.03
Vanilla	3	2.5	3
Sucrose	q.s.	q.s.	q.s.
Distilled water	q.s.	q.s.	q.s.

Table 3 – Formula Table for 50ml syrup

Evaluation :

A] Colour examination :

i)5mL of prepared solution was taken on a watch glass.

ii)Watch glass is placed against a white background in a white tube light.

iii) Colour was observed by naked eyes.

B] Odour examination :

i)2mL of the prepared solution was taken and smelled individually.

ii)The time interval between 2 smelling was 2 minutes to nullify the effect of the previous smelling.

C] Taste examination :

i)A pinch of final solution was taken and examined by taste buds of the tongue.

D]Transparency examination :

i)Take 5mL herbal solution in a test tube.

ii)Observe the herbal solution against bright white background for the colour.

E] pH determination :

i)10mL of the prepared solution is taken in 100mL volumetric flask.

ii)Make up the volume to 100mL by adding distilled water.

iii)Sonicate for 10 minutes.

iv)pH was measured by digital pH meter.

Result -

The Herbal formulation was prepared successfully by admixing the predetermined amount of the aqueous extracts of all the ingredients. Evaluation of polyherbal solution was carried out and result of evaluation study was as follows:

Evaluation Test	**F 1**	**F 2**	**F 3**
Colour examination	Yellowish brown	Yellowish brown	Brownish red
Odour examination	Aromatic	Aromatic	Aromatic
Taste examination	Slightly bitter	Slightly bitter	Slightly bitter
Transparency examination	Translucent	Translucent	Translucent
pH determination	6.5	6.7	6.5

Table 4 – Evaluation Test Results

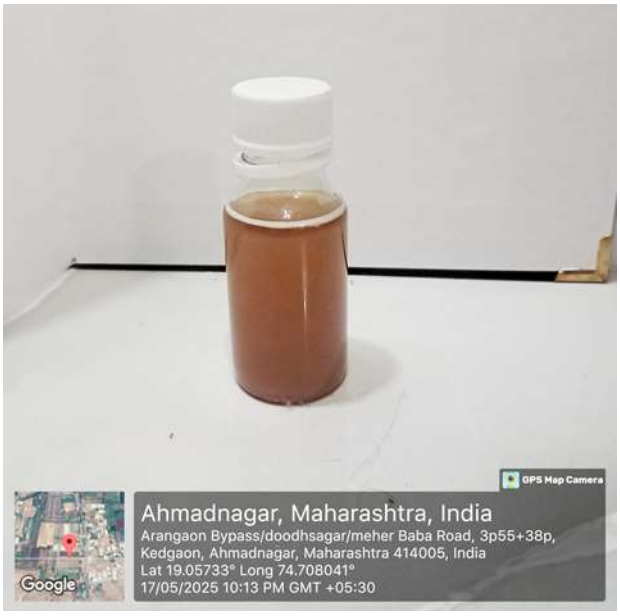

Fig 9 – Prepared syrup

Conclusion –

The present study successfully formulated and evaluated a polyherbal syrup containing extracts of Terminalia arjuna, Centella asiatica, Curcuma longa, Withania somnifera, Ocimum basilicum, Cinnamomum zeylanicum, Glycyrrhiza glabra, and Allium sativum, stabilized with sodium benzoate and incorporating menthol, sucrose, and distilled water. The physicochemical parameters of the syrup were found to be within acceptable limits, suggesting good formulation characteristics. The synergistic potential of these traditionally used medicinal plants, known for their cardioprotective, anti-inflammatory, antioxidant, and immunomodulatory properties, offers a promising complementary approach for the management of Rheumatic Heart Disease (RHD). This formulation provides a palatable and potentially effective means of delivering these beneficial compounds.

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