

# Formulation and Evaluation of Herbal Syrup for Prevention of Side Effect of Isoniazid.

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**Abstract:** *In order to lessen the adverse effects of isoniazid, a herbal syrup including amla (Phyllanthus emblica), ashwagandha (Withania somnifera), brahmi (Bacopa monnieri), licorice (Glycyrrhiza glabra), and pyridoxine hydrochloride was created and tested in this study. Although isoniazid is frequently used to treat tuberculosis, it can result in peripheral neuropathy and liver damage. Pyridoxine hydrochloride aids in preventing nerve injury, and the chosen herbal components have hepatoprotective, neuroprotective, and antioxidant qualities. Good physicochemical characteristics, including a suitable pH, viscosity, stability, and palatability, were demonstrated by the produced syrup. Good preservation was indicated by the absence of microbiological growth. All things considered, the formulation might be helpful as a supportive treatment to lessen isoniazid side effects; however, more clinical research is required to verify its efficacy and safety. The chosen herbs have anti-inflammatory, neuroprotective, hepatoprotective, and antioxidant qualities that may lessen isoniazid's negative effects. The herbal syrup was made with appropriate excipients, such as sugar syrup base, and its physicochemical characteristics, such as pH, viscosity, clarity, stability, and acceptability, were assessed. The syrup may be used as a supporting herbal formulation to lessen isoniazid-induced adverse effects and increase patient compliance, since it shown satisfactory evaluation findings. According to this study, polyherbal formulations may be a safe and effective Addition to treatment for preventative tuberculosis..*

**Keywords:** ashwagandha

## I. INTRODUCTION

Tuberculosis (TB), the most prevalent infectious disease in humans, is a leading cause of illness and death worldwide. This infectious disease is mostly caused by Mycobacterium tuberculosis (M. tuberculosis). TB primarily affects the lungs, although it can also damage the lymphatic, circulatory, and central nervous systems [1]. The two main strategies for preventing tuberculosis are screening programs and immunizations such as the Bacillus Calmette Guerin (BCG) vaccine [2]. Due to inadequate treatment, tuberculosis (TB) is a dreadful illness that spreads throughout the world. After HIV, it is the second most common infectious disease-related cause of mortality globally. Tuberculosis affects a substantial portion of members of marginalized populations and those with poor socioeconomic position [3]. Tuberculosis treatment is a difficult process that requires the long-term use of multiple drugs. A significant problem in infections brought on by multiple drug-resistant tuberculosis (MDR-TB) is antibiotic resistance. [4] Additionally, efforts have been undertaken to treat MDR and XDR-TB by integrating clinical, radiographic, microbiological, and histopathologic features with the appropriate multidrug medicine. DOTS (directly observed therapy, short course), which consists of specific anti-TB drug combinations, is another strategy developed by the World Health Organization (WHO) to fight tuberculosis [5]. Antibiotic resistance is a developing problem in the treatment of tuberculosis. Regarding the DOTS approach, the use of first and second line anti-TB drugs, and cutting-edge drug delivery methods to deal with the problem of resistance.(6)The current status of novel anti-TB drugs and vaccines undergoing clinical development is also covered, along with the most recent WHO, CDC, and recommendations for the treatment of tuberculosis. In order to stop this epidemic's alarming spread due to resistance.



The structural features and therapeutic targets of both conventional drugs and novel anti-TB compounds in the drug research pipeline are also provided.[7] Drug resistance develops in it, and long-term care is necessary. If the patient misses a dosage, the entire course of treatment must be initiated.



### **TYPE OF TUBERCULOSIS**

According to state of mycobacterium tuberculosis

- Latent tuberculosis
- Active tuberculosis
- According to effect on body
- Tubercular lymphadenitis
- Pleural tuberculosis
- Abdominal tuberculosis
- Central nervous system tuberculosis
- Bone and join tuberculosis
- Genito urinary tuberculosis
- Miliary tuberculosis

According to state of mycobacterium tuberculosis

#### **a. Latent Tuberculosis**

- It is present in the form of germs in our body, but in immune system stops them from spreading
- That means there is no symptom and person is not contagious
- The infection is still alive in body and become active

#### **b. Active tuberculosis**

- In these germs multiply and can make sick
- Person can spread the disease to other [13]



**According to effect on body**

**a. Lymphadenitis tubercular**

In 60–90% of instances of tuberculous lymphadenitis, the most common condition, lymphadenitis, is present. The cervical lymph node becomes involved when bacilli spread from primary sources. The tonsils, adenoids, sinusoidal/osteomyelitis of the ethmoid bone, or Ghon's complex infection site. When MTB bacilli first multiply in lymph nodes, the afflicted lymph node exhibits obvious hyperemia, edema, necrosis, and caseation [12]. A. Tuberculosis in the pleura Up to 30% of all EPTB cases in high-burden countries may be pleural TB. Usually, the patient has a high temperature, a productive cough, and pleuritic symptoms.[13] chest pain associated with dyspnea, chills, weakness, weight loss, and sweats at night. The pathogenesis of pleural tuberculosis is thought to be delayed hypersensitivity rather than direct pleural space infection [14].

**b. Tuberculosis in the abdomen**

Abdominal tuberculosis is identified in 11% of EPTB patients, as opposed to 55–90% in the days prior to effective ATT [15].

**c. Abdominal tuberculosis**

The most common place in the digestive system. The following are the reasons why the ileocecal region is affected. A rise in physiological stasis Increased lymphoid tissue (Peyer's patches) The rate of fluid and electrolyte absorption inadequate digestion [16]

**d. Tuberculosis of the central nervous system**

It is a severe form of EPTB that mostly affects newborn infants and is often fatal. The diagnosis of CNS TB is difficult. There are two primary ways that it appears. i. Meningitis caused by TB ii. Tuberculosis within the brain [17]

**e. Tuberculosis in bones and joints**

Ten to fifteen percent of all EPTB cases are caused by it. It results from the reactivation of latent MTB bacilli that have become lodged in any bone, including major joints or the spine, after bacteremia caused by a primary lung infection. Due to their abundant vascular supply, these bacilli have a preference for the spine and major joints. Tuberculous arthritis is caused by an expansion of the primary infection focus from the bone to the joint.[18] f. Genito urinary tuberculosis is associated with 3–4% of PTB patients and 15% of all EPTB cases. Kidney transplant recipients are 20 times more likely to experience it than the general population. Twelve After hematogenous Bacilli leave the active site of the infection—usually the lungs—they settle in the kidney, the most common site of GUTB, and grow into metastatic lesions, or tubercles.[19]

**f. Tuberculosis in the military**

Although autopsy investigations have shown that military TB varies from 0.3% to 13.3%, military TB accounts for less than 2% of all TB cases and up to 20% of all EPTB cases in immunocompetent individuals. The TH2 response plays a major role in the immunopathogenesis of military TB.[20]

**Symptoms of TB**

- Cough that produces sputum (mucus) that may be bloody
- Chest pain
- Fatigue
- Weight loss
- Night sweats
- Fever



**Risk factors**

- > Diabetes mellitus
- > Smoking
- > Alcohol use
- > Illicit drug use

**Diagnosis**

- > Radiology techniques
- > Chest x-rays
- > Microscopic examination
- > Microbiological culture like multiple sputum cultures.
- > Skin test
- > Interferon gamma release assays (IGRAs) of the blood sample [21]

**ADVERSE DRUG REACTIONS**

- a. Hepatotoxicity
- b. Peripheral neuropathy
- c. Hyperuricemia
- d. Optic neuritis
- e. Nephrotoxicity
- f. Ototoxicity
- g. Cardiotoxicity

**Mechanism**

Isoniazid is a powerful first-line antibiotic that is mainly used to treat and prevent Mycobacterium TB-caused tuberculosis. By preventing the formation of mycolic acids, which are crucial parts of the mycobacterial cell wall, it demonstrates bactericidal activity against organisms that are actively proliferating. This disrupts the integrity of the cell wall and causes bacterial mortality. Isoniazid is effective in treating both pulmonary and extrapulmonary tuberculosis because it is quickly and fully absorbed after oral administration and spreads widely throughout bodily fluids and tissues, including the cerebrospinal fluid. The medicine is primarily metabolized in the liver by acetylation, a process that is regulated by genetic variation and categorizes people as either fast or slow acetylators. This can have an impact on the toxicity and plasma drug levels. To stop drug resistance from developing, it is frequently used in conjunction with other antitubercular medications including pyrazinamide and rifampicin. Hepatotoxicity, which can range from modest increase of liver enzymes to severe hepatitis, is one of the main side effects of isoniazid. As a result, monitoring liver function is advised throughout long-term therapy. Peripheral neuropathy is another serious adverse effect that can be avoided by co-administration of pyridoxine (vitamin B6), especially in patients who are malnourished, pregnant, or have diabetes. Rash, fever, and gastrointestinal problems are further adverse effects. Additionally, isoniazid is frequently used as a preventative measure for people who have latent tuberculosis infection or who are at high risk, such as those who are HIV positive.

Hepatoprotective, neuroprotective, antioxidant, and adaptogenic herbal substances are combined with vitamin supplements in the creation and assessment of a herbal syrup intended to avoid the adverse effects of isoniazid. Amla helps lessen oxidative stress and isoniazid-induced liver damage since it is high in vitamin C and has potent antioxidant and hepatoprotective qualities. While Brahmi has neuroprotective properties and improves cognitive function, helping to offset neurological negative effects, Ashwagandha functions as an adaptogen that boosts immunity, lowers stress, and supports general vitality. While turmeric includes curcumin, which has strong anti-inflammatory, antioxidant, and



hepatoprotective effects, licorice has calming, anti-inflammatory, and liver-protective qualities. By adding pyridoxine hydrochloride, a typical side effect of isoniazid therapy, peripheral neuropathy is avoided. These plants' aqueous or hydroalcoholic extracts are usually used to make the syrup, along with an appropriate syrup base (such as sucrose solution), flavoring agents, and preservatives to improve palatability. In addition to phytochemical screening, microbiological load testing, and organoleptic characteristics (color, taste, odor), the prepared syrup is evaluated using physicochemical parameters like pH, viscosity, and stability. Additionally, hepatoprotective evaluation and antioxidant activity investigations can be used to gauge its efficacy. All things considered, this polyherbal formulation provides a helpful treatment strategy to reduce the harmful effects of isoniazid while enhancing patient compliance and general health.

### **Plant profile**

#### **Amala**



**Biological Name:** Phyllanthus emblica

**Family:** Phyllanthaceae

**Part Used:** Fruit

### **Chemical Constituents**

Vitamin C

Tannins (Emblicanin A & B)

Flavonoids

Polyphenols

### **Pharmacological Uses**

Antioxidant

Hepatoprotective

Immunomodulatory

Role in Formulation

Helps prevent liver toxicity caused by isoniazid

Boosts immunity



### Ashwagandha



**Biological Name:** Withania somnifera

**Family:** Solanaceae

**Synonyms Name:** Indian Ginseng

**Part Used:** Root

### Chemical Constituents

Withanolides

Alkaloids

Steroidal lactones

### Pharmacological Uses

Adaptogenic

Anti-stress

Neuroprotective

Role in Formulation

Reduces stress and weakness

Supports nervous system during isoniazid therapy

### Brahmi



**Biological Name:** Bacopa monnieri

**Family:** Plantaginaceae

**Synonyms Name:** Brahmi

**Part Used:** Whole plant

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**Chemical Constituents**

Bacosides  
Saponins  
Alkaloids

**Pharmacological Uses**

Memory enhancer  
Neuroprotective  
Anti-anxiety  
Helps prevent neurological side effects (e.g., neuropathy)

**Licorice**



**Biological Name:** Glycyrrhiza glabra

**Family:** Fabaceae

**Common Name:** Mulethi

**Part Used:** Root

**Chemical Constituents**

Glycyrrhizin  
Flavonoids  
Saponins

**Pharmacological Uses**

Anti-inflammatory  
Hepatoprotective  
Demulcent

**Role in Formulation**

Protects liver  
Improves taste of syrup



## Turmeric



**Biological Name:** *Curcuma longa*

**Family:** Zingiberaceae

**Synonyms Name:** Haldi

**Part Used:** Rhizome

### Chemical Constituents

Curcumin

Volatile oils

Turmerone

### Pharmacological Uses

Anti-inflammatory

Antioxidant

Hepatoprotective

### Role in Formulation

Reduces inflammation

Prevents liver damage

### PLAN OF WORK

1. Literature survey
2. Selection of raw material
3. Processing of raw material
4. Preparation of herbal extracts
5. Formulation of herbal syrup
6. Evaluation of herbal Syrup
7. Final report and conclusion



## II. MATERIAL AND EQUIPMENTS

### Material

Sr no	Ingredient	Uses
1	Amla	Antioxidant, hepatoprotective (protect liver from isoniazid toxicity)
2	Ashwagandha	Anti-inflammatory, support immunity
3	Brahmi	Neuroprotective, improves memory (help prevent isoniazid induce neuropathy)
4	Licorice	Anti-inflammatory, hepatoprotective, soothing effect on GI tract
5	Turmeric	
6	Pyridoxine hydrochloride (vitamin B6)	Prevent peripheral neuropathy cause by isoniazid
7	Sucrose	Sweetening agent
8	Glycerin	Co- solvent, improves viscosity
9	Sodium benzoate	Preservative
10	Flavoring agent	Improve taste and palatability
11	Purified water	Solvent

### Equipment

Sr No	Equipment	Uses
1	Analytical balance	Accurate weighing of ingredient
2	Hot plate	Heating during preparation
3	pH meter	Measuring pH of syrup

## III. METHOD AND EVALUATION

### Method

#### Preparation of turmeric extract

In a clean 250 ml volumetric flask or conical flask, combine 10 g of turmeric powder with 100 ml of distilled water or hydroalcoholic solvent (1:10 ratio). To guarantee adequate extraction, the mixture is firmly sealed and left to remain at room temperature for 48 to 72 hours, stirring occasionally. Following the maceration process, the mixture is filtered via filter paper or muslin fabric. The turmeric extract is the filtrate that is produced.



### **Brahmi**

The decoction process, which entails boiling the plant material in water, can be used to make Brahmi extract. In an appropriate container, combine 100–200 ml of distilled water with 10 g of dried Brahmi powder or roughly broken plant material. In order to effectively extract water-soluble components like bacosides, the mixture is heated and gently boiled for 15 to 30 minutes until the volume is reduced to around half. The mixture is boiled, allowed to cool to room temperature, and then filtered through filter paper or muslin cloth to get rid of any solid residue. The Brahmi decoction extract is the clear filtrate that is produced.



### **Amla**

By boiling the plant material in water, the decoction method is used to create the Amla extract. In a good jar, combine 100–200 ml of distilled water with around 10 g of dried Amla fruit pieces or coarse powder. In order to extract active ingredients like vitamin C and tannins, the mixture is heated and gently simmered for 15 to 30 minutes until the volume drops to almost half. Following boiling, the mixture is allowed to cool to room temperature before solid residues are filtered out using filter paper or muslin cloth. The Amla decoction extract is the clear filtrate that was produced.



### **Ashwagandha**

The maceration process is used to create the ashwagandha extract. In a sterile 250 ml conical flask, combine 10 g of dried ashwagandha root powder with 100 ml of distilled water or hydroalcoholic solvent (1:10). To guarantee that



active ingredients such withanolides are properly extracted, the flask is firmly sealed and left at room temperature for 48 to 72 hours with sporadic stirring. To get rid of plant remnants, the mixture is filtered using muslin cloth or filter paper once the maceration period is over. Ashwagandha extract is the filtrate that was produced.

### **Licorice**

Licorice's dried roots are used in the decoction process to make the extract. In an appropriate container, combine 100–200 ml of distilled water with roughly 10 g of coarsely ground licorice root. In order to effectively extract active ingredients like glycyrrhizin, the mixture is heated and gently simmered for 15 to 30 minutes until the volume is reduced to around half. The mixture is boiled, allowed to cool to room temperature, and then filtered through filter paper or muslin cloth to get rid of any solid residue. The licorice decoction extract is the clear filtrate that is produced.



### **Preparation of syrup formulation**

Choosing appropriate medicinal herbs, such as amla, ashwagandha, brahmi, and licorice, which have antioxidant, hepatoprotective, and neuroprotective qualities, is the first step in making the herbal syrup to lessen the negative effects of isoniazid. To obtain the extract, the powdered dried plant materials are boiled in distilled water (1:8 ratio) for 30 to 45 minutes until the volume is reduced to half. This is followed by chilling and filtration. Separately, sugar (60–70% w/v) is dissolved in filtered water, heated gently, and then cooled to create a syrup basis. After that, the syrup base and herbal extract are gradually combined while being constantly stirred to guarantee even dispersion. In addition to appropriate preservatives such sodium benzoate and optional flavoring ingredients, pyridoxine hydrochloride (Vitamin B6) is added to prevent isoniazid-induced peripheral neuropathy. Distilled water is used to modify the final volume, and any contaminants are filtered out of the syrup. The prepared syrup is put into dry, clean, amber-colored bottles, labeled appropriately, and kept out of direct sunlight in a cool, dry location.





#### FORMULATION TABLE

Sr no	Ingredient	F1	F2	F3
1	Amla	2ml	3ml	4ml
2	Ashwagandha	2ml	3ml	4ml
3	Brahmi	2ml	3ml	4ml
4	Licorice	2ml	3ml	4ml
5	Turmeric	2ml	3ml	4ml
6	Pyridoxine HCL	4mg	4mg	4mg
7	Sucrose	24g	26g	28g
8	Sodium benzoate	0.04g	0.04g	0.04g
9	Glycerin	2ml	2ml	2ml
10	Flavoring agent	q. s	q. s	q. s
11	Purified water	q. s to 40ml	q. s to 40ml	q. s to 40ml

#### Evaluation

The formulated herbal syrup for urinary tract infection are evaluated for the following parameter.

Organoleptic properties

PH determination

Clarity test

Solubility test

Viscosity

#### Evaluation test for herbal syrup for reduce side effect of isoniazid

##### Organoleptic properties

Organoleptic evaluation refers to assessing the syrup based on sensory characteristics such as appearance, colour, odour, taste, and texture. It helps in determining the quality and acceptability of the formulation.



**Appearance:** Clear and free from suspended particles

**Colour:** Yellow to brown

**Odour:** Characteristic aromatic with slight pungent smell of garlic

**Taste:** Sweet with slightly pungent and bitter aftertaste

**Texture:** Smooth, viscous, and free from grittiness

#### PH determination

The pH of the prepared herbal syrup was determined using a calibrated pH meter. About 10 ml of the syrup and required quantity of distilled water were taken in a beaker. The pH meter was calibrated using standard buffer solutions. The electrode was then immersed in the syrup sample, and the pH was recorded.



#### Clarity test

The prepared herbal syrup is observed visually against a light source to check for clarity. The syrup should be clear and free from any suspended particles or turbidity.



#### Solubility test

The prepared herbal syrup is tested for solubility by mixing a small quantity of the syrup in a specified amount of distilled water. The syrup should dissolve completely to form a clear solution without any precipitation.





### **Viscosity test**

The viscosity of the prepared herbal syrup is determined using a viscometer. The syrup is taken in the sample container, and the viscosity is measured at room temperature. The viscosity should be sufficient to ensure proper flow and pourability of the syrup.



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