WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Preparation and Evaluation of Polyherbal Tablet for Dengue

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ABSTRACT:

Dengue is a disease of many tropics and subtropic regions that can occur epidemically, caused by dengue virus, a member of the family "Flaviviridae". Dengue fever, also called dengue, is a potentially serious disease caused by a virus. There are four types of dengue virus that can cause illness in humans Dengue viruses are transmitted between humans by the bite of an infected Aedes mosquito. Dengue is rare in the U.S., but is common and a serious public health threat in warm sub-tropical and tropical areas of the world. These include areas of Central and South America, Africa, Southeast Asia, China, India, the Middle East, Australia, the Caribbean and the South and Central Pacific Dengue fever is most common in urban areas and outbreaks occur commonly during the rainy season when mosquitoes breed heavily in standing water. The incidence of dengue fever is on the rise worldwide, and in some areas of Asia, complications of the disease are a leading cause of serious illness and death in children. Treatment of acute dengue is supportive, using either oral or intravenous rehydration for mild or moderate disease, and intravenous fluids and blood transfusions for more severe cases. The rate of infection has increased dramatically over the last 50 years, with around 50-100 million people being infected yearly.

1. INTRODUCTION:

Dengue is a potentially serious disease caused by the dengue virus, a member of the family Flaviviridae. There are four types of dengue virus that can cause illness in humans. Dengue viruses are transmitted between humans by the bite of an infected Aedes mosquito. Dengue is rare in the United States, but is common and a serious public health threat in warm sub-tropical and tropical areas of the world. These areas include Central and South America, Africa, Southeast Asia, China, India, the Middle East, Australia, the Caribbean, and the South and Central Pacific.

Mosquitoes pick up a dengue virus when they bite a human who is already infected with the virus. The mosquito then carries it in its own blood and spreads it when it bites other humans. After a dengue virus enters the human bloodstream, it spreads throughout the body. Symptoms appear in about eight to ten days after a bite from an infected mosquito. Symptoms are flu-like and can include high fever, nausea, vomiting, body aches, and headache

Fig. 1 Dengue mosquito.

Dengue fever is usually diagnosed by taking a thorough personal and family medical history, including symptoms, and completing a physical examination. Recent travel to sub-tropical or tropical areas of the world is an important clue that may increase the suspicion of a diagnosis of dengue fever. The virus exists in four different types, and an infection with one type usually gives lifelong immunity to that type, but only short-term immunity to the others. There is currently no vaccine available for dengue fever, but measures to reduce the habitat and the number of mosquitoes, and limiting exposure to bites, are used to decrease the incidence of dengue. Treatment of acute dengue is supportive, using either oral or intravenous rehydration for mild or moderate disease, and intravenous fluids and blood transfusions for more severe cases. The rate of infection has increased dramatically. Dengue is usually transmitted by the mosquito Aedes aegypti and rarely Aedes albonictus. Dengue is a global disease and is currently endemic in more than 110 countries.

ETIOPATHOGENESIS:

Dengue fever is a severe flu-like infection that can affect individuals of all age groups, including infants, children, adolescents, and adults . The virus is transmitted among human beings by the mosquito Aedes aegypti, which is most active during the rainy season . Dengue virus gains entry into the host organism through the skin following an infected mosquito bite. The virus primarily replicates in macrophages, and it can also cause direct skin infection or induce immunological and chemical-mediated mechanisms induced by host-viral interaction . The progression of the illness is implicated by humoral, cellular, and innate host immune responses, and the more severe clinical signs occur following the rapid clearance of the virus from the host organism. Hence, the most severe clinical presentation during the infection course does not correlate with a high viral load . Alterations in endothelial microvascular permeability and thrombo regulatory mechanisms lead to an increased loss of protein and plasma. Proposed theories suggest that endothelial cell activation caused by monocytes, T-cells, the complement system, and various inflammatory molecules mediate plasma leakage. Thrombocytopenia may be related to alterations in megakaryocytopoiesis, manifested by infection of human hematopoietic cells and compromised progenitor cell growth. This may cause platelet dysfunction, damage, or depletion, leading to significant hemorrhages.

CLASSIFICATION:

According to the World Health Organization guidelines issued in 1975 and 1997, Dengue is classified into three categories:

(1) Undifferentiated fever

(2) Dengue fever

(3) Dengue hemorrhagic fever

TYPE OF DENGUE:

Dengue fever is caused by four different types of viruses:

- Dengue 1 (DENV-1)
- Dengue 2 (DENV-2)
- Dengue 3 (DENV-3)
- Dengue 4 (DENV-4)

The following are some key characteristics of each type:

DENV-1: This flavivirus is transmitted to humans through the bite of an infected Aedes mosquito, which is common in tropical and subtropical regions around the world. Once the DENV-1 virus enters the human body, it replicates in the liver and lymph nodes. The virus then spreads to the bloodstream, where it can infect other organs and tissues. DENV-1 is the same type of virus that causes yellow fever and Zika.

DENV-2: This virus is also transmitted to humans through the bite of an infected Aedes mosquito. DENV-2 is known to cause more severe disease in children than in adults. The best way to protect yourself from DENV-2 infection is to avoid mosquito bite.

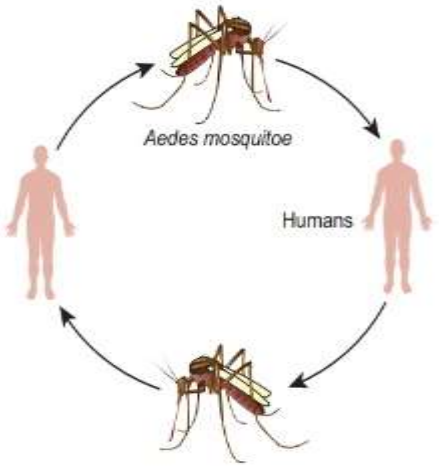
DENV-3: This type of dengue fever is characterized by bleeding, plasma leakage, and shock. It can cause a range of symptoms, from mild dengue fever to severe dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

DENV-4: This virus is also transmitted to humans through the bite of an infected Aedes mosquito. It can cause a range of symptoms, from mild dengue fever to severe DHF and DSS.

It is important to note that there is no specific treatment for dengue fever. However, early detection and proper medical care can significantly reduce the risk of complications and death.

TRANSMISSION:

Fig. 1 Transmission cycle



Transmission through mosquito:

The virus that causes dengue fever is transmitted to humans through the bites of infected female mosquitoes, primarily the **Aedes aegypti** mosquito. Other species within the **Aedes** genus can also act as vectors, but their contribution is secondary to **Aedes aegypti**. After feeding on a person infected with the virus, the virus replicates in the mosquito mid gut before disseminating to secondary tissues, including the salivary glands. The time it takes from ingesting the virus to actual transmission to a new host is termed the extrinsic incubation period (EIP). The EIP takes about **8–12 days** when the ambient temperature is between **25–28°C**. Variations in the extrinsic incubation period are not only influenced by ambient temperature; several factors such as the magnitude of daily temperature fluctuations, virus genotype, and initial viral concentration can also alter the time it takes for a mosquito to transmit the virus. Once infectious, the mosquito can transmit the virus for the rest of its life.

Human to mosquito transmission:

Mosquitoes can become infected with the dengue virus (DENV) when they bite a person who is viremic with DENV. This can happen even if the person is asymptomatic or pre-symptomatic. The transmission from human to mosquito can occur up to 2 days before the onset of symptoms and up to 2 days after the fever has resolved. The risk of mosquito infection is positively associated with high viremia and high fever in the patient. Conversely, high levels of DENV-specific antibodies are associated with a decreased risk of mosquito infection. Most people are viremic for about 4–5 days, but viremia can last as long as 12 days.

Maternal transmission:

Dengue fever is primarily transmitted to humans through mosquito vectors. However, there is evidence of the possibility of maternal transmission (from a pregnant mother to her baby). The risk of vertical transmission appears to be linked to the timing of the dengue infection during the pregnancy, and vertical transmission rates appear low. When a mother contracts DENV during pregnancy, babies may suffer from pre-term birth, low birth weight, and fetal distress.

Other transmission:Dengue fever is primarily transmitted to humans through mosquito vectors, primarily the **Aedes aegypti** mosquito. However, there have been rare cases of transmission via blood products, organ donation, and transfusions. Transovarial transmission of the virus within mosquitoes has also been recorded.

PHASES OF DENGUE:

Mild phase:

To manage mild stages of the infection, **intravenous therapy** may be used. To manage the disease in severe stages, **blood transfusion** may be required. Foods rich in vitamin C such as fruit juices, strawberries, guava, kiwi, and papaya, and nutrients rich in fluids such as sugar cane juice, lime juice, and coconut water are recommended. Solid foods should be avoided.

It is important to avoid anti-inflammatory painkillers like aspirin and ibuprofen, as these medications can increase the risk of bleeding. Instead, over-the-counter pain relievers such as acetaminophen (Tylenol) can be taken to reduce fever and pain . It is also important to drink plenty of fluids to stay hydrated and get plenty rest.

Dengue hemorrhagic fever:

DHF is most common in children under the age of 15, but it can occur in adults as well. DHF is a medical emergency and requires hospitalization. Treatment is focused on stabilizing the patient's vital signs and preventing complications.

This may include:

- **Intravenous fluids-** to replace lost fluids and electrolytes.
- **Blood transfusions-** to replace lost blood cells.
- **Medications -** to control bleeding and prevent shock.

Dengue shock fever:

Dengue shock fever (DSS) is a severe form of dengue fever that can be fatal if not treated promptly. It is characterized by a sudden drop in blood pressure, bleeding, and organ damage. Although DSS is most common in children under the age of 15, it can occur in adults as well, especially in those who have had dengue fever before. It is important to seek medical attention immediately if you or someone you know is exhibiting symptoms of DSS.

MECHANISM :

Dengue fever is a tropical disease caused by a mosquito-borne virus that afflicts millions of people each year. The symptoms include fever, headache, muscle and joint pains, and a characteristic skin rash. In some people, the disease progresses to a severe, often fatal, form known as dengue hemorrhagic fever.

According to Ping Liu of the University of North Carolina at Chapel Hill, the prevention and clinical treatment of dengue infection has been a "dramatic failure in public health compared to other infectious diseases like HIV".

However, new research by Liu and her colleagues, presented at the 58th Annual Biophysical Society Meeting, could offer vital insight into the mechanism of dengue virus entry into cells — and aid vaccine and clinical drug development .

Liu and her colleagues used high-resolution microscopes to examine the expression of a particular protein, known as DC-SIGN (for dendritic cell-specific intercellular adhesion molecule-grabbing nonintegrin), on the surface of immune system cells called dendritic cells. The normal role of DC-SIGN is to capture pathogens so that fragments of those pathogens can be presented as antigens on the surface of the dendritic cells. Such antigens then are recognized by T cells — the workhorse cells of the immune system "which is one of the first steps in the normal immune response," Liu said.

While it has been known for some time that dengue used DC-SIGN to attach to cells, Liu and her colleagues used high-resolution microscopy to study exactly how the viruses used the protein to gain entry into cells. "DC-SIGN has a unique carbohydrate recognition domain on its extracellular portion, which binds to all sorts of carbohydrates on pathogens," she explained.

SIGNS AND SYMPTOMS OF DENGUE:

The symptoms of dengue fever include:

- Sudden onset of high fever
- Severe headache, usually behind the eyes
- Joint and muscle pain
- Skin rash
- Mild bleeding from the nose or gums
- Easy bruising

In severe cases, dengue fever can cause dengue hemorrhagic fever, which is characterized by:

- Severe abdominal pain
- Persistent vomiting
- Bleeding under the skin, which might look like bruising
- Difficulty breathing
- Fatigue
- Blood in the urine, stools, or vomit

PREVENTION OF DENGUE:

To prevent dengue fever, it is important to avoid exposure to mosquitoes. This can be done by:

- Wearing long-sleeved shirts and pants
- Using mosquito repellent
- Sleeping under mosquito nets
- Eliminating standing water around your home, where mosquitoes breed.

Prevention of Dengue Fever is easy, cheap and better. What is required are some simple measures for -

➤ Preventing breeding of Aedes mosquitoes.

➤Protection from Aedes mosquitoes bites.

There are currently no approved vaccines for the dengue virus. Prevention thus depends on control of and protection from the bites of the mosquito that transmits it.

The World Health Organization recommends a Integrated Vector Control program consisting of five elements:

Advocacy, social mobilization and legislation to ensure that public health bodies and communities are strengthened.

Collaboration between the health and other sectors (public and private).An integrated approach to disease control to maximize use of resources. Evidence-based decisions making to ensure any interventions are targeted appropriately.

Capacity-building to ensure an adequate response to the local situation.

The primary method of controlling A aegypti is by eliminating its habitats. This may be done by emptying containers of water or by adding insecticides or biological control agents to these. areas. Reducing open collections of water through environmental modification is the preferred. method of control, given the concerns of negative health effect from insecticides and greater logistical difficulties with control agents. People may prevent mosquito bites by wearing clothing that fully covers the skin and/or the application of insect repellent (DEET being the most effective). A number of novel methods have been used to reduce mosquito numbers with some success including the placement of the fish Poecilia reticulata or copepods in standing water to eat the mosquito larva.

There are ongoing programs working on a dengue vaccine to cover all four serotypes. One of the concerns is that a vaccine may increase the risk of severe disease through antibody-dependent enhancement. The ideal vaccine is safe, effective after one or two injections, covers all serotypes, does not contribute to ADE, is easily transported and stored, and is both affordable and cost-effective. A number of vaccines are currently undergoing testing. It is hoped that the first products will be commercially available by 2015.

Plan of work-

1. Literature survey and analysis of collected data.
2. Selection of dosage form.
3. Designing the formulation.
4. Evaluating the formulation for required result in future.

2. Literature review :-

1. **Ayurvedic and other herbal remedies for dengue of the clinical complimentry medicine and pharmacology by vivek p chavda , anup kumar, rittwika banerji, nayan das**

The review by Chavda et al. provides a comprehensive overview of various Ayurvedic and herbal remedies that show potential in managing dengue fever. These remedies, including Tulsi, Papaya Leaf Extract, Giloy, Neem, Andrographis, Phyllanthus niruri, Eclipta alba, Curcumin, Amalaki, and Guduchi, exhibit antiviral, immunomodulatory, anti-inflammatory, and antipyretic properties that collectively contribute to their efficacy in treating dengue. However, further clinical trials and research are necessary to substantiate these findings and establish standardized treatment protocols.

2. **Pawan kumar singh nad pooja rawat, Evolving herbal formulations in management of dengue fever, j-AIM, doi. 10.1016/j.aim.2017.06.005**

They emphasize the effectiveness of formulations derived from herbs like Papaya Leaf (Carica papaya) for increasing platelet count and Tulsi (Ocimum sanctum) for its antiviral and immunomodulatory properties. The review also highlights Giloy (Tinospora cordifolia) for its immune-boosting effects, Neem (Azadirachta indica) for its antiviral activity, and Andrographis (Andrographis paniculata) for its anti-inflammatory and antiviral benefits. These formulations have shown promise in clinical settings, though the authors call for further research to validate their efficacy and safety in treating dengue fever.

3. **Mamta dhimani ,lakshika shrama, abhishek dadhich , poonam dhawan, traditional knowledge to contemporary medication in the treatment of infectious disease dengue, Frontier in Pharmacology doi.org/10.3389/fphar.2022.750494**

The authors explore the integration of traditional herbal remedies with contemporary medical treatments for dengue. They discuss the efficacy of herbs such as tulsi (ocimum sanctum), known for its antiviral properties, and papaya leaf (carica papaya), effective in increasing platelet count. The review also highlights giloy (tinospora cordifolia) for its immunomodulatory effects and neem (azadirachta indica) for its broad-spectrum antiviral activity. The authors emphasize the need for more clinical studies to bridge traditional knowledge with modern pharmacology, enhancing the treatment protocols for dengue.

4. **Sulochana kaushik, samander kaushik, vikrant shrama, jaya parkash yadav Antiviral antivirus and therapeutic uses of medicinal plant and their derivative against dengue virus from pharmacognosis review Doi. 10.4103/phrev_2_18.**

Examine the potential of various medicinal plants in combating dengue virus infections. They highlight the antiviral properties of Tulsi (Ocimum sanctum) and its bioactive compounds like eugenol. Papaya Leaf Extract (Carica papaya) is noted for its effectiveness in increasing platelet counts, crucial for dengue patients. Giloy (Tinospora cordifolia) is discussed for its immune-boosting and antiviral effects, while Neem (Azadirachta indica) is recognized for its broad-spectrum antiviral properties. The review underscores the importance of these traditional remedies in the development of complementary therapies for dengue, calling for more detailed research and clinical trials to substantiate their efficacy and integrate them into mainstream medical practice.

3. Need of study:-

Dengue fever, a mosquito-borne viral infection, continues to be a significant public health concern, especially in tropical and subtropical regions. With no specific antiviral treatment available, the management of dengue primarily involves supportive care to alleviate symptoms and prevent complications. Traditional medicinal plants such as Tulsi (Ocimum sanctum), Papaya (Carica papaya), Giloy (Tinospora cordifolia), and Amla (Emblica officinalis) have shown promise in individual studies for their therapeutic benefits in managing dengue symptoms and enhancing patient recovery.

Need for Study

1. **Safety and Toxicity Profiling:**
    - **Objective:** To determine the safety profile and any potential toxicity of the herbal combination.
    - **Rationale:** Ensuring the safety of the combined herbal formulation is critical, as interactions between different plant compounds could lead to adverse effects. Comprehensive toxicity studies are necessary to ensure patient safety.
2. **Standardization and Quality Control:**
    - **Objective:** To develop standardized extraction methods and formulation processes that ensure consistent quality and potency of the herbal tablet.
    - **Rationale:** Variability in active compound concentrations can affect the efficacy and safety of herbal products. Standardization is essential for clinical reliability and regulatory approval.
3. **Mechanistic Insights:**
    - **Objective:** To investigate the molecular mechanisms by which the combined herbs exert their therapeutic effects against dengue.
    - **Rationale:** Understanding the underlying mechanisms can help optimize the formulation, improve efficacy, and identify potential biomarkers for monitoring treatment success.
4. **Clinical Validation through Trials:**
    - **Objective:** To conduct randomized controlled trials comparing the herbal tablet's effectiveness against standard care in dengue patients.
    - **Rationale:** Clinical trials are essential to validate preclinical findings, establish the herbal tablet as a viable treatment option, and gather data on efficacy, safety, dosage, and patient outcomes.
5. **Cost-Effectiveness Analysis:**
    - **Objective:** To evaluate the cost-effectiveness of the herbal tablet compared to conventional treatments.
    - **Rationale:** Developing an affordable and effective treatment could be particularly beneficial in resource-limited settings where dengue is prevalent, improving access to care and reducing the economic burden of the disease.
6. **Public Health Impact:**
    - **Objective:** To assess the potential impact of the herbal tablet on dengue incidence and severity at a population level.
    - **Rationale:** An effective herbal treatment could significantly reduce the burden of dengue, lowering hospitalization rates and improving quality of life for affected individuals.

4. AIM AND OBJECTIVES:-

Aim:-

To develop and evaluate a combined herbal tablet of Tulsi, Papaya, Giloy, and Amla for effective and safe management of dengue fever.

Objectives:-

1. Evaluate Efficacy:

- Assess the combined efficacy of Giloy, Tulsi, Amla, and Papaya in reducing dengue viral load and alleviating clinical symptoms.

2. Enhance Platelet Count:

- Determine the effectiveness of the herbal tablet in increasing platelet counts and preventing thrombocytopenia in dengue patients.

3. Safety and Toxicity Assessment:

- Conduct comprehensive safety and toxicity studies to ensure the herbal tablet is safe for consumption without adverse side effects.

4. Standardization and Quality Control:

- Develop and validate standardized extraction and formulation methods to ensure consistent quality, potency, and stability of the herbal tablet

5. Mechanistic Studies:

- Investigate the molecular mechanisms through which the combined herbal ingredients exert their antiviral, immunomodulatory, and anti-inflammatory effects.

6. Clinical Trials:

- Perform randomized controlled trials to compare the herbal tablet's effectiveness against standard dengue treatments and assess patient outcomes.

7. Cost-Effectiveness Analysis:

- Evaluate the cost-effectiveness of the herbal tablet compared to conventional dengue treatments to determine its viability for widespread use, particularly in resource-limited settings.

5. MATERIAL AND METHODOLOGY:-

Creating herbal tablets involving tulsi (holy basil), neem, papaya, and giloy requires careful consideration of ingredients, processes, and proportions. Here's a basic outline:

Materials:

Creating herbal tablets involving tulsi (holy basil), neem, papaya, and giloy requires careful consideration of ingredients, processes, and proportions. Here's a basic outline:

Materials:

1. *Tulsi (Holy Basil)*: Dried leaves or powder.

2. *Neem*: Dried leaves or powder.

3. *Papaya*: Dried leaves or powder.

4. *Giloy*: Dried stems or powder.

5. *Binder*: Options include gum acacia, cellulose, or starch.

6. *Excipients*: Used for proper tablet formation, like magnesium stearate or silicon dioxide.

7. *Equipment*: Mixing equipment, granulator, tablet press, and coating equipment if necessary.

Methodologies:

1. *Preparation*: Ensure all ingredients are thoroughly dried and powdered if not already in powder form.

2. *Mixing*: Combine the powders of tulsi, neem, papaya, and giloy in the desired proportions. The proportion depends on the intended dosage and the potency of each ingredient.

3. *Granulation*: If needed, granulate the mixed powder to improve flow and compression properties.

4. *Binder Addition*: Incorporate a binder into the mix to help the powder hold together during compression.

5. *Compression*: Use a tablet press to form tablets of the desired size and shape.

6. *Drying*: If necessary, dry the tablets to remove excess moisture.

7. *Coating (Optional)*: Apply a coating to improve appearance, taste, or stability.

8. *Packaging*: Package the tablets in suitable containers, ensuring they are airtight and light-resistant to maintain potency.

6. FORMULATION AND EQUIPMENTS:-

HERBS FOR DENGUE:

We can use various herbal ingredients for dengue such as **papaya leaves, Tulsi leaves, giloy, Amla,** etc.

1. **Tulsi:** Tulsi is an ayurvedic herb used to prevent dengue fever, traditionally.

2. **Papaya leaves**: Papaya leaves are known to increase the platelet count in the blood, which is essential for dengue patients. You can consume papaya leaves in the form of juice or tea.
3. **Giloy**: Giloy is an Ayurvedic herb that is known for its antipyretic properties. It can help reduce fever and boost immunity.
4. **Amla:** Amla consumption of food act as a natural cure for dengue promotes antibodies for faster healing and recovery.

HERBS

Tulsi

Fig. 3 Tulsi

- **Synonyms:** Holy Basil, Sacred Basil

- **Biological Source:** It is the dried leave of Ocimum santcum Linn. Family: Labiatae.
- **Geographical Distribution:** The plant is cultivated throughout India especially in Hindu houses and temples for worship. It also grows in Phillipines.
- **Morphological character:**
    - It has an erect growth form which is highly branched. Leaves are broadly elliptical with a slightly toothed leaf margin (1.5-6 cm long, 1-2.5 cm wide).
    - The leaf surface is pubescent (densely covered in short hairs). Crushed leaves emit a musky, slightly minty fragrance.
- **Chemical constituents**: active compounds. Tulsi contains chemical compounds such as eugenol, ursolic acid, rosmarinic acid, chlorophyll, caryophyllene, oleanolic acid and linolenic acid. Nutritional compounds found in tulsi include vitamin A, vitamin C, calcium, iron and zinc.
- **Uses:**

- Leaf extract is effective to treat skin disorders. Dried leaf powder is used for brushing teeth. In the preparation of toothpaste for dental health.
- Tulsi leaves is used for relief from cough and cold. In respiratory disorders like Infuenza are treated with leaf extract.

PAPAYA LEAVES

Fig. 2 papaya

- **Synonyms:** Papayotin, vegetable pepsin, tromasin, arbuz, caroid.

- **Biological Source:** Papain is the dried and purified latex of the green fruits and leaves Of Carica papaya Linn. Family: Caricaceae.
- **Geographical source:** The plant is cultivated in Sri Lanka, Tanzania, Hawai, and Florida.
- **Morphological characters:**

1. It is white or greyish white coloured powder.
2. It is slightly hygroscopic in nature.
3. It is partially soluble in water and glycerol.
4. It is a protein made-up of 212 amino acid and has molecular weight is about 23,000 Dalton
5. It is resistant to heat.
6. In crystalline form, it is most stable in pH 5-7 and gets destroyed at 30°C and below pH 2.5 and above pH 12.

- **Chemical Constituents:**

Papain contains several enzymes such as proteolytic enzymes peptidase. It capable of converting proteins into dipeptides and polypeptides, rennin-like enzyme, clotting enzyme .The enzymes, papain, papayaproteinase, and chymopapain, have been isolated in crystalline form from the latex. It contains 15.5% nitrogen and 1.2% Sulphur.

The leaves possess dehydrocarpaines I and II, fatty acids, carpaine, pseudocarpaine, and carotenoids. The fruits yield lauric, myristoleic, palmitoleic and arachidic acids, 2-phenyl ethyl glucoside, and 4-hydroxy-phenyl-2-ethyl glucoside.

- **Uses:**

1. It is used to treat infected wounds act as an anthelmintic and anti-inflammatory agent

2. It is used in the treatment of intestinal and gastric disorders.

3. It is used in surgery for reducing blood clots and for local treatment of buccal and pharyngeal disorders.

4. It is used as an additive in digestive mixture and liver tonic.

5. Its reduces the enlarged tonsils.

Three potential anti-viral compounds (Quercetin, Kaempferol, and Chlorogenic acid) from papaya leaf extracts against the dengue virus.

∴ we can use papaya in formulation.

GILOY

Fig. 5 Giloy

- **Synonym**: Heartleaved Moonseed, guduchi, amrita, cinnodbhava, jwarari, jwarnashini, kundali, guduchika, jivantika, etc.
- **Biological source:** Giloy (Tinospora cordifolia) is a climbing shrub that grows on other trees, from the botanical family Menispermaceae.
- **Geographical distribution:** indigenous to tropical regions of the Indian subcontinent. It is found throughout India, Bangladesh, Sri Lanka, and Myanmar.
- **Morphological character:**

1. Leaves are simple, alternate, and exstipulate with long petioles up to 15 cm (6 in) long which are roundish and pulvinate.

2. The lamina are broadly ovate or ovate cordate, 10–20 cm (4–8 in) long or 8–15 cm (3–6 in) broad.
3. Flowers are unisexual, small on separate plants and appearing when the plant is leafless, greenish-yellow on axillary and terminal racemes.
4. Male flowers are clustered, but female flowers are usually solitary.
5. It has six sepals in two series of three each.
6. It has six petals which are smaller than sepals, obovate, and membranous.
7. Fruits aggregate in clusters of one to three. They are ovoid smooth drupelets on thick stalks with sub terminal style scars, scarlet or orange colored .

- **Chemical constituents:**

Giloy contains diverse phytochemicals, including alkaloids, phytosterols, glycosides, tinosporide, and various other phytochemicals.

Some of the chemical constituents present in it are choline, palmetin, ethanol, isocolumbin, berberine, aporphine, tembetarine, tinosporin, and mangoflorine.

- **Uses:**

It is used to improve the immunity and Helps to remove toxins from the body.

Improves digestion and absorption.

∴Columbin, tinosporaside, palmatine, berberine, choline is chemical constituent used in treatment of Giloy.

AMLA

Fig.3 Amla

- **Synonyms:** Amlang , Amlaki , Ambala , Amalic , Aunla , Nellikai .
- **Biological source:** This is consists of dried, as well as fresh fruits pericarp of the plant Emblica officinalis Gaerth Phyllanthus emblica Linn. Belonging to family Euphobiaceae. It contains not less than 1.0% w/w of Gallic acid calculated on dry basis.
- **Geographical distribution:**

- A small to medium in size, reaching 1-8m (3 ft 3 in-26 ft 3 in) in height. The trunk is slightly curved and the branches are scattered around.
- Bark: Amla plant is gray with hard reddish wood. It has a yellowish. green or pinkish colour flower.
- Fruit: pale yellow in colour, round in shape and has six vertical strips.
- A ripened Amla fruit is hard and weights approximately between 60 and 70 grams.
- Leaves: lighter in weight, linear and long in shape and smells like lemon and leaflets are arrange in pinnate shape.

- **Morphological character:**

- Deciduous tree medium in height grows up to 8 meter with slightly curved trunk. Branchlets are finely pubescent 10-20 cm long. Leaves are finely and closely set along the branchlets.
- Leaves have pinnate resemblance, very tiny, simple and attached by the base to branchlets.
- Taste of Indian gooseberry is sour, bitter and astringent and edible fruit is a great source of

- Color of flowers are yellowish. This tree contains hard, smooth and spherical fruit yellowish green in color with six vertical stripes of fiber.

➢ **Chemical constituents:** Hydrolysable Tannins, Emblicanin A and B, Punigluconin, Pedunculagin, Chebulinic acid (Ellagitannin), Chebulagic acid (Benzopyran tannin), Corilagin (Ellagitannin), Geraniin (Dehydroellagitannin), Ellagotannin.

➢ **Uses:**

- These are available in season in Indian stores. You can eat amla slices raw with salt and spices, like in India or you can mix a teaspoon of honey. Honey balances the tart taste of amla.
- Dried amla: Dried amla fruit can be chewed on. But be aware that they may have a lot of sugar added to it. In India, the candied pickle is called amla murabba.
- Organic versions are available in the market and can be mixed with water, honey, or yogurt to be made into a hair or face mask.
- This oil helps to strengthen the hair, prevents premature greying and stops hair fall.
- Taking amla juice diluted with water carly in the morning on an empty stomach helps keep the digestive system healthy and aids in managing blood sugar level.

EQUIPTMENTS:

1.weighing balance

Balance Type – Digital

Accuracy- 0.1 gm

Brand- NTF

Usage/Application- Office

Platform Size- 130 mm

Capacity- 600 gm

Product Description

GSM Round Cutter Diameter : 113mm

GSM Scale Capacity : 600 gm

Accuracy : 0.1 gm

Blades : German LUTZ

Body made of : Aluminium

Fig-7 weighing balance

2.Hot air oven

Brand: BTL

Usage/Application: Research department, laboratory

Temperature Range: 50-250 Degree Celsius

Material: stainless steel

Type: Digital

Number of Shelves: 4

Minimum Order Quantity: 1 Piece

Double walled inner made of thick stainless steel / mild steel, outer made of heavy duty mild steel / G.I. duly powder

coated. Temp range 50°C to 250°C Temp accuracy ± 2°C controlled by thermostatic.

Fig- 8 hot air oven

3. pfizer

Brand Name- LAB JUNCTION

Colour- Black, Blue & White

Item Weight- 1.40 kilograms

Model Number- LJ-200

Part Number-Model:LJ-200

Size- Standard

Fig- 9 pfizer

4.Friability test

Brand Name : Labpro

Dimension : 5.08x5.08x5.08 cm

Weight : 20 Kg

Type of Product : Friability Apparatus

Voltage : 230 V AC

Frequency : 50 Hz

STIRRER

Speed 25-200 RPM + 1 RPM

Resolution 1 RPM

Depth Adjustment 25 mm to 40 mm, 2.25 mm + 2

TEMPERATURE

Range 10 – 50 °C

Temperature Control Thermostat 0-85 °C

Fig-10 friability test

5.Dissolution test

Brand- FRINGE LABS

Wattage- 1000 Watts

Style- Compact

Manufacturer- FRINGE LABS

There are seven types of dissolution apparatus. We offer United States Pharmacopeia (USP)

Apparatus

1 (baskets),

2 (paddles),

3 (reciprocating cylinder),

4 (flow throw cell),

Fig-11 dissolution test

5 (paddle over disk),

6 (rotating cylinder), and

7 (reciprocating disk).

6.Tablet punching machine:-

Brand-RIDDHI

Capacity-24000 tablets

Model-RDSRTM

Tablet Dia Maximum-23 mm

Voltage (V)-410 volts

Weight (kg)-2 tons

Depth Of Fill Max-17

Fig- 12 tablet punch machine

7. FORMULATION TABLE:

Sr.no.	Ingredient used	BATCH 1	BATCH 2	Uses
1.	Basil leaves	5gm	10gm	Antipyretic for dengue fever.
2.	Papaya leaves	2gm	7gm	Boost platelets count.
3.	Giloy	5ml	10ml	Boost immune system.
4.	Bael fruit powder	5gm	7gm	Keeps hydrated
5.	Amla powder.	2gm	5gm	Vitamin c.
6.	Sodium starch glycolate	3gm	3gm	Faster disintegration.
7.	lactose	10gm	10gm	To mask unpleasant taste
8.	Starch	1.5%	2%	Binder
9.	Methyl paraben	1 gm	1gm	preservative
10.	Mannitol	1.5gm	1.5gm	Sweetening agent, Bulking agent.
11.	Talc	1gm	1gm	lubricant
12.	Sodium saccharin	1gm	1gm	Sweetening agent
13.	Magnesium stearate.	0.5gm	0.5gm	binder
14.	Calcium carbonate	2gm	2gm	Buffer.
15.	Sodium carbonate	2gm	2gm	Buffer.

8. PROCEDURE:-

- **Formulation and Mixing**

1. Weighing:

- Accurately weigh the tulsi powder, giloy powder, bael powder, amla powder, and aloe vera powder. A common ratio might be equal parts of each powder, but this can be adjusted based on specific requirements.

2. Mixing:

- In a mixing bowl, thoroughly combine the tulsi, giloy, bael, amla, and aloe vera powders to achieve a uniform blend.

- **Adding Binders and Excipients**

3. Binder Preparation:

- Prepare the binder solution by dissolving starch or gum acacia in a small amount of water to form a sticky solution.

4. Mixing with Binder:

- Gradually add the binder solution to the herbal powder mixture. Mix thoroughly until the mixture has a dough-like consistency. This will help in forming cohesive tablets.

5. Adding Excipients:

- Add excipients like lactose or microcrystalline cellulose to improve the tablet's texture and stability. Mix well to ensure even distribution.

6. Wet Granulation:

- If the mixture is too dry, perform wet granulation by adding more binder solution and then passing the mixture through a sieve to form granules.

7. Drying:

- Dry the granules if they were moistened during the previous step. Use a dehydrator or allow them to air dry until they reach the desired consistency.

9. EVALUATION:

Appearance: Visual inspection for colour, shape, and size consistency.

Fig 13- tablet

Elements of tablets	**Colour**	**Shape**	**Size**
Batch 1	Brown	Round/circle	1cm
Batch 2	Brown	Round/circle	1cm

Hardness and Friability: Testing the mechanical strength using hardness testers and friability testers.

Fig 14 - pfizer

Fig 15-dissolution

Fig16-weighing of tablet

Calculate the percentage loss in weight using the formula:

$$\text{Friability (\%)} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

= 1.945-1.940/1.945*100

= 0.257

Element	**Hardness**	**Friability**
Batch 1	40N	0.257
Batch 2	80N	0.854

Disintegration Test: Ensuring tablets disintegrate within a specified time in a simulated gastric environment.

Batch 1

1. Tablet 1: 12 minutes
2. Tablet 2: 12 minutes
3. Tablet 3: 15 minutes
4. Tablet 4: 13 minutes
5. Tablet 5: 14 minutes
6. Tablet 6: 12 minutes

Calculate the average disintegration time:

= 12+12+15+13+14+12/6

= 13

This result indicates that, on average, the herbal tablets disintegrate in 13 minutes, which is within the acceptable limit for uncoated herbal tablets.

Batch 2

1. Tablet 1: 15 minutes
2. Tablet 2: 20 minutes
3. Tablet 3: 18 minutes
4. Tablet 4: 20 minutes
5. Tablet 5: 19 minutes
6. Tablet 6: 20 minutes

Calculate the average disintegration time:

= 15+20+18+20+19+20/6

= 18.66

This result indicates that, on average, the herbal tablets disintegrate in 18.66 minutes, which is within the acceptable limit for uncoated herbal tablets.

Fig17-disintegration

Dissolution Test: Measuring the rate and extent of dissolution of the active ingredient in a simulated digestive fluid.

Dissolution testing evaluates how quickly and efficiently the active ingredients in herbal tablets are released into a solution under standardized conditions. This test is crucial for predicting the bioavailability of the active compounds in the body.

Procedure for Dissolution Testing

1. **Apparatus**:
    - A dissolution tester, often using USP Apparatus 1 (basket) or USP Apparatus 2 (paddle).
    - The apparatus contains a vessel filled with a dissolution medium (e.g., water, acidic buffer, or a specific solvent) maintained at 37°C ± 0.5°C.
2. **Sample Preparation**:
    - Place the tablet in the dissolution tester.
3. **Testing Process**:
    - Operate the apparatus at a specified rotation speed (e.g., 50 rpm for the paddle method).
    - At predetermined time intervals (e.g., 5, 10, 15, 30, 45, 60 minutes), withdraw samples of the dissolution medium.
    - Replace the withdrawn volume with fresh medium to maintain constant volume.
4. **Analysis**:
    - Filter and analyze the samples using appropriate analytical techniques, such as UV spectrophotometry or HPLC (High-Performance Liquid Chromatography), to determine the concentration of the active ingredient.
5. **Calculation**:
    - Calculate the percentage of the active ingredient dissolved at each time point.

10. RESULT AND DISCUSSION:-

Formulating a tablet that combines tulsi (Ocimum sanctum), aloe vera (Aloe barbadensis), bael fruit (Aegle marmelos), giloy (Tinospora cordifolia), and papaya (Carica papaya) for the treatment of dengue fever is an innovative approach that leverages the potential medicinal benefits of these plants. Each of these ingredients has demonstrated certain properties that could be beneficial in the management of dengue fever symptoms and complications. Here is a summary of the potential benefits and the conclusion regarding such a formulation:

1. *Tulsi (Ocimum sanctum)*:

- *Antiviral and Immunomodulatory*: Tulsi is known for its antiviral properties and can help boost the immune system. This could aid in combating the dengue virus and improving the body's overall defense mechanisms.

2. *Aloe Vera (Aloe barbadensis)*:

- *Anti-inflammatory and Immunomodulatory*: Aloe vera has anti-inflammatory properties and can help in soothing and reducing inflammation, which is beneficial in managing fever and pain associated with dengue. It also helps in immune regulation.

3. *Bael Fruit (Aegle marmelos)*:

- *Gastroprotective and Antimicrobial*: Bael fruit is known for its gastroprotective effects, which can be beneficial for the gastrointestinal symptoms often seen in dengue patients. Its antimicrobial properties can help in preventing secondary infections.

4. *Giloy (Tinospora cordifolia)*:

- *Antipyretic and Immunomodulatory*: Giloy is renowned for its fever-reducing properties and immune-boosting effects. It can help lower high fevers and improve the immune response in dengue patients.

5. *Papaya (Carica papaya)*:

- *Platelet-boosting and Anti-inflammatory*: Papaya leaf extract is known for its ability to increase platelet count, which is crucial in dengue treatment as the virus often causes a significant drop in platelets. It also has anti-inflammatory properties.

Discussion-

Combining these five ingredients into a single tablet formulation for the treatment of dengue fever presents a promising complementary approach to managing the disease. The potential benefits include:

- *Enhanced Immune Response*: Tulsi and giloy can synergistically boost the immune system, helping the body to better fight the dengue virus.

- *Symptom Management*: Aloe vera and bael fruit can help in reducing inflammation and protecting the gastrointestinal tract, alleviating common symptoms associated with dengue.

- *Platelet Count Support*: Papaya leaf extract can specifically address the critical issue of platelet count reduction in dengue patients.

- *Fever Reduction*: Giloy's antipyretic properties can help manage high fever, a common and serious symptom of dengue.

11. CONCLUSION:-

From the above evaluation test performed and appearance of tablets and conclusion and uses of ingredients according to the references ,the tablets formulated are beneficial on dengue fever. Batch 1 shows best formulation of dengue herbal tablets as it passes /complies good colour appearance , texture, disintegration test and hardness test and friability test as per standards of herbal uncoated table

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