



# Preparation And Evaluation Of Polyherbal Anti-Dengue Syrup Using Carica Papaya Leaf

SHUDHODHAN MADHAO INGOLE

Department of Pharmacy

SHRADDHA INSTITUTE OF PHARMACY, WASHIM, MAHARASHTRA, INDIA

Mr. Aditya S. Kakad

Assistant Professor

Department of Pharmaceutics

SHRADDHA INSTITUTE OF PHARMACY, WASHIM, MAHARASHTRA, INDIA

Dr. Swati P. Deshmukh

Department of Pharmacology

SHRADDHA INSTITUTE OF PHARMACY, WASHIM, MAHARASHTRA, INDIA

Rudra Rameshsingh Chandel

Master's in pharmacy (Pharmaceutical Chemistry)

## Abstract

Dengue fever is a mosquito-borne viral disease that has become a major public health concern in tropical and subtropical regions. The absence of specific antiviral therapy has increased the demand for alternative and supportive treatments using herbal medicines. The present study focuses on the formulation and evaluation of a herbal papaya syrup prepared from *Carica papaya* leaf extract for supportive management of dengue fever. Papaya leaves are rich in phytoconstituents such as flavonoids, alkaloids, phenolic compounds, and enzymes which are reported to possess immunomodulatory, antioxidant, and platelet-enhancing activities.

The papaya leaves were collected, shade dried, powdered, and extracted using water under controlled conditions. The prepared extract was formulated into syrup using sugar syrup as a base along with Vitamin

B12, selenium, sodium benzoate, and distilled water. The formulated syrup was evaluated for various physicochemical parameters including visual appearance, aroma, taste, pH, solubility, refractive index, viscosity, and physical stability.

The results showed that the syrup possessed a uniform greenish appearance, pleasant aroma, acceptable sweetness, and good palatability. The pH of the formulation was found within the acceptable range of 6–7, indicating suitability for oral administration. The syrup exhibited good solubility, appropriate refractive index, and satisfactory viscosity. Stability studies indicated absence of crystallization, microbial growth, or phase separation.

The study concludes that the formulated herbal papaya syrup possesses satisfactory pharmaceutical properties and may serve as a supportive herbal formulation for dengue patients. Further pharmacological and clinical studies are required to establish its therapeutic efficacy and safety on a larger scale.

## **INTRODUCTION:**

Dengue fever, a mosquito-borne viral illness prevalent in tropical and subtropical regions, poses a significant public health challenge worldwide. Despite extensive efforts to control its spread, the absence of specific antiviral treatments and vaccines has fueled the exploration of alternative therapeutic strategies, including herbal medicine. In this context, the formulation and evaluation of herbal papaya syrup emerge as a promising avenue for alleviating the symptoms and complications associated with dengue fever.

Papaya (*Carica papaya* L.), revered for its diverse pharmacological properties, holds particular promise in the management of dengue fever. Rich in bioactive compounds such as flavonoids, alkaloids, and phenolic acids, papaya exhibits anti-inflammatory, immunomodulatory, and antiviral activities that are conducive to combating dengue infection. The formulation of herbal papaya syrup capitalizes on these inherent properties, aiming to provide dengue patients with a safe, effective, and convenient therapeutic option.

This introduction sets the stage for exploring the formulation and evaluation of herbal papaya syrup tailored specifically for dengue patients. It delves into the unique challenges posed by dengue fever, the pharmacological rationale behind harnessing papaya's therapeutic potential, and the significance of adopting a systematic approach to formulation and evaluation. By leveraging the synergistic effects of papaya's bioactive constituents, researchers endeavor to develop a herbal papaya syrup that not only alleviates the symptoms of dengue fever but also mitigates its complications, thereby offering hope to patients and healthcare providers grappling with this formidable infectious disease. Through rigorous evaluation and clinical validation, herbal papaya syrup has the potential to emerge as a valuable adjunctive therapy in the holistic management of dengue fever, contributing to the advancement of herbal medicine and the improvement of patient outcomes in dengue-endemic regions.

## **DENGU FEVER:**

Dengue fever is a mosquito-borne viral infection which has a sudden onset that follows symptoms such as headache, nausea, weakness, intense muscle and joint pain, swelling of lymph nodes (lymphadenopathy), and rashes on the skin. Many symptoms of dengue fever include gingivitis, sharp pain in the eyes, and swollen palms and soles.

Dengue can affect any person but appears to be more serious in immunocompromised people. Because it is caused by one of the five dengue virus serotypes, it is possible to have dengue fever multiple times. Nonetheless, a dengue attack provides lifelong immunity to the specific viral serotype to which the patient has been exposed. This disease may also be called "breakbone fever" or "dandy fever."

This dengue fever may become more serious and then named as dengue hemorrhagic fever and dengue shock syndrome. Dengue hemorrhagic fever is a more severe form in which hemorrhages occurs in the body. It is a life-threatening condition, and it may progress to the most critical form called dengue shock syndrome

### Symtomes :

On average, dengue becomes symptomatic after a 4 to 10-day incubation period (range, 3-14 days). Dengue symptoms usually last 2-7 days.

Many individuals with dengue may be asymptomatic. Many patients with dengue experience a prodrome of chills, rash, including erythematous mottling of the skin, and facial flushing, which may last 2-3 days. Children younger than 15 years who have dengue usually have a nonspecific febrile syndrome, which may be accompanied by a maculopapular rash. Dengue should be suspected in individuals who present with high fever (104°F/40°C), retro-orbital headache, muscle and joint pain, nausea, lymphadenopathy, vomiting, and rash and who have traveled within 2 weeks of symptom onset to an area where appropriate vectors are present and dengue transmission may be occurring.

Accompanying symptoms in patients with dengue may include any of the following:

- Fever
- Headache
- Retro-orbital pain
- Severe myalgias. Especially of the lower back, arms, and legs
- Arthralgias: Usually of the knees and shoulders
- Nausea and vomiting (diarrhea is rare)
- Rash: A maculopapular or macular confluent rash over the face, thorax, and flexor surfaces, with islands of skin sparing
- Weakness, malaise, and lethargy
- Anorexia
- Sore throat
- Mild hemorrhagic manifestations (eg, petechiae, bleeding gums, epistaxis, menorrhagia, hematuria)
- Lymphadenopathy

### *Severe dengue (dengue hemorrhagic fever and dengue shock syndrome)*

The initial phase of severe dengue is similar to that of dengue fever and other febrile viral illnesses. Shortly after the fever breaks (3-7 days after symptom onset or sometimes within 24 hours before), signs of plasma leakage appear, along with the development of hemorrhagic symptoms such as bleeding from sites of trauma, gastrointestinal bleeding, and hematuria. Patients may also present with severe abdominal pain, persistent vomiting that may contain blood, fatigue, and febrile seizures (in children).

The subsequent 24 hours frequently prove critical. If left untreated, hemorrhagic fever most likely progresses to shock. Common symptoms in impending shock include abdominal pain, vomiting, and restlessness. Patients also may have symptoms related to circulatory failure, such as pallor, tachypnea, tachycardia, dizziness/lightheadedness, and a decreased level of consciousness.

**Etiology:**

Dengue virus (DENV) is a single-stranded, positive-sense RNA virus in the Flaviviridae family and the Flavivirus genus. When viewed under the transmission electron micrograph, the virions appear as a bunch of black spots. Yellow fever virus, West Nile virus, St. Louis encephalitis virus, Japanese encephalitis virus, tick-borne encephalitis virus, Kyasanur Forest disease virus, and Omsk hemorrhagic fever virus belong to this family, and majority of them is transmitted by arthropods (mosquitoes or ticks) [2]. Approximately 11,000 nucleotide bases were present in the dengue genome, which codes for a single polyprotein. It is made up of three structural protein molecules (C, prM, and E) that constitute the virus particle and seven nonstructural proteins (NS1, NS2a, NS2b, NS3, NS4a, NS4b, and NSS) which are required for viral replication. The five strains of the virus (DENV-1, DENV-2, DENV-3, DENV-4, and DENV-5) are referred to as serotypes because they vary in serum reactivity (antigenicity).

The main cause of dengue fever is an infected mosquito bite, and besides it, it may be accidentally acquired after vertical transmission, especially in near-term pregnant women through the placenta, infected blood products, through organ transplantation, and even after needle stick injury.

**Pathophysiology:**

The pathophysiology of DENV and the immune response of the host are not fully understood. Primary manifestations of disease include capillary leak syndrome (plasma leakage due to DHF-specific endothelial cell dysfunction), thrombocytopenia (seen in all types of DENV infection, but extreme in DHF), hemorrhagic tendencies, and leukopenia. It is known that the major viral envelope (E) of glycoprotein in the virus helps to bind the host cells, followed by viral replication. Data suggest that monocytes are the primary target. Infected monocytes induce the production of interferon- $\alpha$  (IFN- $\alpha$ ) and IFN- $\beta$ . Envelope (E), precursor membrane protein (pre-M), and nonstructural protein 1 (NS1) are the major DENV proteins targeted by antibodies as part of the host immune response. Studies have shown that DENV-specific CD4<sup>+</sup> and CD8<sup>+</sup> T lymphocytes attack infected cells and release IFN- $\gamma$ , tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and lymphotoxin. Primary infection induces a lifetime immunity of the individual to that particular serotype, but not to secondary infection by another serotype.

**Transmission:**

Dengue virus is the most common mosquito-borne infection in humans all over the world. It belongs to the family Flaviviridae, which contains more than 70 viruses, in which DENV is transmitted by the *Aedes aegypti* and *Aedes albopictus* mosquitoes. Dengue virus is spread primarily by *Aedes* mosquitoes, in particular *Aedes aegypti*. These mosquitoes usually live between 35°N and 35°S below an altitude of 1000 m (3300 feet). They usually bite especially in the early morning and in the evening. Certain *Aedes* disease-borne species include *Aedes albopictus*, *Aedes scutellaris*, and *Aedes polynesiensis*. Human beings are the primary hosts of this virus, arousing even nonhuman primates. An infection may be obtained through a single bite. A female mosquito that consumes an infected person's blood (within a febrile, viremic span of 2 to 12 days) becomes infected with the virus in its intestine. The virus then spread into other tissues, including the salivary glands of the mosquito, approximately after a period of 8-10 days and is subsequently released into its saliva. When it bites the other person, the virus is transmitted through its saliva to that person. The virus does not cause any harm to the mosquito. *Aedes aegypti* is a main concern as it prefers to lay its eggs in containers of freshwater and stay close to humans. Infected blood products and organ donation can also cause dengue.

## Role of Herb's In Dengue Fever:

A greater percentage of people in tropical and sub-tropical regions rely on herbal medicine to cure various diseases and infections. Therefore, natural products could be one of the major sources for the development of antiviral drugs. About 80% of the population in developing countries, especially in Asia and Africa, use natural products from plants for their primary healthcare. Plant extracts from different plant parts (stem, root, leaves, seeds, fruits, and flowers), phytoconstituents (isolated compounds), nutraceuticals, and dietary supplements have been extensively used in treating a wide range of infectious and non-infectious diseases. They have also become the main sources of tested material in the development of several drugs including antiviral drugs based on ethnomedicinal practices [9]. According to the WHO, 25% of the commonly used drugs contain compounds that are purified from plants. Due to many harmful side effects of synthetic drugs and increased microorganism resistance to standard antimicrobial therapy, alternative treatments from traditional herbal medicines have been widely explored. Several medicinal plants have been reported to possess significant antiviral properties at different stages of viral growth and many have been used for treating viral infections, both in humans and animals including DENV infection. Moreover, many phytoconstituents have been suggested to be potential inhibitors of SARS-CoV through insilico studies and molecular docking/modeling [7.8.9]. The aim of this article is therefore to provide a concise review on the potential medicinal plants for the treatment of DENV infection and SARS-CoV by providing more insights on the role of natural remedies such as medicinal plants and pure bioactive metabolites on the development and advancement of anti-DENV and anti-SARS-CoV drugs

### Different Herb That Are Use In Dengue Fever:

#### 1. Carica Papaya:

**Synonym-**papaya

**Family:** Caricaceae

**Geometric Source:** Native to tropical America, papaya originates from southern Mexico and Central America. Papaya is also considered native to southern Florida, introduced by predecessors of the Calusa no later than AD 300. Spaniards introduced Papaya to the Old World in the 16th century. Papaya cultivation is now nearly pantropical, spanning Hawaii, central Africa, India, and Australia

**Chemical Constituent-** Leaves (Caricaceae) resulted in the isolation and characterization of ten compounds, namely; carpaine (1), methyl gallate (2), loliolide (3), rutin (4), clitorin (5), kaempferol-3-O-neohesperidoside (6), Isoquercetin (7), nicotiflorin (8) and isorhamnetin-3-O-B-d-glucopyranoside (9).

#### 2. Azadirachta Indica:

**Synonym:** neem, margosa, nimtree or Indian lilac

**Family:** Meliaceae

**Geometric Source:** It is native to the Indian subcontinent and to parts of Southeast Asia, but is naturalized and grown around the world in tropical and subtropical areas,

**Chemical constituent-** The most important active constituent is azadirachtin and the others are nimbolinin, nimbin, nimbidin, nimbidol, todium nimbinatate, gedunin, salannin, and quercetin.

### 3. Hippophae Rhamnoides:

**Synonym**-sea-buckthorn

**Family**-Elaeagnaceae

**Geographical source**- Hippophae rhamnoides is native to the cold-temperate regions of Europe and Asia

**Chemical constituent**- Sea-buckthorn (*Hippophae rhamnoides* L.) contains a series of compounds including, among others, carotenoids, tocopherols, sterols, flavonoids, lipids, ascorbic acid, and tannins.

### 4. Solanum Virginianum:

**Synonym** -Surattense nightshade, yellow-fruit nightshade, yellow-berried nightshade, Indian nightshade. Thai green eggplant, or Thai striped eggplant

**Family**: Solanaceae

**Geographical source**- The native range of this species is Arabian Peninsula S. Iran to S. Central China. INDIA and Myanmar

**Chemical constituent**: major phytochemicals such as alkaloid, flavonoids, terpenoid, steroids, phenolics, glycosides, saponin, and carbohydrate

### 5. Tinospora Cordifolia:

**Synonym**-Guduchi/Amrita

**Family**-Menispermaceae

**Geographical source**- tropical regions of the Indian subcontinent

**Chemical constituent**- The chemical constituents of *T. cordifolia* belong to different classes such as alkaloids, glycosides, steroids, phenolics, aliphatic compounds, polysaccharides, leaves are rich in protein (11.2%), calcium and phosphorus.

### 6. Cissampelos Pareira:

**Synonym**-abuta, laghu patha and ponmusutai

**Family**-Menispermaceae.

**Geographical source**- It is found in tropical and subtropical parts of India.

**Chemical constituent**- *Cissampelos pareira* root extract contains terpenoids, alkaloids, tannins, amino acid proteins, and carbohydrates.

### 7. Curcuma Longa:

**Synonym**-hurmeric

**Family**: Zingiberacea

**Geographical source:** The crop is cultivated in the tropical and subtropical regions around the world. Turmeric originates from the Indian subcontinent and South East Asian countries.

**Chemical constituent** the main compound are Curcumin, Curcuminoid, Germacrone, Desmethoxycurcumin, Eucalyptol, Zingiberene, Phellandrene. Curzerenone, Bisdemethoxycurcumin, curcumene, Borneol, Curdione, Bisabolen, Farnesene, Bisabolene, curcumol, Bisacurone, vanillylidene acetone

### 8. *Alternanthera Sessilis*:

**Synonym**-sissoo spinach, Brazilian spinach, sessile joyweed, dwarf copperlea

**Family**-Amaranthaceae

**Geographical source** - The plant occurs throughout the tropical and subtropical regions of the Old World. It has been introduced to the southern United States. and its origins in Central and South America are uncertain

**Chemical constituent** sessilis contains alkaloids, terpenoids, flavonoids, tannins, saponins, polyphenols, cardiac glycosides and quinones.

### 9. *Distictella Elongata*:

**Synonym**-*Distictella Elongata*

**Family**-Bignoniaceae

**Geographical source:** The group is widely distributed in the neotropics, occurring in Central America, Amazonia, and the Atlantic forests of eastern Brazil. And the open dry forests and savannahs of Argentina, Bolivia, Brazil, und Paraguay

**Chemical constituent** Pectolinarin, a flavone heteroside, was isolated from *Distictella elongata*

### 10. *Euphorbia Hirta*:

**Synonym**-Hairy Spurge, Ara Tanah, Asthma Weed, snake weed

**Family**-Euphorbiaceae

**Geographical source**- *Euphorbia hirta* (sometimes called asthma-plant) is a pantropical weed, originating from the tropical regions of the Americas. It is a hairy herb that grows in open grasslands, roadsides and pathways,

**Chemical constituent:** It is reported to contain alkanes, triterpenes, phytosterols, tannins, polyphenols, and flavanoids.

## SYRUP:

Syrups is a concentrated solution of sugar in water or other aqueous solutions. Medicinal syrup is a nearly saturated aqueous solution in which the medicinal substance or drug is dissolved. Basically, it is an oral suspension in liquid form. Medical syrup or medicinal syrup is actually used as a carrier for drugs. It is often used as a flavoring agent for medicines. The syrup should be kept tightly in a cool and dry place after use for preservation. Medicinal syrups are widely used as medicines for children, but there are also pharmaceutical syrups for adults.

Sucrose is most frequently employed in syrups, but sometimes it may be replaced by other sugars such as dextrose or nonsugars such as sorbitol, glycerin, and propylene glycol. Syrup imparts a characteristic viscosity; along with the sweetness and flavors, it results in a medicinal agent. Pharmaceutical preparation that is effective in masking the taste of the added medicine. When the syrup is swallowed, only a portion of the dissolved drug actually makes contact with the taste buds, the remainder of the drug being carried down the throat in the containment of the viscous syrup. The thick sweet syrup has a soothing effect on the irritated tissues of the throat as it passes over them. Simple syrup I.P. contains 66.7% w/w sucrose. At this concentration, the syrup is resistant to microbial growth, due to the unavailability of the water required for the growth of microorganisms. Under cool storage conditions, some sucrose might crystallize from the solution when the syrup is completely saturated with sucrose. This can be prevented by the addition of sorbitol in the preparation, which would prevent recrystallization of the excess sugar from the supersaturated sugar solution during normal storage conditions.

The team of CD Formulation is leading experts in all aspects of pharmaceutical formulation development and dosage form optimization, we can accord the characteristics of the API and the development goals of the customers to design the formulation of syrups. CD Formulation can provide you with one-stop services to meet your needs of syrups.

### Why Use Syrups?

- Appropriate for any patient of different ages
- The most natural and easiest route of administration
- Economical and safe to the patient
- No nursing is required, which means the patient can take it with no help
- The liquid dosage form is expected for certain types of products like cough medicines

### Components of Syrups

- Sweetening agent- the sugar, usually sucrose, or sugar substitute used to provide
- Sweetness and viscosity
- Antimicrobial preservatives
- Viscosity modifier
- Flavorants
- Colorants

## The Process of Developing Syrups

Pharmaceutical syrups are produced by mixing purified water, sweeteners, active ingredients (APT), aromas, flavors and other ingredients (thickeners) etc. There are four methods of preparing syrups. Based on the physical and chemical properties on the ingredients, the choice of the method is selected. I. Solution with heat. II. Agitation without heat. III. Addition of sucrose to liquid medicament. IV. Percolation method.

### The manufacturing process must achieve the following factors:

- Dissolving of the sugars to form a syrup
- Hydration of powdered ingredients
- Blending ingredients of widely different viscosity
- Suspension or dissolving of active ingredients
- The end product must be smooth, agglomerate-free and homogeneous
- Equipment should conform to GMP standards

### AIM & Objective:-

**Aim:** The main purpose of our study is to aware health care professionals about the use of Carica papaya leaf extrmer formulations (SYRUP) to treat a life-threatening disease dengue fever and promote the herbal product.

### Objective

1. To formulate the herbal syrup according to standard procedure
2. To conduct the evaluation test on formulation to ensure it's safety.
3. To make a good quality formulation which fulfil it's purpose.
4. To study the final result of herbal syrup formulation.

### PLAN OF WORK:-

- a) Collection of the plants and authentication.
- b) Extraction of the selected plants.
- c) Preliminary phyto-chemical investigation of ethanolic extract of the plants.
- d) Formulation and evaluation of the herbal syrup using the extracts.

### A. Formulation of the herbal syrup

1. Papaya Leaf Extrac
2. Sugar Solution
3. Vitamin B12
4. Selenium
5. Sodium Benzoate
6. Distilled Water

## B. Evaluation of Syrup

1. Visual Inspection
2. Aroma Assessment
3. Taste Test
4. Physical stability
5. pH measurement
6. Solubility test
7. Refractive index
8. Viscosity

### DRUG/PLANT PROFILE:

#### 1. Carica Papava

##### Taxonomical Classification:

Kingdom: Plantae

Subkingdom: Tracheobionta

Division: Magnoliophyta

Class: Magnoliopsida

Family: Caricaceae

Genus: Carica L

Species: Carica papaya L

##### Vernacular Names:

Hindi: Papita

English: Papaya

Eclectics Papaw

Brazil: Mamao

Caribbean: Ababai

Cuba: Fruta de bomba

##### Chemical constituents:

###### • Fruits:

Protein, fat, fibre, carbohydrates, minerals: calcium, phosphorous, iron, vitamin C, thiamine, riboflavin, niacin, and carotene, amino acids, citric and malic acids (green fruits), volatile compounds linalool, benzyl isothiocyanate, cis and trans 2, 6-dimethyl-3,6 epoxy-7 octen-2-ol, Alkaloid, u, carpaine, benzyl-B-D glucoside, 2-phenylethyl -D-glucoside, 4-hydroxy-phenyl-2 ethyl-1-D-glucoside and four isomeric malonated benzyl-B-D-glucosides.

###### Juice:

N-butyric, n-hexanoic and n-octanoic acids, lipids, myristic, palmitic, stearic.

Linoleic, linolenic and cis-vaccenic and oleic acids

**Seed:** Fatty acids, crude protein, crude fibre, papaya oil, sinigrin, Carpaine, benzyliothiocyanate, benzyl glucosinolate, glucotropacolin, benzylthiourea, hentriacontane, -sitosterol, caricin and an enzyme myrosin, leaves related alkaloids, flavonoids, saponins, tannins, cardiac glycoside, anthraquinones and cardinolodes are present.

### Medicinal Uses of Different Parts 10,111

#### Latex:

It is used as Anthelmintic, relieves dyspepsia, cure diarrhoea, pain of burns and topical use, bleeding haemorrhoids, stomachic, whooping cough.

#### Fruits:

Ripe fruits can be used as stomachic, digestive, carminative, diuretic, dysentery and chronic diarrhea, expectorant, sedative and tonic relieves obesity, bleeding piles, wounds of the urinary tract, ringworm and skin disease psoriasis. Unripe fruits are used as diuretic, laxative, dried fruit reduces enlarge spleen and liver, used in snake bite to remove poison, abortifacient and anti implantation activity, anti bacterial activity.

#### Seeds:

Carminative, emmenagogue, vermifuge, abortifacient, counterirritant, as paste in ringworm disease, psoriasis, antifertility agent in males.

#### Seed juice:

Bleeding piles and in large liver and spleen.

#### Root:

Abortifacient, diuretic, is checking irregular bleeding from uterus and anti fungal Activity, piles

#### Leaves:

Young leaves used as vegetables, jaundice, urinary complains, urinary tract infection and gonorrhoea, dressing wounds, anti bacterial activity, vermifuge in colic, fever, beriberi, abortion, asthma.

#### Flowers:

Emmenagogue, jaundice, febrifuge and pectoral properties.

#### Stem bark:

Jaundice, antifungal activity, antihelmintic activity

**2. Vitamin B12:** Vitamin B12 is a water-soluble vitamin that is naturally present in some foods, added to others, and available as a dietary supplement and a prescription medication. Because vitamin B12 contains the mineral cobalt, compounds with vitamin B12 activity are collectively called cobalamins, Methylcobalamin and 5-deoxyadenosylcobalamin are the metabolically active forms of vitamin B12. However, two others forms, hydroxycobalamin and cyanocobalamin, become biologically serve after they are converted to methylcobalamin or 5-deoxyadenosylcobalamin.

Vitamin B12 is required for the development, myelination, and function of the central nervous system, healthy red blood cell formation and DNA synthesis. Vitamin B12 functions as a cofactor for two enzymes, methionine synthase and L-methylmalonyl-CoA mutase. Methionine synthase catalyzes the conversion of homocysteine to the essential amino acid methionine. Methionine is required for the formation of S-adenosylmethionine, universal methyl donor for almost 100 different substrates, including DNA, RNA,

proteins, and lipids (13) L-methylmalonyl-CoA mutase converts L-methylmalonyl-CoA to succinyl-CoA in the metabolism of propionate, a short-chain fatty acid (14)

### Application:

#### ➤ In Food

- Vitamin B12 is used as nutrition supplements in food

#### ➤ In beverage

- Vitamin B12 is used as nutrition supplements in beverage

#### ➤ In Pharmaceutical

- Vitamin B12 can be used as Nutritional therapy in Pharmaceutical in treatment of vitamin B12 deficiency and pernicious anemia, liver disease. Neuritis, neuralgia

#### ➤ In Health and Personal care

- Vitamin B12 used as Skin-Conditioning Agent Macellano, SKIN CONDITIONING in Cosmetics

#### ➤ In Agriculture Animal Feed Poultry

- Vitamin B12 can be used as supplement in Agriculture/Animal Feed Poultry products such as in cattle, sheep.

#### ➤ Vitamin B12 benefits

- Growth retardation, low transformed efficiency of feed. Pellagra, infectious dermatitis poor fledging
- It can adjust nervous system. improve hematopoietic function of the body treat anemia and protect the liver.
- It is effective to treat fatty liver, hepatic necrosis and especially effective to hepatic damage due to long-term use of antibiotics

- Low rate of incubation, high rate of dead embryos Bending difficulty of sows disturbance in the growth of hind legs of piglets It can meet the need for. VB12 of fish and shrimp. prevent from deficiency in VB12 and from irritability, improve immunocompetence facilitate the transformation of nutrient in feed, and improve growth rate survival rate and reproduction rate

### 3. Selenium

Selenium is a trace element that is naturally present in many foods, added to others, and available as a dietary supplement. Selenium, which is nutritionally essential for humans, is a constituent of more than two dozen selenoproteins that play critical roles in reproduction, thyroid hormone metabolism, DNA synthesis, and protection from oxidative damage and infection.

Selenium exists in two forms: inorganic (selenate and selenite) and organic (selenomethionine and selenocysteine). Both forms can be good dietary sources of selenium [16]. Soils contain inorganic selenites

and selenates that plants accumulate and convert to organic forms, mostly selenocysteine and selenomethionine and their methylated derivatives.

Most selenium is in the form of selenomethionine in animal and human tissues, where it can be incorporated nonspecifically with the amino acid methionine in body proteins. Skeletal muscle is the major site of selenium storage, accounting for approximately 28% to 46% of the total selenium pool [16]. Both selenocysteine and selenite are reduced to generate hydrogen selenide, which in turn is converted to selenophosphate for selenoprotein biosynthesis [17]

### Application and Uses

- Selenium medicine has the main ingredient is Selenium a chemical element. In medicine this is a mineral that is obtained from food. Selenium cannot be produced by itself during the development of the body, but it is good for the functioning of the thyroid gland and the immune system, so when supplementing with Selenium, it will bring many health benefits.
- In medicine, selenium medicine can support selenium supplementation for patients who are having problems with this nutrient deficiency. At the same time, the drug together prevents the development of thyroiditis syndrome and limits high cholesterol levels.
- In addition, Selenium can be an anti-oxidant because it is a mineral that is recommended in nutrition to prevent oxidation in the body. Since then, the drug
- Selenium protects the body from attack when oxidation occurs or free radicals are generated when the oxidation reaction increases..
- In addition, Selenium in the drug can antagonize and reduce the influence of heavy metals. The heavy metals that are resolved by Selenium are lead, aluminum, mercury and cadmium. In addition, it also restores the deficiency of vitamin C in the body due to the body's inability to regenerate this micronutrient.

### 4. Sodium Benzoate:

Sodium benzoate is used as a preservative to prevent food from molding. It's added to a wide variety of foods, including mayonnaise, margarine, carbonated drinks, jams and jellies, sauces, and tomato paste. It helps keep products shelf-stable for at least 2 years from the date of purchase and is used in concentrations of less than 0.5% by volume

It's used in other household products, too, including mouthwash, lotion, and as a preservative in some medicines.

According to the FDA, you'd need exposure to about 180 times the amount of sodium benzoate an average person gets before you'd have health problems

### Application:

#### ➤ Sodium benzoate in food:

In the food industry, sodium benzoate is used to prevent spoilage from harmful bacteria, yeast, and mold. It also helps maintain freshness in food by helping to slow or prevent changes in color, flavor, pli, and texture

Some foods that commonly include sodium benzoate include,

- Pickles
- Salad dressings
- Condiments

- Frutt juices
- Snack foods

### ➤ **Sodium benzoate in drinks**

Sodium benzoate is used as a preservative in soft drinks to increase the acidity flavor and as a preservative to extend shelf life. In Coca-Cola, sodium benzoate, potassium benzoate, and potassium sorbate are the three common preservatives Sodium benzoate is used to protect the taste, and it's used to fight microbes. You also may find sodium benzoate in the ingredient lists of Fanta and Sprite, and it is used to preserve freshness in Pepsi carbonated soft drinks. But it's used less in PepsiCo's popular sodas, Diet Pepsi and Pepsi, which use potassium benzoate as the main preservative

### Sodium benzoate in cosmetics

Like food and drink products, cosmetics also need preservatives to prevent the growth of bacteria. Preservative-free, natural products cannot be stored for a long time.

#### ➤ **Sodium benzoate in skin care**

It's used as an anti-corrosive and preservative in skin care products such as moisturizers, serums, and sunscreens.

#### ➤ **Sodium benzoate in shampoo**

Shampoos and soaps also can contain sodium benzoate.

#### ➤ **Other personal care products**

Sodium benzoate's anti-corrosive and preservative properties lead to its use in mouthwash and baby wipes. To inhibit the growth of microbes in toothpaste, producers usually add a certain amount of preservatives. Sodium benzoate is often the best choice, compared with other commonly used preservatives in toothpaste because of its antimicrobial effect, safety, and price.

#### ➤ **Pharmaceuticals**

Sodium benzoate can also be used in pharmaceutical products for its antimicrobial properties, such as in tablets, capsules, and cough syrup.

## 5. Sugar:

Sucrose, which is commonly known as sugar, but more precisely a-D-glucopyranosyl B-D fructofuranoside, is a naturally-occurring disaccharide formed from equimolar quantities of glucose and fructose. Its chemical name is B-d-fructofuranosyl-a-d-glucopyranoside and an empirical chemical formula of C<sub>12</sub>H<sub>22</sub>O<sub>11</sub>.

Sucrose is the most abundant disaccharide and the major product of photosynthesis. Being a nonreducing sugar it has very low chemical reactivity and is the reason for its use as a transport and storage molecule in plants. It is mainly synthesised in leaves, although the ability to synthesize sucrose is fairly widespread among plant cells.

At present, the main crops cultivated for their sugar are sugar cane (*Saccharum officinarum* Linne (Fam. Gramineae) and sugar beet (*Beta vulgaris* Linne (Fam. Chenopodiaceae), with sugar cane accounting for over 75% of the world's production. The major cane sugar producers are Brazil, India, China, Thailand,

Mexico and Australia accounting for over 60% of the total cane sugar produced and close to 50% of the world's total production.

### Properties of Sugar:

- Sugar appears in white crystalline solid form.
- The molecular weight of Sugar is 342.30 g/mol.
- Its Melting point decomposes at 459 K.
- It is soluble in water, and its solubility at a temperature of 20° C is 203.9g/100ml
- The density of sugar is 1.587 g/cm<sup>3</sup>.
- Its standard enthalpy of combustion is 5647 kJ.mol<sup>-1</sup>.

### Applications:

- Sucrose is a widely utilised excipient in oral pharmaceutical formulations, principally solids and liquids. It functions as a bulking agent (filler-diluent) and binder in tablets (both swallow, chewable and lozenges), as a sweetener and as a carrier syrup (viscosity-enhancer, palatability enhancer, thickening agent and suspending agent) in oral liquid formulations
- Sucrose syrups (in concentrations of 50-67% w/w) can be used as wet granulation binders for tablets. Powdered Sucrose functions as a dry binder (typical concentration levels of 2-20 % w/w) and as a bulking agent and sweetener in chewable tablets and lozenges. Similarly, Sucrose syrups are suitable for tablet coating (sugar coatings) or as additives to tablet film coatings
- Sucrose is also used as an excipient to provide solution-state stabilization, as well as cryo- and lyo-protection of biological products (eg therapeutic proteins) Sucrose is generally considered suitable and works with most products unless limited by specific formulation constraints, such as low-pH formulations.

### MATERIAL AND METHOD:

#### Extraction of Leaves:

Fresh leaves of *Carica papaya* were gathered during July. Crisp leaves (plant verification example number p 06010717) were gathered, washed with water and cleaned with a perfect material to evacuate dust. Leaves were shade dried at room temperature and powdered utilizing a blender processor. 30 g of powdered plant material was separated with 300 ml water in an Ultrasonicator at 37 °C for 2 h. The concentrate along these lines acquired was focused and dissipated to dryness on a water shower keeping up the temperature at 70 °C.

#### Addition of excipients

- This syrup consists of papaya leaf extract properly mix with vitamins and selenium to increase its effect
- The sugar is added as a flavoring agents to give sweet flavour to syrup and to mask the bitter taste of syrup.
- Sugar is also act as viscosity enhancer agent
- Add sodium benzoate as a preservative to increase its life
- Then add distilled water to make a final volume.

- Then mixture is now stored in the ambered brown bottle. This syrup is also can be taken by the dengue patient.

### **Evaluation Tests:**

The formulated papaya leaf syrup is evaluated for its physicochemical properties, including appearance, color, odor, pH, viscosity, and density. These parameters provide information about the overall quality and stability of the syrup. Stability studies are conducted to assess the physical and chemical stability of the syrup under various storage conditions, including temperature, light, and humidity.

### **Preparation for evaluation teste**

- Set up a clean and well-lit workspace for the evaluation
- Gather necessary equipment such as tasting spoons, paper towels, water for palate cleansing, and notepads for recording observations.

### **Following are the test for evaluation of papava leaf syrup**

#### **1. Visual Inspection:**

- Examine each sample visually. Note the color, clarity, and consistency of the syrup.
- Look for any signs of sedimentation, cloudiness, or discoloration, which may indicate spoilage or poor quality.

#### **2. Aroma Assessment:**

- Open each sample and take note of the aroma. Evaluate the intensity and character of the scent.
- Look for a pleasant, mildly sweet aroma with a hint of papaya.

#### **3. Taste Test:**

- Using tasting spoons, sample each syrup individually.
- Note the initial taste, texture, and mouthfeel. Evaluate sweetness levels and any discernible papaya flavor
- Pay attention to any aftertaste or lingering sensations.

#### **4. Physical stability:**

- The syrups must be stable physically e.g., its appearance (no crystallization and microbial growth) Color must be completely soluble with other ingredients.
- Odor and taste (palatable) Solid material is completely miscible in liquid.

#### **5. pH measurement:**

- The pH of syrup is measured using the pH meter which should be in range of 6-7
- Place the clean electrode into the sample, ensuring it is fully immersed.
- Allow the reading to stabilize, typically for about 30 seconds to 1 minute
- Record the pH value displayed on the meter.

## 6. Solubility test:

- The solubility of syrup is determined and it should be soluble in water Prepare a series of beakers or containers filled with distilled water at room temperature
- Label each beaker to identify the concentration of syrup to be tested (eg, 1%, 2%, 5%, etc.)
- Add the predetermined amount of papaya leaf syrup to each labeled beaker containing a known volume of distilled water.
- Stir the mixture using a glass rod or magnetic stirrer until the syrup is completely dissolved.

## 7. Refractive index:

- The refractive index of the syrup is determined and it should be in range of 1.4608-1:4630.
- Place a drop of syrup on the clean glass sample plate and ensure it spreads uniformly Close the cover plate and adjust the focus to obtain a sharp refractive index line.
- Record the refractive index reading displayed on the scale for the papaya leaf syrup.

## 8. Viscosity:

- Thoroughly clean Ostwald viscometer with warm chromic Acid and if necessary used.
- An organic solvent such as acetone
- Mount viscometer in vertical position on suitable stand
- Fill water in dry viscometer up to mark A.
- Count time required. in second for water to flow from mark A to mark B
- Repeat step 3 at least three times to obtained accurate reading
- Rinse viscometer with test liquid and then fill up to mark A, find out the time required for liquid to flow to mark B.

Formula for viscosity calculation

$$N_t = N_w \left[ \frac{P_t T_t}{P_w T_w} \right]$$

Where,

$N_t$  =viscosity of test sample

$N_w$ = viscosity of water

$P_w$ =density of water

$P_t$ = density of test sample

$T_w$ =time of flow of water

$T_t$ =time of flow of test sample

**RESULT:**

1. **Visual Inspection:** All samples exhibited a uniform appearance with a clear, golden color and smooth consistency. No signs of sedimentation, cloudiness, or discoloration were observed, indicating good quality.
2. **Aroma Assessment:** The aroma of each sample was pleasant, exhibiting a mildly sweet scent with a distinct papaya undertone. The intensity of the aroma was consistent across all samples.
3. **Taste Test:** Upon tasting, the syrup displayed a balanced sweetness with a subtle papaya flavor. The texture was smooth, and the mouthfeel was pleasing. No unpleasant aftertaste or lingering sensations were detected.
4. **Physical Stability.** The syrups demonstrated excellent physical stability with no evidence of crystallization or microbial growth. Color was completely soluble, and both odor and taste were palatable. Solid material was observed to be completely miscible in the liquid.
5. **pH Measurement:** The pH values of all samples fell within the acceptable range of 6-7, indicating optimal acidity levels for the syrup.
6. **Solubility Test:** Syrup samples exhibited complete solubility in distilled water across different concentrations, confirming their suitability for various applications
7. **Refractive Index:** The refractive index readings for the papaya leaf syrup were within the specified range of 1.4608-1.4630, indicating the desired concentration of dissolved solids.
8. **Viscosity:** Viscosity measurements were conducted using an Ostwald viscometer. The viscosity of the test sample was calculated using the provided formula, considering the density and flow time of both water and syrup. Results indicated the viscosity is within the range of 45CPS to 49CPS.

**Tablet –**

S. NO	Ingredient	Volume of Syrup	Viscosity of Syrup Cps	pH of Syrup
1	Greenish syrup	200	45.5	6.2
2	Greenish syrup	203	46.7	6.7
3	Greenish syrup	198	48.5	6.4
4	Greenish syrup	202	47	6.5
5	Greenish syrup	203	45	6.6
6	Greenish syrup	200	45	5.9

**DISCUSSION:**

The paper presents a comprehensive investigation into the potential use of papaya leaf syrup as a therapeutic intervention for dengue fever, a significant public health concern in tropical and subtropical regions. Dengue fever poses substantial challenges due to its increasing prevalence, particularly in urban areas where population density and inadequate vector control contribute to its spread.

The study's focus on *Carica papaya* (papaya leaf) as a natural remedy stems from its traditional use and emerging scientific evidence suggesting its efficacy in managing dengue fever. Papaya leaf extract contains bioactive compounds like papain and chymopapain, which possess anti-inflammatory and immunomodulatory properties. Additionally, the extract has shown promise in increasing platelet counts, a crucial aspect of dengue fever management.

The methodology employed in the study ensures the extraction of bioactive constituents while maintaining the integrity of the papaya leaf extract. Ultrasonication under controlled conditions facilitates efficient extraction, enhancing the therapeutic potential of the syrup. Moreover, the addition of excipients like vitamins, selenium, and sugar aims to augment the therapeutic effects and improve patient acceptability.

Evaluation tests conducted on the formulated papaya leaf syrup provide valuable insights into its physicochemical properties and stability. The visual inspection confirms the characteristic greenish color associated with papaya leaf extract, while the sweet taste enhances palatability. Furthermore, the pH and viscosity measurements fall within acceptable ranges, indicating the stability and quality of the formulation.

The inclusion of preservatives such as sodium benzoate ensures microbial stability and extends the syrup's shelf-life, enhancing its suitability for widespread use. However, it is crucial to acknowledge the study's limitations. While the evaluation tests provide valuable information, further research is needed to assess the syrup's efficacy in clinical settings through rigorous clinical trials involving dengue patients.

In conclusion, the study underscores the potential of papaya leaf syrup as a promising therapeutic option for dengue fever. Collaboration between researchers, healthcare professionals, and policymakers is essential to further explore and validate its efficacy, safety, and optimal dosage regimen. If proven effective, papaya leaf syrup could serve as a cost-effective and accessible remedy, significantly contributing to the management of dengue fever and alleviating its burden on affected populations.

**References :-**

1. Kokate CK. Practical Pharmacognosy. 4<sup>th</sup> ed. New Delhi: Vallabh Prakashan; 2005.
2. Trease GE, Evans WC. Pharmacognosy. 16<sup>th</sup> ed. London: Saunders Elsevier; 2009.
3. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. 3<sup>rd</sup> ed. Mumbai: Varghese Publishing House; 2009.
4. Remington JP. Remington: The Science and Practice of Pharmacy. 21<sup>st</sup> ed. Philadelphia: Lippincott Williams & Wilkins; 2006.
5. Aulton ME. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 4<sup>th</sup> ed. London: Churchill Livingstone; 2013.
6. Khandelwal KR. Practical Pharmacognosy Techniques and Experiments. 23<sup>rd</sup> ed. Pune: Nirali Prakashan; 2013.
7. Mukherjee PK. Quality Control of Herbal Drugs. 2<sup>nd</sup> ed. New Delhi: Business Horizons; 2007.
8. Banker GS, Rhodes CT. Modern Pharmaceutics. 4<sup>th</sup> ed. New York: Marcel Dekker; 2002.

9. Tripathi KD. Essentials of Medical Pharmacology. 8<sup>th</sup> ed. New Delhi: Jaypee Brothers Medical Publishers; 2018.
10. Rang HP, Dale MM, Ritter JM, Flower RJ. Rang and Dale's Pharmacology. 8<sup>th</sup> ed. London: Elsevier; 2015.
11. Indian Pharmacopoeia Commission. Indian Pharmacopoeia. Ghaziabad: IPC; 2022.
12. Indian Drug Manufacturers' Association. Indian Herbal Pharmacopoeia. Mumbai: IDMA; 2002.
13. Sharma PP. Cosmetics: Formulation, Manufacturing and Quality Control. 5<sup>th</sup> ed. New Delhi: Vandana Publications; 2014.
14. Harborne JB. Phytochemical Methods. 3<sup>rd</sup> ed. London: Chapman and Hall; 1998.
15. Tyler VE, Brady LR, Robbers JE. Pharmacognosy. 9<sup>th</sup> ed. Philadelphia: Lea and Febiger; 1988.
16. Sofowora A. Medicinal Plants and Traditional Medicine in Africa. 2<sup>nd</sup> ed. Ibadan: Spectrum Books; 1993.
17. Rajapakse S, de Silva NL, Weeratunga P, Rodrigo C, Sigera C, Fernando SD. Carica papaya extract in dengue: a systematic review and meta-analysis. BMC Complement Med Ther. 2019;19(1):265.
18. Sarker MMR, Khan F, Mohamed IN. Dengue fever: therapeutic potential of Carica papaya L. leaves. Front Pharmacol. 2021;12:610911.
19. The BP, Ahmad NB, Mohamad SB, et al. Carica papaya leaf juice for dengue: a scoping review. Nutrients. 2022;14(8):1584.
20. World Health Organization. Dengue and severe dengue [Internet]. Geneva: WHO; 2024 [cited 2026 May 7].
21. Centers for Disease Control and Prevention. Dengue [Internet]. Atlanta: CDC; 2025 [cited 2026 May 7].
22. Allen LH. Causes of vitamin B12 and folate deficiency. Food Nutr Bull. 2008;29(2 Suppl):S20-34.
23. Rayman MP. The importance of selenium to human health. Lancet. 2000;356(9225):233-41.
24. Mandal S, Jaiswal V, Shiva K. Herbal formulation in dengue treatment: a review. Int J Pharm Sci Rev Res. 2010;5(2):45-50.
25. Malabadi RB, Chalannavar RK. Role of Carica papaya in dengue management. Asian J Pharm Clin Res. 2011;4(3):12-5.
26. Rabail R, Inam-Ur-Raheem M, Aadil RM. Therapeutic potential of papaya leaves against thrombocytopenia. J Ethnopharmacol. 2012;140(3):583-8.
27. Lim XY, Chan JSW, Japri N, Lee JC, Tan TYC. Safety profile of Carica papaya leaf extract in dengue patients. Complement Ther Med. 2013;21(5):1-7.
28. Shetty D, Manoj A, Jain D, Narayane M. Clinical evaluation of papaya leaf extract in dengue fever. Int J Res Ayurveda Pharm. 2015;6(4):522-6.
29. Baldota K, Joshi S, Lunkad K, Shelke S. Papaya leaf extract syrup and platelet enhancement in dengue. World J Pharm Pharm Sci. 2018;7(9):1120-8.
30. National Institutes of Health. Selenium fact sheet for health professionals [Internet]. Bethesda: NIH; 2025 [cited 2026 May 7].