

# An Overview on Formulation and Evaluation of Disodium Hydrogen Citrate Syrup

Tirth Kaushik kumar Patel, Akshitaben Vijaykumar Patel,  
HirMaheshkumar Patel, Nikita Manilal Patel,  
Parthiben Navneetbhai Patel

Guide :- Mrs. Varsha V Chaudhary  
Shri Sarvajani Pharmacy College, Mehsana, Gujarat

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## ABSTRACT:

**Objective:** The objective of project is to review in detail about disodium hydrogen citrate API, disodium hydrogen citrate syrup, various method of preparation, equipments and evaluation parameters.

**Aim:** An Overview on Formulation and Evaluation of Disodium Hydrogen Citrate Syrup

**Conclusion:** Welable Healthcare helped us to imbibe the information and detail about disodium hydrogen citrate syrup. we were given all the required knowledge on the formulation and evaluation of disodium hydrogen citrate syrup it is a urinary alkanizer which is used to treat urinary tract infection, gout, painful urination and kidney stones. If overdose one can have side effect that include tiredness, vomiting, nausea and others. Thus the syrup has been prepared using various equipments like mixers, stirrer and other filling and sealing machine and has been evaluated for parameter like physical stability, pH, solubility, assay, refractive index etc.

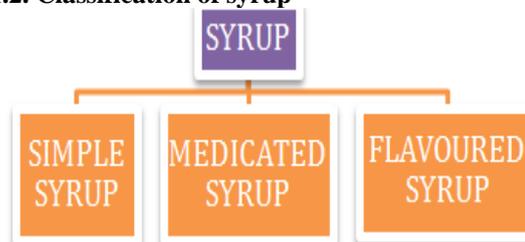
**KEYWORDS:** Disodium Hydrogen Citrate, Colloidal Mill, Stirrer, Bottle Filling Machine, Bottle Sealing Machine, Automatic Labelling Machine.

## I. INTRODUCTION

### 1.1. Syrup<sup>[1]</sup>

Syrup is a concentrated solution of sugar in water or other aqueous liquid. syrup is a type of medication that is formulated in a liquid form for oral administration. It typically contains a concentrated solution of sugar, water, active ingredients that are intended to treat a specific medicinal condition. syrups are generally easy to swallow and are commonly used for children or individuals who have difficulty swallowing pills or capsules. They are available in various flavours and colors to make them more appealing to taste buds to patients.

### 1.2. Classification of syrup<sup>[1]</sup>



Classification of Syrup

#### A. Simple Syrup :

It is a concentrated sucrose solution in purified water.

E.g. Simple Syrup I.P.

#### Rx

Sucrose	66.7 g
Purified Water	100 ml
Make: Syrup	Send : 60 ml

#### B. Medicated Syrup :

When preparation contains added medicinal substances.

E.g. Codeine phosphate syrup, Ginger syrup, Ferrous sulphate Syrup, Ephedrine sulphate syrup, Chlorpheniraminemelate syrup

#### Rx

Codeine phosphate	5 g
Chloroform spirit	25 ml
Purified Water	50 ml
Syrup....q.s....	1000 ml
Make : Syrup	Send 60 ml

Directions : one tablespoonful to be taken, two times a day.

#### C. Flavoured syrup :

Non-medicated syrup containing aromatic or flavoured ingredients.

E.g. Orange Syrup

**Rx**

Orange Syrup                    6 ml  
Syrup q...s....                100 ml  
Make : Syrup                    Send 60 ml

**1.3. Advantages of Syrup<sup>[2]</sup>**

- Syrup is having easiest route of administration.
- Syrups are simple & fast to formulate.
- Syrups are economic & safe to Patient.
- Syrups are used for any age of patient
- No nursing is required, which means the patient can take it with no Help.
- Syrup are easy to take so it is easy to formulate in syrup
- The liquid dosage form is expected for certain types of products like cough medicines.
- Syrup are easy to swallow, making them a good choice for Individuals who have difficulty swallowing pills or capsules.
- Many syrups are formulated with pleasant flavors and colors to make them more appealing to children and adults.
- Syrups are usually absorbed more quickly by the body than other dosage form, which can result in faster onset of action and faster relief of symptoms.
- Syrup can be formulated to contain a wide range of drugs, making them a versatile dosage form for variety of medicinal conditions.
- Syrup prevent decomposition of many vegetable drugs.

**1.4. Disadvantages of Syrup<sup>[2]</sup>**

- Not convenient for patient with GIT disorder such as diarrhea, constipation.
- Syrup are bulky, so difficult to transport and store.
- When expose to direct sunlight it may undergo hydrolysis
- Can't avoid first pass metabolism.
- Not suitable in emergency and for unconscious patients.
- Syrups have shorter shelf life compared to tablets or capsules and may need to discarded after a certain period of time.
- Some sugar contain a high concentration of sugar, which may not be suitable for individuals with diabetes or those who need to limit their sugar intake.
- Syrups can be easily overused or misused, which can lead to adverse effects or even overdose.

- Some syrups may contains alcohol, which may not be suitable for children or individuals who need to avoid alcohol.

**1.5. Ideal Properties of Syrup<sup>[3]</sup>**

- Physiologically inert
- Physiologically stable
- Do not impart any undesired taste, colour & odour
- Non-toxic
- Non-irritant
- Non-sensitizing
- Effective in low concentrations
- Free from microorganisms
- Not interfere with bioavailability of the drug
- Mask bitter or unpleasant taste of drugs.

E.g. Acacia syrup USP, Raspberry

Syrup USP

- Syrups with sucrose concentration of 65% w/w is bacteriostatic.
- When syrup or sucrose is overheated, it caramelizes.
- High sugar content increase stability of product.
- High sugar content increase viscosity and decrease incompatibility.

**1.6. Methods of Preparation of Syrup<sup>[4]</sup>**

Syrups are Prepared by 4 Methods :

1. Solution with Heat
2. Solution by Agitation
3. Addition of Sucrose to a Liquid Medication
4. Percolation

**1. Solution with Heat**

This method is suitable, if the constituents are not volatile or not degraded by heat. Purified Water is heated to 80-85 °C, and then removed from its heat source. Weight desired amount of sucrose is added with vigorous agitation. Then, other required heat stable components are added to the hot syrup. The mixture is allowed to cool, and its volume is adjusted to proper level by the addition of purified water. In instances in which heat-labile agents or volatile substance, such as flavours and alcohol, are added, they are incorporated in to the syrup after cooling to room temperature.

E.g. Syrup IP, Acacia Syrup NF, Cocoa Syrup NF

**2. Solution by Agitation**

In this method heating is not involved so this method is used for the heat laibleand volatile substances. In this method Sucrose and other

ingredients are dissolved in purified water through Agitation. {without heat}  
E.g. Sulphate syrup

**3. Addition of Sucrose to a liquid medication or Flavoured liquid**

This method is often used with fluid extract or tinctures. Fluid extract or tincture are added to a syrup. Addition of these may cause precipitation of alcohol soluble material due to dilution.  
E.g. aromatic eridictyon syrup

**4. Percolation {cold process}**

In this method, either purified water or medicinal component is passed slowly through bed of crystalline sucrose, thus dissolving it and forming a syrup. Sucrose is placed in suitable percolator. Purified water (with medicament) is allowed to slowly pass through sucrose. Final Volume is adjusted by purified water.

**1.7. Formulation of Syrups<sup>[5]</sup>**

Different excipients used in syrup are like

1)	Vehicles	Purified water, Glycerin
2)	Chemical stabilizer	a) Poly-hydric alcohols Glycerin Sorbitol Propylene glycol (prevent the crystallization of sucrose)  b) Surfactant (e.g. Tweens) used to dissolve certain ingredients in the syrup, to make clear solution.
3)	Colouring agents	a) Amaranth solution b) compound tartrazine.
4)	Flavouring agents	a) Tinctures: Tincture of Lemon Tincture of Ginger b) Fruit Juices: Raspberry juice Wild cherry juice c) Essences: Vanilla flavor, Orange flavour
5)	Preservatives	a) Benzoic acid b) Sodium benzoate c) Methyl paraben

**Formulations of Syrup**

**1.8. Preservatives of Syrup<sup>[6]</sup>**

Syrups are self-preservatives. Because they contain concentration solution of sucrose. Generally, Benzoic acid, Sodium benzoate, methyl paraben can be used as a preservative.

**1.9. Storage of Syrup<sup>[6]</sup>**

Stored in a well dried, screw cap fitted, and well-stoppered bottle in a cool dark place. Store at a temperature not exceeding 25 °C .



**Syrup Bottle**

**1.10. Dispensing of Syrup<sup>[7]</sup>**

Simple Flavoured Syrups are dispensed in bulk volumes, but medicated syrups should be dispensed in small volumes. Syrups should be dispensed in well dried, completely filled and well

stoppered bottles because, moisture present in wet bottles and atmospheric moisture causes fermentation of the sucrose. Therefore they should be dispensed in narrow mouthed, amber coloured (light resistant) bottles, fitted with white, poly propylene moulded or black thermosetting plastic screw cap bottle.

### 1.11. Label of Syrup<sup>[7]</sup>

The label must bear all necessary requirements of liquid dosage forms. In addition it should contain auxiliary label like “Store at fairly cool temperature, not exceeding 25 °C in dark place”.



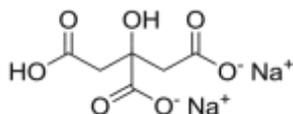
Label of Syrup

## II. INTRODUCTION OF DISODIUM HYDROGEN CITRATE<sup>[8-16]</sup>

### 2.1 Introduction

**Name:** Disodium Hydrogen Citrate

**Structure:**



**Appearance:** White Crystalline Powder

**Colour:** White Crystalline Powder

**Purity:** 98%

**Odour:** Odourless

**Taste:** Unpleasant

**Molecular Formula:** C<sub>6</sub>H<sub>6</sub>Na<sub>2</sub>O<sub>7</sub>

**Molecular Weight:** 236.09 g/mol

**Category:** Urinary Alaklinizer

**BCS Class:** Class 1

**λ max:** 232 nm

**PKa:** 3.13-4.76 at 25<sup>0</sup>c

**Log P:** 1.3

**Half-life:** 4-6 Hrs

**Shelf Life:** 24 Months

**Route of Elimination:** Renal Route

**pH:** 4.9 to 5.2

**Melting Point:** 149<sup>0</sup>C

**Pharmacokinetics:** Disodium hydrogen citrate is metabolized after absorption to sodium bicarbonate. Oxidation is virtually complete, less than 5% of citrate is excreted unchanged in the urine.

**Solubility:** Freely Soluble in Water and practically insoluble in Methanol. 269 g/litre at 20<sup>0</sup>C.

**Pharmacodynamics:** Disodium hydrogen citrate, also known as sodium acid citrate, is a urinary alkalinizer. It renders the urine less acidic and promotes a mild diuresis.

**Mechanism of Action:** Disodium Hydrogen Citrate works by decreasing the acidity of urine and helps the kidneys to get rid of uric acid, thereby preventing gout and kidney stones. It prevent certain kinds of bacteria from sticking to the walls of urinary tract and prevents infections.

**Dose:** Adults:30 ml (two teaspoonfuls) 4 times daily. Children 6 to 12 years:10 or 15 ml (two or three teaspoonfuls). To be taken in water or milk. Adults may take 3 to 4 times daily.

**Absorption:** It is absorbed by oral route of administration.

**Metabolism:** It is metabolized in liver.

**Contraindications:** Disodium Hydrogen Citrate is contraindicated in patients with severe renal impairment and associated oliguria, azotemia or anuria, untreated Addison’s disease, acute dehydration, heat cramps, and severe myocardial damage. In addition, sodium salts are contraindicated in patients on sodium restricted diet.

**Special Warnings and Special Precautions**

**For Use:**Disodium Hydrogen Citrate should be used with caution in patients with edematous sodium retaining states, congestive heart failure, hypertension, pulmonary or peripheral edema or toxemia of pregnancy. Serum electrolytes, particularly serum bicarbonate levels, should be monitored in patients with renal disease. Caution is advised in patients with low urinary output or reduced glomerular filtration rates. Precaution is also advised while using blood products containing citrate in patients with acute liver failure.

#### ☐ **Interactions With Other Medicaments and Other Form of Interaction**

Concurrent administration of aluminium antacids and citrate salts is not recommended, especially in patients with renal insufficiency. Citrate salts taken orally can enhance absorption of aluminium from the gastrointestinal tract. This may lead to increased serum concentration of aluminium and encephalopathy especially in the elderly. It is recommended that if concurrent use cannot be avoided, patients should be monitored for possible acute aluminium toxicity (e.g. encephalopathy, seizures, coma) and doses should be adjusted accordingly. Urinary alkalinizers including disodium hydrogen citrate may increase the excretion and decrease the serum levels of chlorpropamide, lithium, methotrexate, methenamine, salicylates and tetracyclines. This may lead to a decrease in the pharmacologic effects of these drugs upon concomitant administration. Urinary alkalinizers have also been reported to decrease the excretion and increase the serum levels of drugs such as mecamylamine, flecainide, quinidine and sympathomimetics, possibly increasing their pharmacologic effects.

#### ☐ **Pregnancy and Lactation**

Safety of Disodium Hydrogen Citrate for use in human pregnancy and lactation has not been established. Use in pregnancy or in nursing mothers should be considered only when the possible benefits outweigh the potential risks.

#### ☐ **Undesirable Side Effects**

Excessive administration of bicarbonate or bicarbonate forming compounds may lead to the following : In patients with acute hepatic failure, impaired citrate utilization and clearance can result in hypocalcemia. Hypokalemia and metabolic alkalosis especially in patients with impaired renal function, especially in the presence of hypocalcemia or when excessive doses are given. Symptoms include mood changes, tiredness, shortness of breath, muscle weakness, and irregular heartbeat. Excessive doses of sodium salts may also lead to sodium overload and hyperosmolarity. Large doses of oral citrate salts may result in gastrointestinal events such as diarrhoea, nausea and vomiting, and a laxative effect. Diluting with large amounts of water and administration after meals can minimize these effects.

#### ☐ **Overdose**

Overdosage with sodium salts may cause serious electrolyte disturbances. Ingestion of large amounts of disodium hydrogen citrate irritates the gastrointestinal mucosa, and may result in diarrhoea, nausea, vomiting, hypernoia (excessive mental activity), edema and convulsions. Treatment includes usual supportive measures such as providing an adequate airway and ventilation and maintaining vascular volume and tissue perfusion. Magnesium sulphate may be given as a cathartic.

#### ☐ **Therapeutic Indications**

To render the urine alkaline in conditions such as pyelitis, cystitis, urethritis, urolithiasis and during treatment of urinary tract infections with antibiotics whose action is enhanced by an alkaline pH such as sulphonamides and fluoroquinolones; or to overcome the tendency to acute or chronic metabolic acidosis in acute infections and dehydration.

#### ☐ **Drug Interactions**

- 1) **Drug-Drug Interactions:** Disodium Hydrogen Citrate may interact with diuretics (furosemide), antibiotics (tetracycline), anti-arrhythmic (quinidine), adrenergic agonist (ephedrine), decongestant (pseudoephedrine), barbiturates, salicylates, and corticosteroids.
- 2) **Drug-Food Interactions:** No interactions found.
- 3) **Drug-Disease Interactions:** Inform your doctor if you have hyperkalaemia (high levels of potassium), hypocalcaemia (low blood calcium levels), high blood pressure, edema, increased alkalinity in the blood, urinary tract infection, or kidney dysfunction.

#### ☐ **Uses of Disodium Hydrogen Citrate<sup>[17]</sup>**

##### 1) **Kidney stones**

Kidney stones are a small, hard deposit of minerals and acid salts that stick together in concentrated urine. They can be painful when passing through the urinary tract, but usually do not cause permanent damage. The most common symptom is severe pain usually in the side of your abdomen, which is often associated with nausea. Disodium Hydrogen Citrate is used for the treatment of uric acid and calcium oxalate kidney stones. It is also used to dissolve kidney stones in people with renal tubular acidosis, a condition that occurs when the kidneys fail to remove acids into the urine.

## 2) Urinary tract infection

Urinary tract infections are more common in women. These infections are observed in any part of the urinary system (kidneys, bladder or urethra). A bladder infection may cause pelvic pain, increased urge to urinate, pain with urination and blood in the urine. A kidney infection may cause back pain, nausea, vomiting and fever. Disodium Hydrogen Citrate makes the urine more alkaline and thereby helps to prevent bacterial growth and relieves the discomfort due to urinary tract infections.

## 3) Painful urination

Painful urination is a condition in which there is discomfort while urinating. The most common cause of painful urination is swelling of the lower urinary tract that is caused by bacterial infections. Disodium Hydrogen Citrate helps to relieve painful or difficult urination by preventing bacterial growth.

## 4) Gout

Gout is a form of arthritis characterised by severe pain, redness and tenderness in joints. Pain and swelling occur when too much uric acid crystallises and deposits in your joints, most often in the big toe. Disodium Hydrogen Citrate reduces the levels of uric acid in your blood, prevents the formation of crystals at joints, thus it treats gout.

## ☐ Benefits of Disodium Hydrogen Citrate<sup>[18]</sup>

### 1) Effective for Kidney stones

Minerals and acid salts in concentrated urine can crystallize into what are known as kidney stones. While going through the urinary tract, they can be uncomfortable, they often do not produce any lasting harm. Severe pain, most commonly on one side of the abdomen, frequently accompanied by nausea, is the hallmark symptom. Those who suffer from kidney stones caused by uric acid or calcium oxalate can benefit from using Disodium Hydrogen Citrate Sugar Free Liquid. Renal tubular acidosis is a condition where the kidneys are unable to excrete acids into the urine this medication is used to dissolve kidney stones in patients with this disease. To increase the urine's alkalinity, many people utilize disodium hydrogen citrate, an acidic salt of citric acid. The urinary tract infection and kidney stone remedies of disodium hydrogen citrate syrup are widely available.

## 2) Removing Urinary Tract infections

Women are more likely to suffer from urinary tract infections than males. Any portion of the urinary system is susceptible to these infections (kidneys, bladder or urethra). There may be blood in the urine, an increased need to urinate, discomfort when urinating, and pelvic pain if there is a bladder infection. Pain in the back, nausea, vomiting, and a high temperature could all be symptoms of a kidney infection. By increasing the urine's alkalinity, Citrate syrup aids in the prevention of urinary tract infections and the associated discomfort. For urinary tract infections, try using Citrate Syrup from disodium hydrogen citrate syrup. This medication works by neutralizing the acidity of the urine, which relieves urinary tract infection symptoms. E. coli is a common cause of urinary tract infections, which can occur at any time but are especially risky for pregnant women. Both the mother and the unborn child are at risk for complications if this is not handled. The recommended dosage of disodium hydrogen citrate is one tablet taken after a meal with a full glass of water. The duration of disodium hydrogen citrate treatment is determined by your doctor and is condition-specific.

## 3) Use in Painful Urination

In cases of painful urine, voiding causes pain or discomfort. Inflammation of the lower urinary tract due to bacterial infections is the most prevalent cause of painful urination. By inhibiting the growth of bacteria, citrate disodium hydrate syrup eases the discomfort of urination in people who find it difficult or uncomfortable. The urine's acidity is reduced and its pH is raised thanks to this. An additional use for Citrate Syrup is in the treatment of urinary tract infections. Use this drug exactly as directed. Do not take more of this or take it more regularly without first consulting your doctor. The best results from this drug should be achieved by using it consistently. Taking it at the same times every day will help you remember to do so.

## 4) Gouts

Those who suffer from gout have excruciating pain, swelling, and soreness in their joints. Uric acid crystallizes and deposits in joints, most commonly the big toe, causing pain and swelling. Gout can be treated with Citrate Syrup because it lowers uric acid levels in the blood and stops crystals from forming in the joints. Drugs containing citric acid or citrate salts (which contain

sodium and potassium) are classified as urinary alkalizers. Your doctor's product recommendation may be affected by the amount of potassium and sodium you can take, as these nutrients are contraindicated in certain medical situations.

#### 5) **Treats Renal Tubular Acidosis**

When the kidneys fail to excrete uric acid from the body, a condition known as renal tubular acidosis (RTA) develops. This leads to acidosis, or an abnormally high concentration of blood acids. While a slight amount of acid in the blood is typical, excessive levels can disrupt several body processes. Generally speaking, RTAs can be divided into three categories. Renal tubular acidosis and kidney stones are two of the conditions for which disodium hydrogen citrate syrup is recommended. It's also useful for soothing the pain of a burning bladder. Concentrated urine can form small, hard deposits called kidney stones, which are composed of minerals and acid salts like calcium and phosphate. In renal tubular acidosis, the kidneys are unable to filter acids out of the blood into the urine, leading to a too acidic blood pH. Magnesium citrate, potassium citrate, and pyridoxine are the three medications that make up disodium hydrogen citrate syrup. Taking a daily dose of disodium hydrogen citrate syrup has been shown to reduce the formation, development, and accumulation of stone-forming ions in the urinary tract by increasing urine pH, potassium, magnesium, and citric acid.

#### 6) **An Antioxidant**

Both as a standalone antioxidant and to boost the effectiveness of other antioxidants, it finds widespread application in the food industry. Preservative  $\text{Na}_2\text{H}(\text{C}_3\text{H}_5\text{O}(\text{COO})_3)$  is the chemical formula for disodium citrate, also known as disodium hydrogen citrate, which is the sodium acid salt of citric acid (sodium citrate). It is a citrate salt, one of three types. Disodium hydrogen citrate syrup uses can also be used as a sequestrant and acidity regulator. Jam, confectionery, gelatin, fizzy drinks, milk powder, ice cream, wine, and processed cheeses are examples of products that fall into this category. It has anti-aging properties and boosts the effectiveness of other antioxidants when used in meals. It can also be used as a sequestrant and acidity regulator.

#### 7) **Best for Gastric Problem**

Due to the potential for colonic perforation, Disodium Hydrogen Citrate should be taken with extreme caution in patients with stomach issues

(hole in the large intestine). As you take this medication, your clinical status will need to be regularly checked. Many conditions, including urinary tract infection symptoms, gas, bloating, acid reflux, constipation, and a number of others, can be alleviated with the use of this medicine. The syrup has dual purposes as an acid neutralizer and a buffer. Because of the potential for adverse effects on health, it is recommended that you take it only after consulting with a medical professional. UTI symptoms can be alleviated and even cured when urine has an alkaline pH, which inhibits the growth of bacteria and other microorganisms. Disodium hydrogen citrate syrup side effects increase the solubility of cysteine in urine and converts uric acid to urate ions, both of which inhibit the development of kidney stones. You have got the idea about the benefits of using Disodium hydrogen citrate syrup. Now you can add this in your daily life. Depending on your situation, your doctor may recommend that you take disodium hydrogen citrate syrup for an extended period of time. Common adverse reactions include gastrointestinal distress, diarrhea, nausea, and vomiting. Most of these unwanted symptoms are temporary and will go away without any intervention. It is recommended, however, that you consult a medical professional if any of these side effects continue or intensify.

#### ❑ **Expert Advice For Disodium Hydrogen Citrate<sup>[19]</sup>**

- 1) Doctors recommend Disodium Hydrogen Citrate to treat gout and kidney stone.
- 2) It is recommended that this medication is taken after meals, along with a full glass of water, to avoid stomach upset.
- 3) If you want to maximise the benefits of this medication, keep taking it as recommended by your doctor.
- 4) When you take this medication, you might have stomach pain. Consult your doctor if it continues to affect you.
- 5) If you're taking this medication, you should avoid alcoholic beverages because they can cause you to be drowsy and have stomach problems.
- 6) You should notify your doctor if you are pregnant, planning to become pregnant, or already breastfeeding.
- 7) This medication may cause Diarrhoea as a side effect. The addition of probiotics to this medication regimen may be beneficial. You should consult a doctor if you experience stomach pain or observe blood in your faeces.

8) Do not use the remaining medication to treat any future infections. Before taking any medication, it is important to consult your doctor.

☐ **Disodium Hydrogen Citrate<sup>[20]</sup>**

Disodium Hydrogen Citrate is a medicine that contains Disodium hydrogen citrate. It is mainly used for the treatment of urinary tract infections, painful or difficult urination, kidney stones, urinary acidosis and gout. Disodium Hydrogen Citrate works by removing excess uric acid from the blood through urine. Disodium Hydrogen Citrate shows some side effects like diarrhoea, nausea, stomach pain, vomiting, increased urination and tiredness. If any of these symptoms do not resolve with time or worsen, consult your doctor for a dose adjustment or alternative treatment. The most common side effect of Disodium Hydrogen Citrate is stomach pain, inform your doctor if it stays for a long duration. Disodium Hydrogen Citrate is usually taken after a meal with plenty of water or as prescribed by your doctor. The effect of this medicine can be seen quickly. Disodium Hydrogen Citrate is not recommended for use in pregnant and breastfeeding women as there is not enough safety and efficacy

data available. It is also not recommended in people with severe kidney impairment.

☐ **Disodium Hydrogen Citrate Syrup<sup>[21]</sup>**

Disodium Hydrogen Citrate Syrup is a urinary alkaliser which helps in the treatment of renal tubular acidosis. It is a condition in which the stones are formed in the kidney which disturbs the action of heroin hence causing the blood formation. The syrup reduces the formation of the stones. Kidney stones might be small but are the hard deposits of calcium, phosphorus and other minerals that combine together in the urine thereby causing trouble. Disodium Hydrogen Citrate Syrup is only composed to provide relief from the issues of the kidney stones. The contents of the syrup are Disodium Hydrogen Citrate which specializes in increasing the pH levels of urine thereby making it less acidic. It also helps get rid of the excessive uric acid which further prevents the gout and other types of kidney stones. The usage of the syrup has to be based on the recommendation of the clinician. One should follow the precaution while undergoing the procedure of the medication as it won't be feasible to the desired amount of dose or discontinuing the medication without the complication.

**2.2 Marketed Products**

Brand Name	Composition	Company name
Alkarate (1.37g/5ml)	Disodium Hydrogen Citrate BP 1.37g	Macleods Pharmaceuticals Ltd.
Alkasol (1.4g/5mL)	Disodium Hydrogen Citrate BP 1.4g	StadmedPvt Ltd.
Citalika (1.53g/5mL)	Disodium Hydrogen Citrate BP 1.53g	Pfizer Limited
Oricital (1.37g/5mL)	Disodium Hydrogen Citrate BP 1.37g	TTK Healthcare Ltd.
Cital (1.37g/5mL)	Disodium Hydrogen Citrate BP 1.37g	Indoco Remedies Ltd.

**Marketed Products**



**Alkarate Syrup**



**Alkasol Syrup**



Citralka Syrup



Oricitral Syrup



Cital Syrup

### III. REVIEW OF LITERATURE

VM Waghulkar<sup>[22]</sup> et.al reviewed on “Formulation and Evaluation of Diuretic Herbal Liquid Syrup from Hemidesmusindicus.” Plant medicines are traditionally used for the treatment of some renal diseases and also have been reported to show significant diuretic activity. In the present study powder of Hemidesmusindicus root was extracted with distilled water to get aqueous extract. During development of syrup, several combinations of sucrose, sorbitol, glycerin, methyl paraben,

propyl paraben and distilled water were tried. The formulation was checked for its stability and consistency. Depending upon the results of evaluation, the formula had been finalized for liquid syrup preparation. Among different compositions, good consistency was obtained using sucrose, sorbitol, glycerin, methyl paraben, propyl paraben in the ratio 30:10:2.2:0.07:0.03. Also, better acceptability was obtained by incorporation of mint flavor (0.2%). The specific gravity of syrup was found to be 1.06068 g/ml. The refractive index and viscosity was found to be 1.339 and 2.4216cp. The pH was found to be 5.62. The single drug preparation can be used for diuretic activity for elderly patients since oral route for single drug preparation is one of the simplest and claimed to be safest.

IK Simpson<sup>[23]</sup> et.al reviewed on “Pharmaceutical Applications of Glucose Syrup.” Pharmaceutical oral solutions are preparations in which the active ingredients are dissolved in suitable liquid vehicles such as syrups. This study sought to determine the potential of glucose syrup produced from high quality cassava flour (HQCF) as a vehicle or sweetener in the preparation of paracetamol syrup and simple linctus. Four formulations (two paracetamol syrups and two simple linctus formulations) were prepared using glucose syrup from HQCF as vehicle or sweetener while two controls were prepared for each group using sucrose syrup as vehicle or sweetener. Two brands of paracetamol syrup and simple linctus were purchased from retail pharmacies to serve as standards. Physical and organoleptic parameters such as pH, taste and color, microbial load, and drug content of all formulations were determined. All formulations passed the microbial load and drug content tests as specified by the British Pharmacopoeia. The paracetamol syrups were all sweet with characteristic bitter aftertastes except formulation which was sweetened with sucralose. All the simple linctus formulations were sweet except (sweetened with sucralose) which was very sweet. The taste masking capacity of the glucose syrup produced from HQCF matched that of the sucrose syrup in the products formulated. Therefore, glucose syrup from HQCF could be a suitable alternative to sucrose syrup as a vehicle or sweetener in oral liquid formulations and can ultimately reduce the cost of these oral liquid formulations.

**LA Karpenko**<sup>[24]</sup> et.al reviewed on “Studying of Syrup with Acorus Calamus Rhizome Extract.” This article includes the description of obtaining of Acorus Calamus rhizome extract by the percolation method and the formulation of this extract in the syrup as a pharmaceutical dosage form. The percolation rate was 0.8 ml/min. The extraction of raw materials fraction with a particles size 0.25-3 mm has been investigated. It was found that the using of 50% ethanol as the extractant maximizes raw material exhaustion at a ratio of raw material: extractant 1:6. The results of the syrup development with the Acorus Calamus extract have been shown that the optimal base was sugar syrup. Such physical-chemical data as description, density, identification of the syrup have been determined.

**PS Bhandare**<sup>[25]</sup> et.al reviewed on “Dry Syrups For Pediatrics.” Suspensions may be defined as preparations containing finely divided drug particles (the suspensoid) distributed somewhat uniformly throughout a vehicle with or without stabilizers and other additives in which drug exhibits a minimum degree of solubility hence conventional oral suspension can be administered immediately (ready to use form) and not requiring reconstitution at the time of dispensing are simply designated as Oral Suspension.

There is an important category of suspension that are available as dry powders intended for suspension in liquid vehicles. These are dry mixtures containing the drug and suitable suspending and dispersing agents to be diluted and agitated with a specific quantity of vehicle, most often purified water. Drugs that are instable if maintained for extended periods in the presence of aqueous vehicle (eg. many antibiotic drugs) are frequently supplied as dry powder mixtures for reconstitution at the time of dispensing. This type of preparation is designated in the USP by a title “for Oral Suspension”. The reconstituted system is the formulation of choice when the drug stability is a major concern. After reconstitution, these systems have a short but acceptable life if stored at refrigerator temperatures. Reconstitutable oral systems show the adequate chemical stability of the drug during shelf life, avoids the physical stability problems related to solubility, pH and incompatibilities with other ingredients and also reduce the weight of the final product because the aqueous vehicle is absent and consequently the transportation expenses may be reduced.

Dry syrup form of the drug is also useful in case of bioavailability as it has high bioavailability

rather than tablets and capsules as it disintegrates in water outside of the oral cavity and directly the suspension is gone through the gastrointestinal tract. So the suspension easily absorbs in the GIT.

A number of commercial and official preparations are available as dry powder mixtures. The present review gives an account of the excipients used, methods of preparation of dry syrups along with their evaluations, their packaging, examples of research articles, few marketed preparations.

**AG Nerkar**<sup>[26]</sup> et.al reviewed on “Formulation and evaluation of herbal syrup of Indian mulberry (Noni).” *Morinda citrifolia* is a fruit-bearing tree in the coffee belonging to the family, Rubiaceae. Its native range extends through Southeast Asia and Australasia, and become spread through the Pacific by Polynesian sailors. The species is now cultivated all through the tropics and widely naturalized. Among a few one hundred names for the fruit throughout special areas different areas are the more common English names are morinda, Indian mulberry, noni, beach mulberry, and cheese fruit. Indian Mulberry has various pharmacological properties such as anticancer, antidiabetic, antistress, antioxidant, anxiolytic, immunomodulatory, cholesterol lowering, lipid lowering, nephroprotective, hepatoprotective and anti-cancer plant which help in maintaining body strength and curing cancer causing germ cells by eradicating them. The syrup is most used and a popular dosage form. It has many applications and many of the treatments are based on the usage of syrup for patients’ compliance at every age. The herbal syrup was formulated using extract of Indian Mulberry or Noni as the main ingredient along with invert sugar base. Indian Mulberry or Noni has been used in the treatment of cancer because of many stresses condition and other oxidative reaction in body the free radical is generated by using these, syrup the condition is overcome. Formulation at laboratory scale was done of herbal syrup and evaluated for number of parameters such as pH, viscosity, density, stability testing during evaluation formulation found to be stable and ready formulas viz. F1, F2, F3 and F4 were prepared with variation in the amount of ingredients such as alcohol, sugar and a final amount of syrup. All formulations were prepared according to parameters such as density, specific gravity, pH, organoleptic properties. Results show that Herbal Syrup Formula 4 (F4) is more stable than other forms.

**MV Pavane**<sup>[27]</sup> et.al reviewed on “Formulation, Development And Evaluation Of Oral Reconstitutable Dry Syrup.” Taste masking and development of palatable dosage forms of bitter drugs constitutes the objective of many a research project in the field of pharmaceutical technology. Taste is an important factor in the development of dosage form. The problem of bitter and obnoxious taste of drug in pediatric patient can create a bad psychological effect on mind. The purpose of this research was to mask the intensely bitter taste of Ciprofloxacin is a broad spectrum antibiotic. It is extremely bitter taste resulting in poor patient’s compliance. The aim of present work was to prepare drug resin complex (DRC) using ion exchange resin (Indion 234) for taste masking and formulate oral reconstitutable dry syrup of DRC. DRC was evaluated for effect of variables like drug resin ratio, pH, temperature, soaking time of resin and stirring time reconstitutable dry syrup was prepared by using xanthan gum and microcrystalline cellulose as suspending agent formulated reconstitutable dry syrup was evaluated for before reconstitution parameters like flow properties, particle size and drug content and after reconstitution parameter like sedimentation rate redispersibility particle size, viscosity, pH and drug content. Formulated ciprofloxacin reconstitutable dry syrup has acceptable sedimentation properties. In evaluating period of 14 days no significant change was observed in pH, viscosity, particle size and drug content. From the results it concluded that effective taste masking of ciprofloxacin was achieved using indion 234 and successfully evaluated in reconstitutable dry syrup.

**AK Ghosh**<sup>[28]</sup> et.al reviewed on “Effect Of Alkalinisation Of Urine Of The Efficacy Of Levofloxacin in Urinary Tract Infection.” Physicians commonly prescribe an alkaliniser along with fluoroquinolones (FQ) in treatment of UTI. The combined effect of these two drugs in our body is unknown. So, we conducted two studies with two different FQ (Pefloxacin and Levofloxacin) with an alkali solution in two separate medical colleges at Kolkata to find out their efficacy in presence of alkali in the treatment of UTI. Materials and methods In our 1<sup>st</sup> study at SSKM Hospital Kolkata, patients with uncomplicated lower UTI were prescribed Pefloxacin 400 mg (Group-A) and Pefloxacin 400 mg + disodium hydrogen citrate (Group-B). In our 2<sup>nd</sup> study at RG Kar Medical college, Kolkata patients with uncomplicated lower UTI were prescribed Levofloxacin 250 mg (Group

A) and Levofloxacin 250 mg + disodium hydrogen citrate (Group-B).

**JG Selwyn**<sup>[29]</sup> et.al reviewed on “Inhibition of Rh Agglutination by Disodium Hydrogen Citrate.” It was found that Rh-positive (that is D-positive) red blood cells suspended in an anti-coagulant preservative solution (2% disodium hydrogen citrate or 'acid citra' 2.5% dextrose) were not agglutinated by anti-D) grouping sera. Investigating this inhibition, 2% D-positive cell suspensions were titrated with a strong anti-D) serum. The titre of cells in isotonic (0.85 %) saline and in isotonic (5%) dextrose was 320, but in isotonic mixtures of acid citrate and sodium chloride or dextrose the titre was reduced according to the acid citrate concentration.

#### IV. AIM AND OBJECTIVE

##### 4.1 Aim of Present Work

An Overview on Formulation and Evaluation of Disodium Hydrogen Citrate Syrup

##### 4.2 Objective

The objective of project is to review in detail about disodium hydrogen citrate API, disodium hydrogen citrate syrup, various method of preparation, equipments and evaluation parameters.

#### V. EXPERIMENTAL WORK

##### 5.1 Syrup

This drug containing Syrup Disodium Hydrogen Citrate is a given a brand name of Alkawel Syrup.

##### 5.2 Methods of Preparation of Alkawel Syrup

##### A. Preparation of Disodium Hydrogen Citrate Syrup

- ☐ Take required amount of demineralized water in SS tank add the preservative and stir until it dissolved completely. Add required amount of sucrose to the tank stir well until it gets dissolved completely.
- ☐ Take Disodium Hydrogen Citrate dissolve in hot 50-60 °C Demineralized water with constant stirring for 3 hrs.
- ☐ Take Sodium benzoate, Sodium Methyl Paraben, Sodium Propyl Paraben and dissolve it in demineralized water main tank.
- ☐ Add to Sorbitol 70% solution in main tank during stirring.
- ☐ Take Aspartame in hot 80 °C demineralized water then transfer to main tank by continuous stirring.
- ☐ Then Add tartrazine supracolour and pineapple essence.

### 5.3 Formulation of Disodium Hydrogen Citrate Syrup

Sr No.	Ingredients	Quantity	Specification	Usage
1.	Disodium Hydrogen Citrate	1.1284 gm	BP	API
2.	Sodium Benzoate	0.12 gm	IP	Preservative
3.	Sodium Methyl Paraben	0.09 gm	IP	Preservative
4.	Sodium Propyl Paraben	0.05 gm	IP	Preservative
5.	Aspartame	0.10 gm	IP	Sweetner
6.	Sorbitol 70% Solution	0.04 gm	IP	Artificial Sweetner
7.	Tartrazine Supracolour	q.s.	IH	Colouring Agents
8.	Pineapple Essence	q.s.	IP	Flavouring Agents
9.	Water	q.s.	IP	

### Formulation of Disodium Hydrogen Citrate Syrup

### 5.4 List of Equipments Used in Present Investigation

Sr No.	Equipments	Supplier/Manufacturer
1.	Colloidal Mill	Dwarkesh
2.	SS Stirrer	Dwarkesh
3.	Bottle Filling Machine	N.K.
4.	Bottle Sealing Machine	N.K.
5.	Automatic labeling Machine	Garuda

### List of Equipments used in present investigation



**Collidal Mill**



**SS Stirrer**



**Bottle Filling Machine**



**Bottle Sealing Machine**



**Automatic labeling Machine**

### 5.5 Evaluation Parameters<sup>[30-31]</sup>

Following tests are specified for the evaluation of syrups:

- (1) Physical Stability
- (2) pH determination
- (3) Consistency
- (4) Refractive index
- (5) Solubility
- (6) Identification of active contents

- (7) Assay of active contents
- (8) Light Transmittance Test
- (9) Determination of Sucrose Concentration
- (10) Content Uniformity

- 1) **Physical Stability** - The syrup must be clear. No solid particle should be present in syrup.
- 2) **pH determination** - Determine the pH of syrup by litmus paper or pH meter. The pH values of syrup ranges between 4.35 to 6.87.
- 3) **Consistency** - Should be clear solution. there should be no solid particles.
- 4) **Refractive index** - The value of refractive index should be in the range of 1.4608 to 1.4630.
- 5) **Solubility** - Soluble in water.
- 6) **Identification of active contents** - Identify the active contents of syrup by suitable means e.g. invert syrups dissolve with 10 ml of water and 5ml of potassium cupric tartrate solution. A red precipitate is produced.
- 7) **Assay of active contents of Syrup** - Mix 8 grams with 100ml of water and titrate with 0.1M NaOH using phenolphthalein as an indicator. Each ml of 0.1M NaOH = 0.007005 grams of citric acid monohydrate.
- 8) **Light Transmittance Test** - A Light transmittance meter is used to check the color of Syrup. In this, a Syrup sample is checked for colour by passing the light through the sample and observed by naked eye. The percent of transmitted light is compared for light transmittance rates for different grades.
- 9) **Determination of Sucrose Concentration** - Concentration of sucrose is very important in syrup because high amount of sucrose in syrup may cause crystallization of syrup while low amount may cause loss of preservative property of syrup. The concentration of sucrose in syrup is determined using analytical tools HPLC or UV Spectrophotometer.
- 10) **Content Uniformity** - In this, take 10 containers having syrup and emptied content of each container. then determine the drug assay of content of each container as per method prescribed in monograph of that drug in pharmacopoeia. The preparation complies with the test if not more than one value is outside the 85%-115% limit of average value and none value is outside the 75-125% limit. If 1-3 values are outside the 85-115% limit value but none is outside the 75-125% the limit of average value then test is performed for another 20 containers. Then not more than 3 values should be outside

the 85-115% limit and none should be 75-125% limit of average value.

## VI. CONCLUSION

- ☐ Welable Healthcare helped us to imbibe the information and detail about disodium hydrogen citrate syrup.
- ☐ We were given all the required knowledge on the formulation and evaluation of disodium hydrogen citrate syrup it is a urinary alkalinizer which is used to treat urinary tract infection, gout, painful urination and kidney stones.
- ☐ If overdose one can have side effect that include Tiredness, Vomiting, Nausea and others.
- ☐ Thus the syrup has been prepared using various equipments like mixers, stirrer and other filling and sealing machine and has been evaluated for parameter like physical stability, pH, solubility, assay, refractive index etc.

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