"THE DEVELOPMENT AND EVALUATION OF CANDY BASED MEDICATED LOLLIPOP: A NOVEL DRUG DELIVERY SYSTEM"

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ABSTRACT -

The oral route is the most popular method for administering medications due to its affordability, simplicity, patient compliance, and adaptability in formulation. For some patients, particularly those who are young or elderly, taking oral medications is highly unpleasant. The advantages of the current research effort include increased oral dosage form retention time, increased bioavailability, and a decrease in stomach irritability by skipping first pass metabolism and for anti-inflammatory activities in body. Lollipops are flavoured medication dose forms that are meant to be retained in the throat or mouth while being sucked. They often include one or more medications in the sweetened base. The purpose of the medicated lollipops is to increase patient acceptance and compliance. Patients, doctors, and the pharmaceutical business always gain from new drug designs in this field. The lollipops were made using sucrose,methylcellulose and citric acid as the polymer and were then heated and congealed.The medication is contained in a sweetened and flavoured base in lollipop-style solid dosage forms that are meant to dissolve gradually in the tongue. Medicated lollipops have a slow-dissolving delivery method. Within one to ten minutes, they disintegrate in the mouth. Having two type of lollipop based on nature of drug in which one is having synthetic drugs (Itraconazol) and another is herbal drugs (Ginger ,Tulsi, Clove,Honey and Lemon Juice) showing anti-inflammatory ,antifungal,antiseptics, in respiratory disorders, repectively.

KEYWORDS- Lollipop, pediatric, Itraconazol, Ginger ,Tulsi, Clove,Honey ,Lemon Juice, sugar syrup.

INTRODUCTION- There are numerous scientific issues surrounding oral medication administration that could be researched for many years to come. Additionally, novel dosage forms that raise the bar for drug delivery must be created using ground-breaking technology.Tablets are the most extensively used dosage form, and oral drug delivery is the most flavorful method of pharmaceutical administration. Solid dosage forms are well-liked because they are simple to administer, precise in amount, allow for self-medication, reduce pain, and most significantly, encourage patient compliance.

Having trouble swallowing is one of the main issues that many patients have with the traditional tablet dosing form. This issue becomes more obvious when a patient taking medication does not have easy access to drinking water. Dispersible pill distribution systems are distinguished by rapid release, quick disintegration, and enhanced patient compliance. Dysphagia, or trouble swallowing, affects people of all ages, but it is most prevalent in the elderly and in young children due to physiological changes in those populations. Additionally, people who are mentally ill, uncooperative, or who experience nausea, motion sickness, abrupt episodes of allergic response, or coughing, have difficulty taking standard oral dosage forms. Due to a lack of water, it may occasionally be difficult to swallow conventional items. These issues prompted the creation of a unique type of solid oral dosage form, so appealing, flavor-masking formulations are now essential.

MEDICATED LOLLIPOP- Lollipops are solid dosage forms for medication that are meant to dissolve gradually in the mouth. They typically contain additives including sweeteners, flavours, colours, opacifiers, and stabilising agents in addition to the medication.The distribution technique for medicated lollipops is sluggish to dissolve. Within 1 to 10 minutes, they disintegrate in the mouth.Lollipops are huge, boiled sugar candies in a variety of flavours that are attached to a plastic stick and may be enjoyed slowly by sucking them. To keep the confection (medication) together, a plastic stick is utilised. Lollipops are a type of solid unit dose that is intended to dissolve in the mouth or pharynx. The creation of lollipops dates to the 20th century and they are still manufactured for sale. The majority of the preparations for lollipops are available as over-the-counter medicines.Lollipops offer a tasty way to administer dose forms, and they have a strong presence in the pharmaceutical industry thanks to a number of benefits. However, they also have certain drawbacks. Usually in a flavoured, sweetened basis, they contain one (or) more medications. The majority of the time, lollipops are employed for immediate effects in the mouth. Additionally, if the medication is effectively absorbed via the buccal lining, they can be employed for systemic effects.

- **Advantages of Medicated Lollipops-**

1. Do not require administration with water intake. Parenteral uses a minimally invasive technique.
2. The simplest foods to prepare early on with little effort and time are lollipops.
3. Lollipops can be given to those patients who have difficulty in swallowing.
4. Having formulas that are easy to change and can be patient specific.
5. It can reduce dosing frequency.

- **Disadvantages of Medicated Lollipops-**

1. Because of the high temperatures needed for production, medicines that are heat labile cannot be utilised in this formulation.
2. Drugs having minimum bitter taste are suitable.
3. Heat stable drugs are suitable.
4. Such dose forms have 'Dysphasia', or difficulty swallowing, which is a significant downside. A third of the population—nearly 35%—is thought to be affected by this. A number of other illnesses, such as Parkinsonism, motion sickness, unconsciousness, elderly patients, children, and a lack of hydration are all connected to this disorder.

The way that the medicated lollipops work-

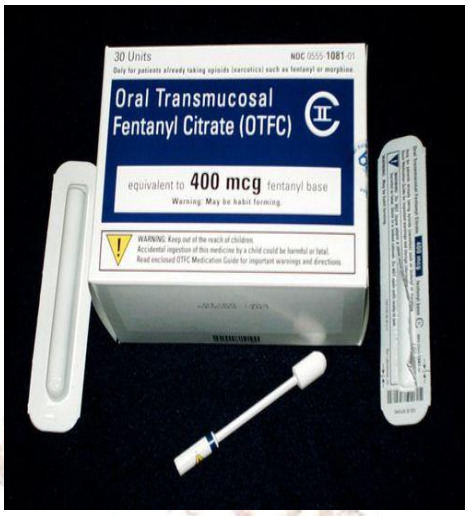
When a medicine is administered using our lollipop delivery system, it is absorbed more quickly through the oral mucosa than when it is ingested and absorbed through the digestive system. By giving a lollipop until the desired result is obtained, the dose can be readily regulated. enjoyable to ingest. They can also be taken anywhere and at any time because they don't need water.

Medicated lollipops release drugs slowly as a patient sucks or rotates a lollipop in the mouth. The medicine acts locally or systemically after absorption by buccal mucosa.

The ideal characteristics of an excipient which used in preparation are given as:

- Chemically stable.
- Non-reactive.
- Low equipment and process.
- Sensitive.
- Inert to human body.
- Non toxic.
- Acceptable with regards to organoleptic.
- Characteristics Economical.
- Having efficiency in regards with the intended use.

Heral (Organic) Lollipop



Synthetic Lollipop

Based on physical form they classified as

- **Hard lollipop-** Hard lollipops could be called solid sugar syrups. Sugars and other materials are heated together before being poured into a mould to make these dosage forms.

- **Soft lollipop-** Soft lollipops have grown in popularity due to their ease of preparation and their suitability for a wide range of medications. The basis is typically made up of a combination of several PEGs, acacia (or) comparable materials, glycerol gelatin (or) an acacia: basis of sucrose.

METHODOLOGY

1.HERBAL LOLLIPOP:

1. Herbal lollipop can be made in home with less ingredient and in less cost.

2. 20 ml of ginger juice in pure form pour in dry container.

3. Take clove oil mixed with ginger juice

4. Add tulsi leaf and lemon juice as vitamin source

5. Add honey (sugar)for softness of lollipop and for sweetness ,also honey having number of property like they has anti-inflammatory, antioxidant, and antibacterial properties. Honey is often used topically to treat burns and enhance wound healing as well as orally to cure coughs.

6. Add colouring agent if essential.

7. All ingredient are mixed well including excipients and heat them above 130-150 degree Celsius.

8. After heating give the shap to concentrated syrup.

9. After cooling ,syrup form in lollipop shape .

10. Packaging and storage take place in dry ,clean place,at room temperature and prevent form moisture.

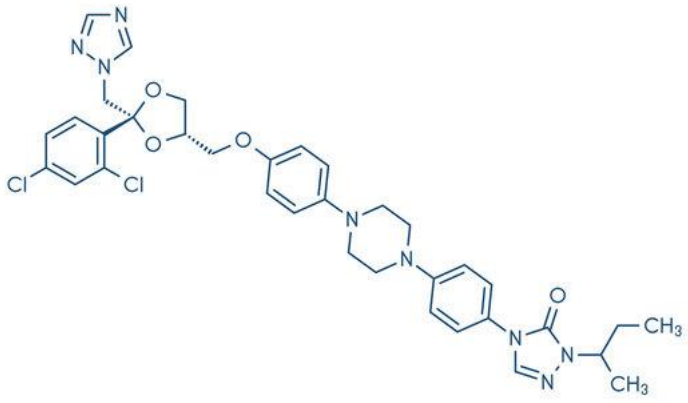
Herbal lollipop

Benefits of Herbal lollipop: Antifungal research have revealed that clove oil kills fungal infections quickly and effectively. Gingerols and shogaols are anti-inflammatory and antifungal components found in ginger roots. In addition, ginger gives important liver support as your body detoxifies the Candida infection. Methylcellulose is a polymer that functions as a thickening and emulsifier. It is non-toxic and does not cause allergies. Citric acid is commonly used as an acidifier, flavouring agent, and chelating agent.

As a result, a herbal lollipop containing ginger juice and clove oil will provide therapeutic efficacy against oral thrush , effective against respiratory disorders

- **SYNTHETIC LOLLIPOP(**using drug)

The main ingredient is itraconazole drug wich showing anti-fungal activity



itraconazole

Physicochemical Properties of Itraconazole

Chemical Name	(2R,4S)-rel-1-(butan-2-yl)-4-{4-[4-(4-{[(2R,4S)-2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl] methoxy}phenyl) piperazin-1-yl]phenyl}-4,5-dihydro-1H-1,2,4-triazol-5-one
Appearance	Itraconazole is a white or almost white powder.
Molecular weight	705.63 g/mol
Molecular formula	$C_{35}H_{38}Cl_2N_8O_4$
Half life	21hrs
Category	For the treatment of the following fungal infections in immunocompromised and nonimmunocompromised patients: pulmonary and extrapulmonary blastomycosis, histoplasmosis, aspergillosis, and onychomycosis.
Solubility	

	Practically insoluble in water, freely soluble in Methylene chloride, sparingly soluble in Tetrahydrofuran, very slightly soluble in alcohol
Melting point	168°C- 170°C
Dose	100 mg/day for 2 weeks by Oral route.
Therapeutic uses	Used as an antifungal agent.

- **Pharmacokinetics of drug**

- **Absorption**

Itraconazole has a maximum oral bioavailability of 55% when taken with a full meal.

- **Distribution**

Itraconazole is widely transported throughout the body, with a reported apparent distribution volume of 10.7 L kg. This process is largely dependent on the drug's physicochemical qualities. It is extremely well bound to serum proteins, particularly serum albumin, with a binding fraction of 99.8%. Itraconazole and/or its metabolites are detected in very high concentrations in several bodily tissues, including the skin, lungs, muscle, and liver.

Data on the medication's disposal following inhalation have confirmed that the parent drug and its hydroxy metabolite reach tissue concentrations greater than concurrent plasma levels.

- **Metabolism**

Itraconazole is extensively metabolised by the liver into a huge variety of metabolites, the most important of which being hydroxyitraconazole. The primary metabolic routes include dioxolane ring oxidative scission, aliphatic oxidation at the 1-methylpropyl substituent, N-dealkylation of this 1-methylpropyl substituent, piperazine ring oxidative degradation, and triazolone scission.

- **Elimination**

Itraconazole is primarily metabolised in the liver by the cytochrome P450 3A4 isoenzyme system (CYP3A4), resulting in the creation of numerous metabolites, the most important of which is hydroxyitraconazole.The parent drug's faecal excretion ranges from 3 to 18% of the dose.The parent medication is excreted in the urine in less than 0.03% of the dose. Approximately 40% of the dosage is eliminated in the urine as inactive metabolites. No single excreted metabolite accounts for more than 5% of the dosage.

- **Pharmacodynamics**

Itraconazole is an antifungal drug of the imidazole/triazole class. Itraconazole works by inhibiting the enzyme cytochrome P450 14demethylase to prevent fungal cytochrome P450 sterol C-14 demethylation. This enzyme converts lanosterol to ergosterol and is essential for the formation of fungal cell walls. The consequent loss of normal sterols correlates with the buildup of 14-methyl sterols in fungus and may be responsible for fluconazole's fungistatic effect.Demethylation in mammalian cells is substantially less responsive to fluconazole suppression. In vitro, itraconazole inhibits Cryptococcus neoformans and Candida spp. Fungistatic action has also been established in normal and immunocompromised animal models for systemic and intracranial Cryptococcus neoformans infections, as well as systemic Candida albicans infections.

- **Mechanism of action**

Itraconazole binds to 14-demethylase, a cytochrome P-450 enzyme required for the conversion of lanosterol to ergosterol. Because ergosterol is a key component of the fungal cell membrane, inhibiting its synthesis increases cellular permeability, resulting in cellular content leakage. Itraconazole may also reduce endogenous respiration, interact with membrane

phospholipids, inhibit yeast mycelial transformation, limit purine uptake, and affect triglyceride and/or phospholipid production.

- **Side effect**

Nausea/vomiting, diarrhoea, headache, stomach discomfort, or dizziness are all possible side effects. Inform your doctor or chemist right away if any of these symptoms persist or worsen. Remember that your doctor has prescribed this medication because the benefit to you outweighs the risk of adverse effects. Many persons who use this drug have no major adverse effects.

Notify your doctor immediately if you experience any serious side effects, such as numbness/tingling in your arms/legs, hearing loss, or mental/mood disorders (such as depression).

Itraconazole has infrequently caused potentially deadly liver damage. Notify your doctor right once if you experience any of the following signs of liver disease: persistent nausea/vomiting, loss of appetite, stomach/abdominal discomfort, yellowing eyes/skin, or dark urine.

- **Toxicity**

Itraconazole was administered orally to mice and rats at 320 mg/kg and to dogs at 200 mg/kg with no substantial mortality seen.

- **Use**

Itraconazole is a medication used to treat fungal infections. It belongs to the azole antifungals class of medicines. It acts by inhibiting the growth of fungus. It is especially effective against Aspergillus, which fluconazole is not. It's also approved for the treatment of blastomycosis, sporotrichosis, histoplasmosis, and onychomycosis.

Itraconazole is highly protein-bound and has almost no penetration into the cerebral fluid. As a result, it should not be used to treat meningitis or other infections of the central nervous system. According to the Johns Hopkins Abx Guide, it has minimal CSF penetration, however treatment for cryptococcal and coccidioidal meningitis has been successful. It is also used to treat systemic infections such as aspergillosis and cryptococcosis when other antifungal medications are either inappropriate or ineffective.

- **OBJECTIVE**

The objectives of present study are

- To formulate the medicated lollipop containing drug for the treatment of children.
- To study drug excipients compatibility study.
- To evaluate the physiochemical properties.
- To study the in-vitro drug release.
- To analyze the effect of polymer on release pattern of drug.
- To study the stability of optimize batches

- **Identification test for Itraconazole**

Identification was performed by various parameters like colour, odour, solubility, Melting point range and FT Infrared spectrophotometer etc.

- **Estimation of Itraconazole:**

Ultra-Violet Spectroscopy: Electronic excitation happens in the ultraviolet spectrum between 200 and 800 nm and involves the promotion of electrons to higher energy molecular orbitals. It is quite beneficial to count the quantity of conjugate double bonds and aromatic conjugation inside diverse compounds. It also differentiates between conjugated and unconjugated systems.

Preparation of Stock solution

In a volumetric flask, 20 mg of itraconazole was carefully weighed and dissolved in pH 6.8 Phosphate Buffer, then the volume was increased to 100 ml with 6.8 phosphate buffer. This was a stock solution with a concentration of 200 g/ml.

Formulation of candy based Itraconazole lollipops(synthetic lollipop)

Step – 1 Preparation of Syrup base**:**

Syrup foundation was made by dissolving 67.56% w/v sucrose in filtered water at 110^0C and stirring continuously for around 90 minutes.

Step – 2 Preparation of medicated lollipops:

The heating and congealing procedure was used to make 3 gm of itraconazole lollipops. In a beaker, the needed amounts of sucrose were dissolved in water while heating and stirring at 110 degree Celsius for around 90 minutes. Dextrose was added, and stirring was continued for 2 hours while the temperature was raised to 140 degree Celsius. The material was placed on a cooling surface, and the temperature was reduced to 90°C until a plastic mass was formed. The substance was mixed for 30 minutes after the drug, polymer, colour, and flavour were introduced. The material was roped on moving rollers before being sized into 3 gms. Lollipops are air dried in a drying chamber for roughly 2 hours. Polythene wraps were used to seal the prepared lollipops.

- **Procedure for evaluation of medicated lollipops:**

Size, thickness, shape, hardness, friability, weight variation, moisture content, drug content, and an in vitro drug release research were all evaluated.

Colour -Prepared lollipop formulations were observed for colour.

Method: Colour comparisons require that a sample be compared against some colour standard.

Thickness and Shape- The shape and thickness were measured with a sliding Calliper scale.

Method: Five or ten lollipop recipes from each batch were chosen and their crown thickness was measured using a sliding Calliper scale. The shapes of the lollipops were observed.

Hardness: Lollipop compositions must be strong or hard enough to survive mechanical shocks during production, packing, and shipment.

Method : The Monsanto hardness tester is made out of a barrel with a compressible spring held between two plungers. The lower plunger is pressed against the lollipop formulation, and a zero reading is taken.

Turning the threaded bolt forces the upper plunger against a spring until the pills break. A pointer rides along a gauge in the barrel to indicate the force as the spring is squeezed. The force of the break is recorded, and a reading of zero force is subtracted from it.

Friability: The Roche Friabilator was used to examine the friability of lollipop compositions.

It is critical to understand the mechanical strength of the tablet when handling it.

Method: Twenty lollipop formulations were weighed initially and transferred to the Friabilator

. **Identification test for Itraconazole**

Organoleptic Properties: The test was performed as per procedure given in material and method. The result is illustrated in following table.

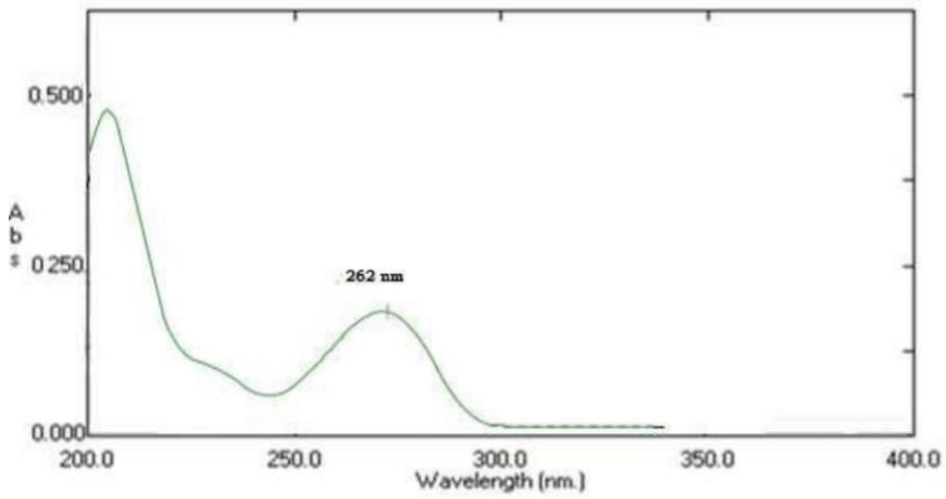
Tests	Observations	IP Specifications
Colour	White powder	Complies
Taste	Unpleasant taste	Complies
Odour	Odourless	Complies
Melting point	168°C-170°C	Complies

Solubility study of Itraconazole in different solvents: Solubility study of Itraconazole was done in aqueous and non-aqueous media.

Sr. No.	Solvents	Solubility (mg/ml)
1.	Water	0.005
2.	pH 6.8 Phosphate Buffer	8.121
3.	Methanol	0.786

Determination of wavelength (λmax) of Itraconazole

10g/ml in 6.8 phosphate buffer was prepared and scanned in the range of 200-400 nm, and the wavelength maxima was obtained using the Shimandzu U.V. Spectrophotometer depicted in Figure 6, and it was 262 nm.



➢ DISCUSSION

The current study intended to design and test a novel system of drug delivery based on candy-based medicated lollipops in order to improve bioavailability and patient compliance.

- Actiza Pharmaceuticals Pvt. Ltd., Surat, provided itraconazole medication. Organoleptic properties such as colour, taste, aroma, and melting point of the obtained Itraconazole sample were found to be in accordance with IP.
- The retention of basic characteristics peaks in the FTIR of a physical mixture of Itraconazole with Hydroxy Propyl Methyl Cellulose K4M and Sodium Carboxy Methyl Cellulose at 1690 cm^{-1}, 1635 cm^{-1}, 1125 cm^{-1}, 1700 cm^{-1}, and 2900 cm^{-1} for - C=C of aromatic groups, C = N stretching, C-N Vibrations, C = O stretching, Alkane, aromatic CH group
- Medicated lollipops containing Itraconazole was prepared in batches using different types with 15%, 20% and 25% concentrations of polymer (Hydroxy Propyl Methyl Cellulose K4M and Sodium Carboxy Methyl Cellulose) by heating and congealing technique method.
- Prepared lollipop batches were evaluated for size, thickness, hardness, friability, weight variation, moisture content, drug content and in vitro drug release study and found to be complies as per specification given in I.P.
- The optimized formulation was subjected to stability study when stored at 40± 20C temperature with relative humidity of 75±5% for a period of three months. No significant change in physiochemical properties, drug release profile as well as drug content indicating there was no degradation and change in composition of system.

Final product

➢CONCLUSION

Various characterisation and evaluation investigations confirmed that candy-based medicated lollipops of antifungal agent (Itraconazole) were made utilising different types and quantities of polymer by heating and congealing procedure method. When compared to Hydroxy Propyl Methyl Cellulose K4M, Sodium Carboxy Methyl Cellulose as a polymer produces better results. Itraconazole is released in 30 minutes by candy-based medicated lollipops, which have a nicer tongue feel.Such dosage formulations are well received by both parents and children, while still retaining good efficacy and bioavailability and, most importantly, increasing patient compliance. Furthermore, it is a simple, inexpensive, and time-saving procedure.

In other words, medicated lollipops will be ideal dosage forms for paediatric patients because they provide many additional benefits such as patient compliance, convenience, and comforts for efficient treatment, such as a low dose, immediate onset of action, a reduced dosage regimen, and an economical factor. These will provide a more novel dosing form.

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