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DEVELOPMENT AND IN VITRO EVALUATION OF MEDICATED LOLIPOP CONTAINING CEFIXIME FOR PEDIATRICS

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ABSRACT

Introduction: The oral route is the most common route of administration of drugs because of the low cost of therapy, ease of administration, patient compliance, and flexibility in formulation. Taking oral medicine is extremely odious to some patients, such as paediatric and geriatric patients. Cefixime is one of the most used antibacterial drugs, used in the treatment of the cough and cold. Difficulty in swallowing (dysphagia) is common among paediatrics and geriatric patients. Accordingly, there is a need for a solid form of medicine that is in a form easy to take and swallow, such as lollipops. **Objective:** The main objective of the present research study is to provide a solid form of medicine that is in a form that makes it pleasant to take and swallow by paediatrics, geriatric, and bedridden patients, and avoid the dangers of being swallowed as do the other solid forms in those patients. However, lollipop is designed to improve patient compliance, acceptability, transportation, etc. **Materials and Method** In the present research study, an attempt has been made to prepare sugar-based cefixime medicated lollipops for paediatrics, geriatrics, and bedridden patients to overcome the administration problem. The cefixime medicated lollipops were prepared using dextrose and sucrose. All the formulations prepared were subjected to various physicochemical parameters like hardness, friability, weight variation, drug content, etc. **Result:** Drug-excipient compatibility study was carried out using FTIR. All the formulations were subjected to various physicochemical evaluations like weight variation, hardness, drug content, friability etc. The in-vitro dissolution study of F3 was carried out by two method a) Paddle method b) flow through cell method. The in-vitro permeation study of F3 was found to be 68.5% at 20 min. Stability study was carried out as per ICH Guidelines (Q1A) at 25±2ºC /60±5% RH and 40±2ºC /75±5% RH.

Conclusion: From present study it can be concluded that the combination of dextrose, sucrose and HPMC K4M shows the best result of evaluation parameters and greater stability than other combinations.

Keywords: Medicated lollipop, Cefixime, Pediatric, FTIR, ICH Guidelines

INTRODUCTION

In oral drug delivery, there are many scientific challenges that could be studied for years to come and breakthrough technologies are oval dosage forms raising drug delivery to higher level **[1]**. Oral drug delivery is the most flavoured route for the administration of various medications and tablets are the most widely accepted dosage form. Solid dosage forms are popular because of the ease of administration, accurate dosage, self-medication, pain avoidance, and most importantly patient compliance.

Among the major problems faced by many patients with conventional tablet dosage form is difficulty in swallowing. This problem is more apparent when drinking water is not easily available to the patient taking medicine. Dispersible tablet delivery system is characterized by fast disintegration, quick dissolving, rapid release and improved patient compliance. Difficulty in swallowing (dysphagia) is a common problem of all age groups, especially the elderly and paediatrics, because of physiological changes associated with those groups. Other categories that experience problems in using conventional oral dosage forms include the mentally ill, uncooperative and patients suffering from nausea, motion sickness, sudden episodes of allergic attack or coughing. Sometimes it may be difficult to swallow conventional products due to non-availability of water. These problems led to the development of a novel type of solid oral dosage form hence, an attractive, taste masking formulations are the need of the hour **[2]**.

Anatomy of Buccal Mucosa

The buccal mucosa is comprised of the mucosal surfaces of the cheeks and lips, which form the anterolateral boundaries of the oral vestibule. It is contiguous with the mucosa that lines the floor of mouth and alveolar ridges. There are approximately 800–1000 minor salivary glands located throughout the buccal mucosa as well as other parts of the contiguous oral mucosa. The thickness of the epithelium in the buccal area in adult human is about 500-800m and of 100cm an average surface area. Buccal mucosa becomes recently a very attractive site for the administration of various pharmaceutical dosage forms due to the potential benefits offered by this route **[3, 34]**.

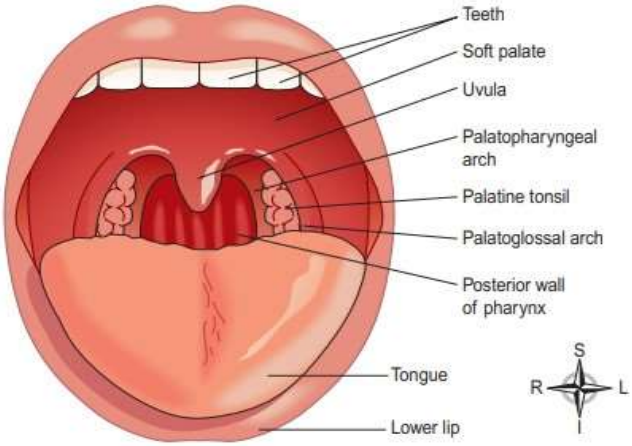


Figure 1: Anatomy of oral cavity [32]

Advantages and Disadvantages of Drug Delivery Via the Oral Mucosa

Conventional, have certain advantages. The oral mucosa is highly accessible and rapidly heals itself after trauma or damage. Such short recovery time reduces adverse drug effects induced by long-term topical drug delivery. The possibility of allergic responses is limited in oral mucosal delivery due to fewer Langerhans cells in the oral mucosa than the skin. The oral cavity is a highly hydrated environment that facilitates drug dissolution. Furthermore, the small surface area of the oral membrane is beneficial for sustained drug delivery, particularly for drugs of high potency. The oral mucosa is highly vascularized and there- fore allows the drug to gain direct access to systemic circulation via capillaries and venous drainage. Disadvantages associated with localized drug delivery to the oral cavity should also be considered. Saliva secretions may wash away the drug and/or dose form before absorption can occur. The delivery device may be dislodged by mastication and speech. Enzymatic degradation may retard absorption. **[4, 33]**.

Medicated Lollipop

Lollipops are solid dosage forms, containing the medicament in a sweetened and flavoured base, intended to dissolve slowly in the mouth. in the Lollipops have mainly contained the additives like sweetening agent, flavouring agent, the colouring agent, opacifier and stabilizing agent **[5]**. medicated lollipops are slow dissolving delivery system. They dissolve in oral cavity within 1 to 10 minutes **[6, 37]**. Lollipops are large sugar boiled confectionary of various flavours attached to a plastic stick which can be consumed over a long period of time through licking. The plastic stick is used to hold the confection (medicament) together. Lollipops are solid unit dosage form of medicament which is meant to be dissolved in mouth (or) pharynx. Development of

lollipops dates back to 20th century and is still in commercial production. Most of the lollipop's preparations are available as over the counter medications. Lollipops provide a palatable means of dosage forms administration and enjoy its position in pharmaceutical market owing to its several advantages but it suffers from certain disadvantages too. They contain one (or) more medicament usually in a flavoured, sweetened base **[38]**. Lollipops are most often used for localized effects in the mouth. They can also be used for systemic effects if the drug is well absorbed through the buccal lining **[7, 35]**.

Mechanism of action of Medicated Lollipop

With our lollipop delivery system, a drug is absorbed more rapidly through the mucosa of the mouth, than when the drug is swallowed and absorbed via the digestive system. The dose can be easily controlled by administering a lollipop until the desired effect is achieved. fun to consume. Additionally, they don't require water, which means they can be taken anywhere and anytime.

How does it work?

Medicated lollipops release drugs slowly as a patient suck or rotates a lollipop in the mouth. The medicine acts locally or systemically after absorption by buccal mucosa **[8]**.

Suitable drug Candidate for Medicated Lollipop

paediatrics, geriatrics and bedridden patients show inconvenience swallowing conventional tablets or capsules due to difficulties in swallowing with lesser amounts of water with the medication, unable to tolerate the taste of many drugs when formulated as liquid dosage forms, resulting in poor patient compliance. The medicated lollipops are flavoured medicated dosage forms intended to be sucked and hold in the mouth or pharynx. The illness is associated with fever headache and body aches so to cure the above, there was need to administer the drug to the individuals but in case of paediatric patients it was difficult to administer the dose forms like tablet, capsule, etc. These preparations are commonly used for the purpose of local effect or systemic effect. Medicated lollipops are prepared heating and congealing method. paediatrics is the most suitable candidate for he medicated lollipop. A small medicated candy intended to be dissolved slowly in the mouth to lubricate the irritated tissues of the tract. A small flavoured tablet made sugar (or) syrup and often medicated. A small medicinal tablet in the shape of lollipop is taken for sore throat. Lollipops are large sugar boiled confectionary of various flavours attached to a plastic stick which can be consumed over a long period of time through licking. The

plastic stick is used to hold the confection (medicament) together Lollipops are the dosage forms that are intended to be dissolved slowly on the mouth (or), that can be easily swallowed are gaining popularity especially among paediatric patients. Lollipops are solid unit dosage form of medicament which is meant to be dissolved in mouth (or) pharynx. Development of lollipops dates to 20th century and is still in commercial production. Most of the lollipop preparations are available as over the counter medications. Lollipops provide a palatable means of dosage forms administration and enjoy its position in pharmaceutical market owing to its several advantages **[7]**.

Cefixime is fulfilling all the criteria given above, a small dose of cefixime can be given to paediatrics, thus it can be chosen to make a lollipop.

Cefixime

Cefixime is an orally active semi synthetic third generation cephalosporin antibiotic. Clinically it is used in the treatment of susceptible infections including gonorrhoea, otitis media, pharyngitis, tonsillitis, lower respiratory-tract infections such as bronchitis, and urinary-tract infections **[9, 10, 11]**.

Antimicrobial Activity

Cefixime's activity is not affected by changes in pH between 5 and 8, or by increases in sodium, calcium, or magnesium concentrations. The presence of urine or serum also has no effect on its activity. Tolerance, indicated by differences between minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs), is not evident in most Enterobacteriaceae, with the exception of some Enterobacter, Morgan Ella, and Serratia strains **[12]**.

Antibacterial Activity

Most tested strains of Escherichia coli. Klebsiella pneumoniae, Klebsiella oxytoca, Proteus mirabilis, Proteus vulgaris. Citrobacter diversus and Providencia rettgeri were inhibited in vitro by cefixime I mg/L or less. Haemophilus influenzas, Branhamella catarrhaiis and Neisseria gonorrhoeae were also inhibited by low concentrations of cefixime. A study of large numbers of Enterobacteriaceae conducted in the USA noted that the M1Cso was below I mg/L for most clinical isolates of all species other than *Citrobacter fteundii, Enterobacter cloacae*. *Hafnia alvei* and *Morgan Ella tnorganii*.

Cefixime is active against *Streptococcus pyogenes, S. pneumoniae, S. agalactiae* and most strains of streptococci belonging to Lancefield group C, but Lancefield groups F and G are only moderately sensitive and *Staphylococcus aureus, S. epidermidis* and *Enterococcus coli* are generally resistant. *Pseudomonas aeruginosa* is resistant to cefixime, as are most strains of the

Bacteroides species. and many strains of Pepto streptococcus species and Flavobacterium species **[13]**.

Mechanism of Action and Resistance

Like other cephalosporins, cefixime appears to inhibit bacterial cell wall synthesis in a manner equivalent to penicillin. It has a high affinity for penicillin-binding protein-3 (PBP-3), the major binding site for cephems, and for PBP-Ib, the killing site of the beta-lactams' It is stable to the common plasmid-mediated beta-Lactamases such as TEM-I, TEM-2, SHY-I, and HMS, t.7 and is also not hydrolysed by most of the chromosomal beta-lactamases, The resistance of staphylococcal species is due to cefixime's poor binding to the PBP-2 of Staphylococcus aureus. Its inactivity against enterococci and Listeria monocytogenes is similarly a result of inability to bind to the PBPs of those species:" The lack of activity against Bacteroides spp. is related to hydrolysis by beta-lactamases produced by organisms in this species. Pseudomonas spp. and Acinetobacter spp. are not inhibited by cefixime because of resistance to penetration through their outer cell membrane **[12, 14, 15]**.

Adverse Effects

cefixime have usually been mild to moderate in severity, and transient. Diarrhoea and stool changes (as dist. inct from diarrhoea) have been the most commonly reported adverse effects. In about two-thirds of instances diarrhoea and stool changes were evident within 4 days of beginning treatment, which is contrary to the pattern usually encountered with changes in bowel flora **[13]**.

MATERIAL AND METHODS

Cefixime, Hydroxypropyl methylcellulose K4M was procured from Yarrow chem. Products Mumbai, Sucrose, dextrose, Citric acid were procured from HI media Mumbai, Vanilla flavouring agent and Colouring agent were procured from Classics aromatics.

Phase-1 studies

Pre-formulation studies of cefixime

Pre-formulation phase focuses on the concepts of physicochemical properties of the pure drug substance and when it is mixed with excipients. Pre-formulation studies are the first step in the rational development of a drug molecule to develop a safe, effective, and stable dosage form **[16, 17]**.

Phosphate Buffer (pH 6.8) was prepared according to the procedure available online resource **[18]**.

Pharmacokinetic Properties

Confirmation tests of cefixime were carried out including melting point, the solubility in different solvents, IR etc. The melting point of cefixime was determined using the capillary method and found at 218-225°C **[19]**. The solubility of the cefixime was determined in different solvents as the

following: A semiquantitative determination of solubility was tested by adding approximately 10 mg of cefixime to a fixed volume of solvents like phosphate buffer (pH 6.8), cefixime found to be freely soluble in methanol and propylene glycol, partially soluble in ethanol and acetone does not dissolve in ether and ethyl acetate, hexane or water **[20]**.

Following oral administration peak plasma concentrations of cefixime are generally attained in 3 or 4 hours and are about 2.0 to 2.6 mg/L (mean) after a single 200mg dose. Other than a delay to peak plasma concentrations the pharmacokinetics of cefixime are not influenced by food. There is no evidence of drug accumulation following administration of 200mg twice daily or 400mg once daily for 15 days. In children, the pharmacokinetics of cefixime 8 mg/kg **[13]**.

Dosage and Administration

In children, cefixime 8 rug/kg/day once daily or in 2 divided doses has been the most widely used dosage for treating acute otitis media, acute tonsillitis and acute pharyngitis. In patients with severe renal dysfunction (creatinine clearance < 20 ml/min) half the standard dose of cefixime should be administered once daily **[13]**.

Phase-2 studies

preparation of medicated lollipops

Preparation of syrup base

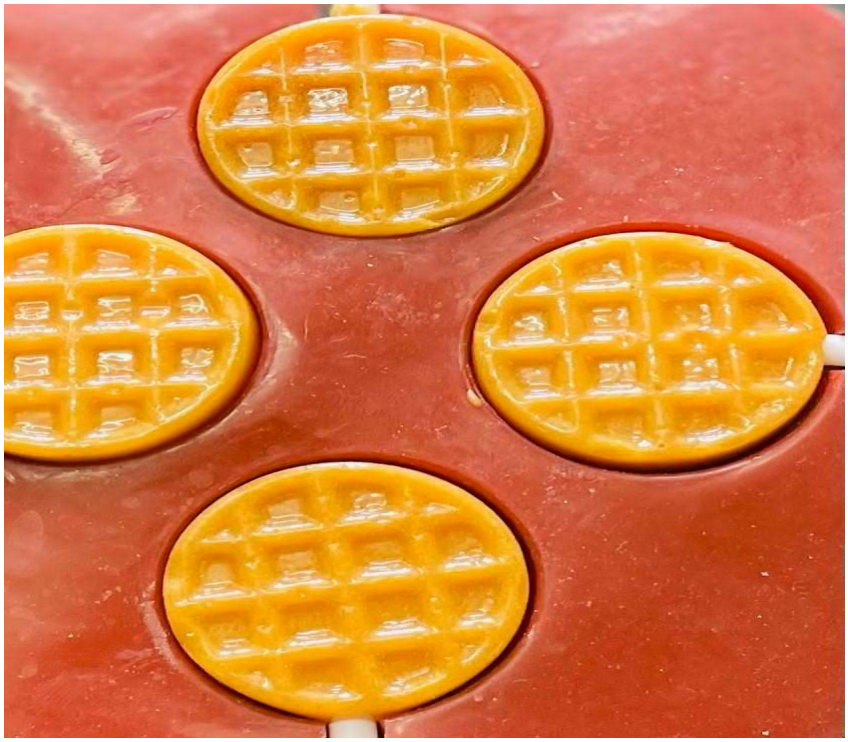
Syrup base was prepared by dissolving 66.66% w/v sucrose in purified water at 110 °C and continue stirring for about 30 min. Scaled downtime to appropriate with the quantity of material used was notice **[21, 36]**.

Heating and congealing method

The dextrose syrup was poured in to the sugar syrup and heated to 160 C till the colour changes to golden yellow. Flavour was added between 120 C to 135 C then temperature was bought down to 90 C and drug, polymer and other ingredients were added and mixed it well. The prepared mixture was poured in to the calibrated mould a kept it for air dry for 1-2 hr. The prepared lollipop was stored wrapped in aluminium foil and stored in desiccators to prevent moisture uptake **[22, 23, 29]**.

Table 1: Formulation chart for medicated lollipop

Ingredients	F0	F1	F2	F3	F4
Cefixime (mg)	100	100	100	100	100
Methylcellulose(mg)	-	300	400	-	-
HPMC K4M(mg)	-	-	-	300	400
Sucrose(mg)	3450	3150	3050	3150	3050
Dextrose(mg)	1400	1400	1400	1400	1400
Citric acid(mg)	50	50	50	50	50
Vanilla flavour	qs	qs	qs	qs	qs
Total weight(gm)	5	5	5	5	5



Fgure 2: Moulding of lollipop

Figure 3: Prepared lollipop

Evaluation test of lollipop

Drug-excipient interaction study

For studying drug-excipients interaction, prepared lollipop was subjected for FTIR studies **[24, 30]**.

Hardness

Hardness indicates the ability of a lollipop to withstand mechanical shocks while handling the hardness of the lollipop was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Three lollipops were randomly picked and hardness of the lollipops was determined **[25, 30]**.

Friability(F)

Roche Friabilator was used for testing the friability. Twenty lollipops were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm. After 4 min., the lollipops were weighed and the percentage loss in lollipops weight was Determined. **[25, 30]**

F = Wt. initial – Wt. final / Wt. initial× 100

Thickness and Diameter

Thickness and diameter were measured using Vernier Callipers. It was determined by checking the thickness and diameter of ten lollipops of each formulation. The extent to which the thickness of each lollipop deviated from ± 5% of the standard value was determined **[25, 31]**.

Weight Variation

Lollipops were randomly checked to ensure that uniform weight Lollipops were being made. 20 Lollipops formulations, weighed individually and average weight and % weight variation was calculated. The requirements are met if the weights of not more than 2 of the Lollipops differ from the average weight by more than the percentage listed in the accompanying table and no lollipops differs in weight by more than double that percentage. In present total weight of lollipop is 1000 mg. So, as per USP maximum difference allowed will be 10% for each lollipop **[25, 31]**.

Drug content

lollipops were selected randomly and powdered. A quantity of these powder corresponding to 300mg of cefixime was dissolved in 100ml of PBS pH 6.8 in a 100ml volumetric flask (stock solution A). From (stock solution A) 1ml is diluted with PBS pH 6.8 up to 100ml volumetric flask (stock solution B). From (stock solution B) 1ml is diluted with PBS pH 6.8 up to 10ml volumetric flask (stock solution C) and absorbance will be recorded at λmax **[26]**.

In-vitro dissolution study for medicated lollipops [26]

Paddle Method

In-vitro release studies were carried using USP-II dissolution apparatus. 900ml of PBS pH 6.8 at 37+ 0.5°C is taken as dissolution media. The rpm of the paddle was fixed at 100. Aliquot of 10ml was withdrawn at an interval of 5min up to 30min and absorbance was recorded at λmax **[26]**.

Flow Through Method

A Flow through cell dissolution model assembly was designed in our laboratory which maintains perfect sink conditions facilitating better in-vitro evaluation. An intravenous infusion set was attached to a bottle containing PBS pH 6.8. The flow rate was adjusted to 2ml/min using a flow regulator. 10ml of PBS was always maintained in the donor cell containing lollipop throughout the experiment. The lollipop was supported on a small mesh (40) in the donor cell of the infusion set. The flow of the release medium was the PBS bottle through the lollipop containing cell and to the receiver. The samples 10ml was withdrawn at an interval of 5min up to 30 min and absorbance was recorded at λmax **[27]**.

In-vitro permeation study

In-vitro permeation studies were conducted by using Franz diffusion assembly. 100mg equivalent weight of lollipop was placed in dialysis membrane between donor and receptor compartment of diffusion cell assembly. The receptor compartment was filled with PBS pH 6.8, Magnetically stirred at 200 rpm.10ml of samples were withdrawn at suitable time interval from donor compartment. The percentage of cefixime permeated was determined by measuring the absorbance in UV spectrophotometer at λmax **[28, 40]**.

Stability study

Stability study was carried out as per ICH-Guidelines (Q1A) at 25±2°C/60±5% RH and 40±2°C/75±5% RH. For every 45days the parameters like physical appearance, weight variation, hardness, friability, drug content, in-vitro release studies and in-vitro permeation studies were determined **[29, 40]**.

RESULTS AND DISCUSSION

In the present study, an attempt was made to develop medicated lollipop of cefixime. Formulations were subjected to various parameters such as weight variation, thickness, diameter, hardness, drug content, friability, in-vitro dissolution study, in-vitro permeation study. Stability studies were performed as per ICH-Guidelines (Q1A).

The percentage friability was found to be in range of 0.35% to 0.44% which was found to be well within maximum 1% limit.

The results of hardness Drug-excipient interaction study

Figure 1 and Figure 2 shows the FT-IR spectra of pure drug and excipient which showed that there is no interaction found between drug and excipient. All the formulations showed good physical appearance.

Weight Variation

The weight variation was found to be in range of 4.98±0.01gm to 4.99±0.05gm.

Thickness and Diameter

Thickness was found to be in the range of 8.45±0.01mm to 8.50±0.03mm.

Hardness

Hardness was found to be in the range of 7.45±0.05kg/cm2 to 7.51±0.17kg/cm2

Friability(F)

and friability indicated that the lollipops are mechanically stable.

Drug content

The drug content was found to be in range of 84±0.567% to 97±0.952% which is within acceptable range as specified in Indian Pharmacopoeia.

The results of hardness, friability and drug content, weight variation and thickness showed in **Table 2**.

In-vitro dissolution study

Paddle method

The in-vitro dissolution study of formulation F0 (without polymer) was found to be 81.3% at 20min. Individual formulations F1and F2 (containing methyl cellulose) showed the percentage cumulative drug release of 89.23% at 20min and 82.90% at 20min respectively, The formulation F3and F4 (containing HPMC K4M) showed the percentage cumulative drug release of 95.54% at 20min and 90.52% at 20 min respectively. The details of in-vitro dissolution studies (Paddle method) showed in **Table 3**.

Flow through method The in-vitro dissolution study of formulation F0 (without polymer) was found to be 81.2% at 20min. Individual formulations F1and F2 (containing methyl cellulose) showed the percentage cumulative drug release of 73.1% at 20min and 75.4% at 20 min respectively, The formulation F3and F4 (containing Hydroxypropyl methylcellulose K4M) showed the percentage cumulative drug release of 85.3% at 20min and 74.7% at 20 min respectively. The details of in-vitro dissolution studies (Flow through method) showed in **Table 4**.

In-vitro permeation study

The in-vitro permeation study of formulation F0 (without polymer) was found to be 59.7 % at 20min. Individual formulations F1and F2 (containing methyl cellulose) showed the percentage cumulative drug release of 65.4 % at 20min and 60.1 % at 20 min respectively, the formulation F3and F4 (containing Hydroxypropyl methylcellulose K4M) showed the percentage cumulative drug release of 68.5% at 20min and 62.4 % at 20 min respectively. The details of in-vitro permeation study showed in **Table 5**.

Stability

The stability studies were carried out for F3 formulation at 25±2oC/60±5% RH and 40±2oC/75±5% RH for two months. The results indicated that the lollipops did not show any physical changes (weight variation, thickness, hardness and friability) during the study period and the drug content

was found at the end of two month. The details of Physico-chemical characterization of formulation during stability studies showed in **Table 6(a) and (b)**. There were no significant differences found in the percentage cumulative drug release after stability studies.

The details of in-vitro dissolution studies of formulation during stability studies showed in **Table 7 and 8**.

There were no significant differences found in the in-vitro permeation drug release after stability studies. The details of in-vitro permeation studies of formulation during stability studies showed in **Table 9**.

The stability studies showed very slight changes in dissolution and in-vitro permeation studies. **Figure 3 and 4** shows the comparison of drug release profile of all formulations. **Figure 5** shows the comparison of in-vitro permeation study of all formulations. This indicates that lollipops are fairly stable at storage condition. HPMC K4M is a hydrophilic polymer, hence facilitates quick release of drug. But as the concentration crosses the optimum quantity it retards drug release.

Table 2 : Evaluation Parameters of Medicated Lollipop of cefixime

Parameters	F0	F1	F2	F3	F4
Weight variation(gm)	4.98±0.01	4.98±0.04	4.98±0.03	4.99±0.03	4.99±0.05
Thickness(mm)	8.49±0.03	8.50 ±0.04	8.48±0.02	8.45±0.01	8.47±0.04
Hardness(kg/cm^2)	7.49±0.05	7.45±0.05	7.46±0.12	7.51±0.17	7.50±0.10
% Friability	0.41	0.44	0.40	0.35	0.37
% Drug content	84±0.567	90.6±0.669	93±0.392	97±0.952	88±0.484

Table 3: In-vitro drug release data of formulation F0 to F4(Paddle method)

Time (min)	F0	F1	F2	F3	F4
0	0	0	0	0	0
5	20.4	29.9	21.6	32.3	30.6
10	41.5	47.5	44.3	49.3	48.6
15	58.7	65.4	61.7	69.5	67.4
20	81.3	89.2	82.9	95.5	90.5

Table 4: In-vitro drug release data of formulation F0 to F4 (Flow through method)

Time(min)	F0	F1	F2	F3	F4
0	0	0	0	0	0
5	26.8	22.5	24	28.3	22.9
10	44.5	36.8	41.3	45.9	38.4
15	62.7	54.8	58.4	66.9	56.2
20	81.2	73.1	75.4	85.3	74.7

Table 5: In-vitro permeation study data of formulation F0 to F4

Time(min)	F0	F1	F2	F3	F4
0	0	0	0	0	0
5	13.9	15.6	12.8	20.9	14.5
10	30.5	35	31.5	39.7	32.4
15	46.7	52.1	48.6	59.5	49.7
20	59.7	65.4	60.1	68.5	62.4

Table 6: (a) and (b) Physicochemical characterization of formulation during stability studies

Time days		Weight variation (gm)	Thickness (mm)
		F3	F3
0		4.99	8.45
30	At 25±2˚C/60±5% RH	4.99	8.44
	At 40±2˚C/75±5%RH	4.88	8.39
60	AT 25±2˚C/60±5%RH	4.96	8.43
AT 40±2˚C/75±5%RH		4.82	8.37

Time days		Hardness (kg/cm)	Friability (%)	Drug content(%)
		F3	F3	F3
0		7.51	0.35	97.9
30	At 25±2˚C/60±5%RH	7.50	0.34	95.8
At 40±2˚C/75±5%RH		7.46	0.32	97.1
60	AT 25±2˚C/60±5%RH	7.48	0.34	94.7
AT 40±2˚C/75±5%RH		7.44	0.31	96.9

Table 7: In-vitro drug release data of medicated lollipops of cefixime formulations after stability studies (Paddle method)

Formulation	Cumulative drug release (%) at time 30 min				
	At 0 day	At 30 day		After 60 day	
	-	A *	B**	A *	B**
F3	95.54	94.98	93.60	94.96	93.55

A *:25±2˚C and 60±5%RH, B**:40±2˚C and 75±5%RH

Table 8: In-vitro drug release data of medicated lollipops of cefixime formulations after stability studies (Flow through method)

Formulation	Cumulative drug release (%) at time 30 min				
	At 0 day	At 30 days		After 60 days	
	-	A *	B**	A *	B**
F3	85.34	84.49	83.30	84.45	80.25

A *:25±2˚C and 60±5%RH, B:40±2˚C and 75±5%RH**

Table 9: In-vitro permeation data of medicated lollipops of cefixime formulations after stability studies

Formulation	Cumulative drug release (%) at time 30 min				
	At 0 day	At 30 days		After 60 days	
	-	A *	B**	A *	B**
F3	68.51	67.42	65.38	67.39	65.24

A *:25±2˚C and 60±5%RH, B:40±2˚C and 75±5%RH**

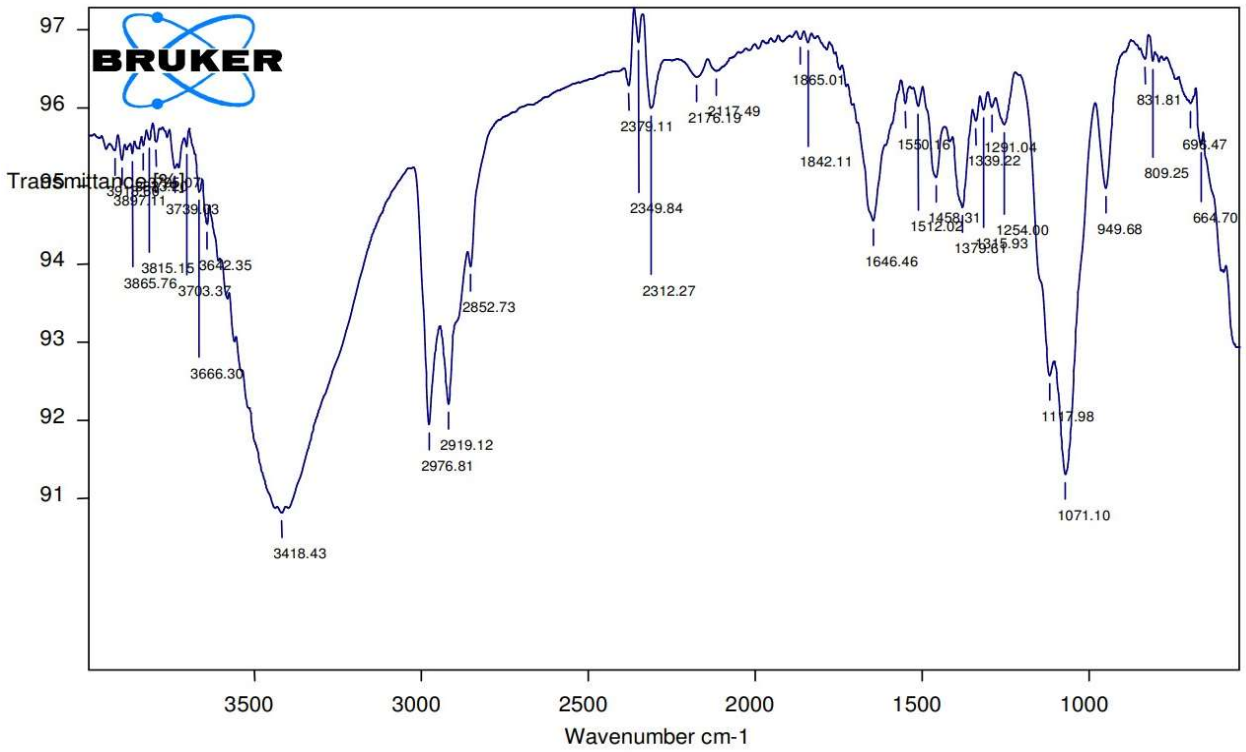


Figure 4: FTIR spectra of cefixime

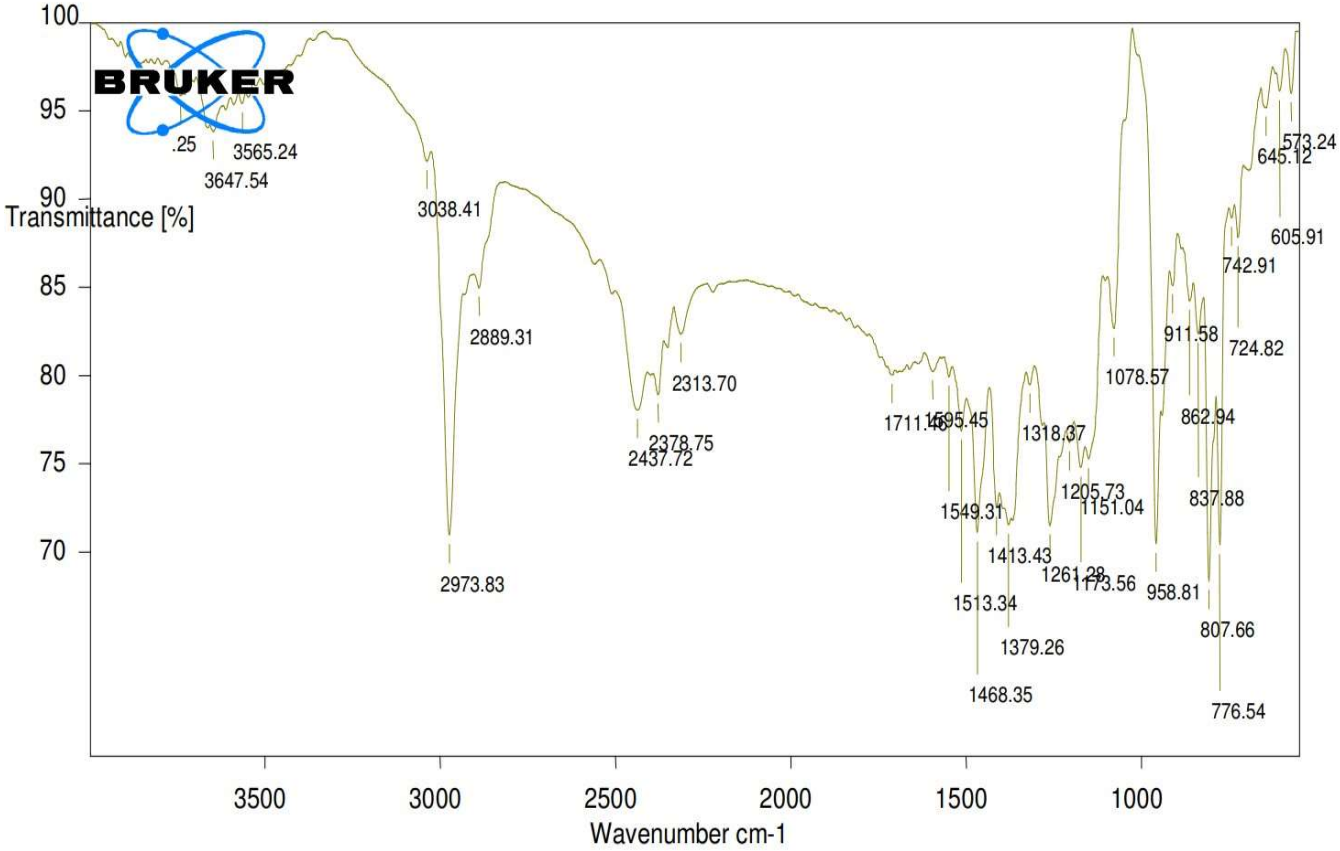


Figure 5: FTIR spectra of Cefixime + HPMC K4M

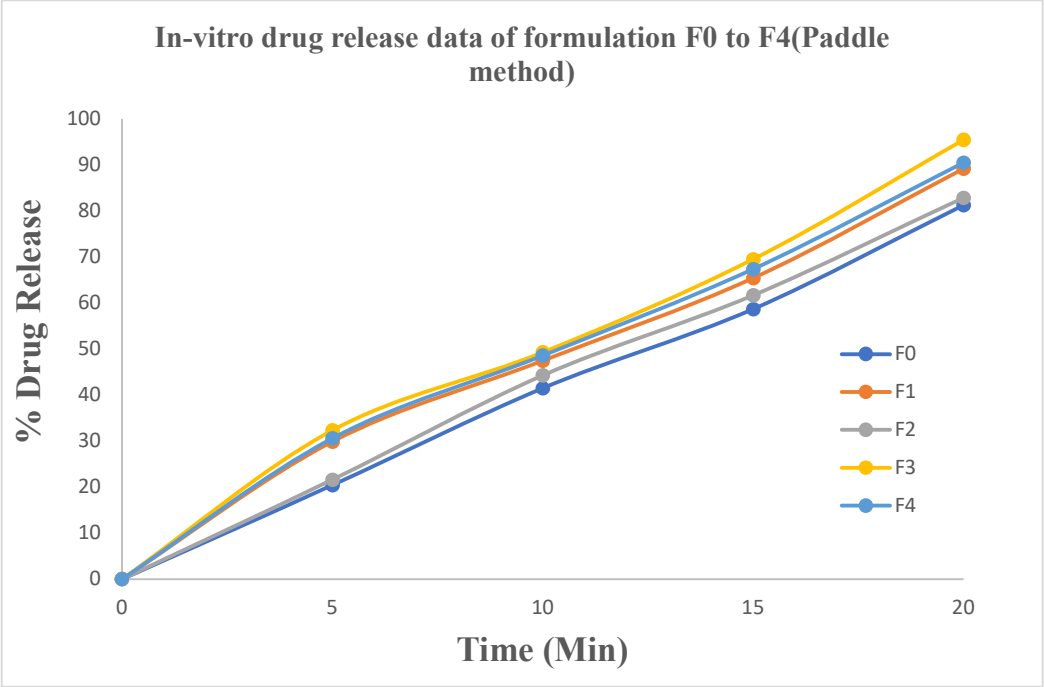


Figure 6: In-vitro release study data of formulation F0 toF4 (Paddle method)

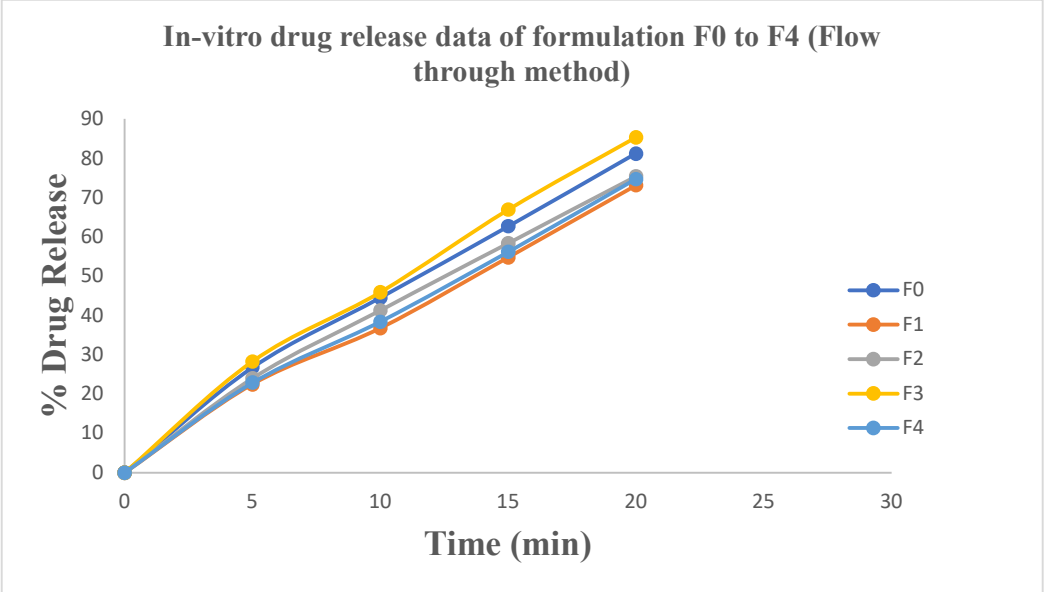


Figure 7: In-vitro release study data of formulation F0 toF4 (Flow through method)

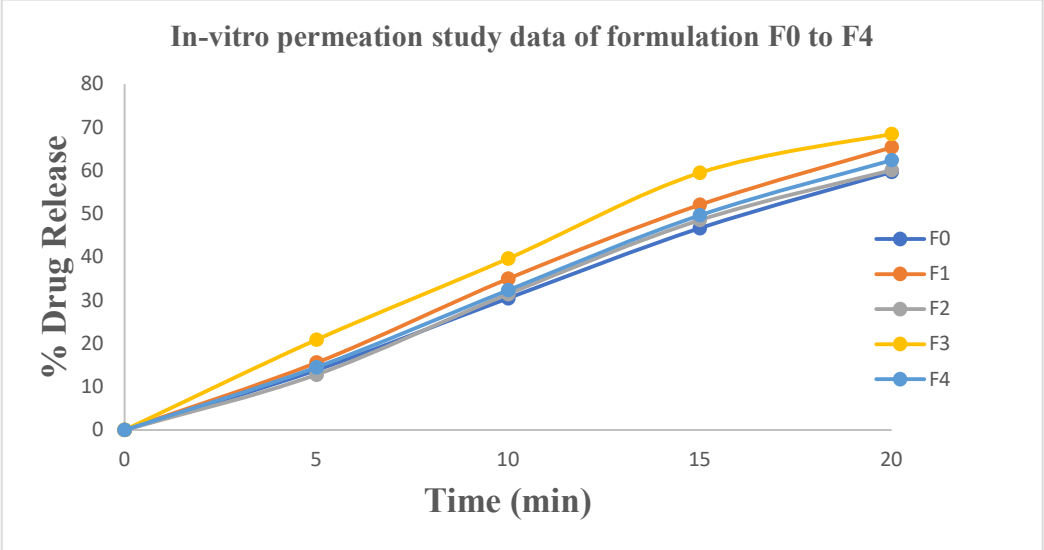


Figure 8: In-vitro permeation study data of formulation F0 toF4

CONCLUSION

In the present study, an attempt was made to formulate and evaluate candy based medicated lollipops of cefixime for the treatment of dry cough. The main interest in such a dosage form was for the development of new dosage form and the effect of different polymers on the in-vitro release of the drug and their stability. At the outset, estimation of drug by UV visible spectrophotometer was carried out. The possible interaction between the drug and excipient was studied by FT-IR spectroscopy which showed that there was no interaction between the selected drug and polymers under study.

A Candy based medicated lollipops of cefixime was prepared by Heating and congealing method. In this study, various formulations were developed using Methyl cellulose, HPMC K4M, sucrose, dextrose, citric acid and vanilla. Evaluation parameters like thickness, weight variation, hardness show that they were within the limits. Drug content uniformity was also found to be within the limit. In vitro release rate studies showed that the drug release was maximum in formulation F3. The rate of release of F3 by paddle method and flow throw cell method was 95.5% and 85.3% respectively at 20 minutes.

It can be concluded that the formulations F3 containing combination of saccharides and polymer HPMC K4M show better taste masking and improved drug release compare to the combination of saccharide and polymer methyl cellulose.

Hence it may be considered as preferred formulations. All the formulations were found to be stable over the storage period and at different conditions tested.

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