RESEARCH ARTICLE

Formulation and Evaluation of Cefixime Pediatric Medicated Lollipops

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Received: 11th Aug, 2024; Revised: 26th Sep, 2024; Accepted: 25th Nov, 2024; Available Online: 25th Dec, 2024

ABSTRACT

The study explores the formulation and evaluation of Cefixime medicated lollipops as a novel solution for paediatric oral drug delivery. The developed lollipops demonstrated desirable physical and pharmaceutical attributes, including consistent drug content, optimal hardness, and adherence to weight variation standards. Fourier-transform infrared spectroscopy confirmed the absence of significant drug-excipient interactions, ensuring formulation stability. Among the tested formulations, F2 exhibited the most promising results, achieving 100.05% cumulative drug release within 15 minutes during *In vitro* dissolution studies. Stability assessments over three months under accelerated conditions confirmed the lollipops' physical and chemical integrity, with drug content remaining within acceptable limits.This innovative dosage form addresses common challenges in pediatric drug administration by enhancing palatability, simplifying administration, and improving patient compliance. Additionally, the reduced dosing frequency associated with the formulation offers practical advantages for paediatric care. These findings position Cefixime medicated lollipops as a patient-friendly and efficient alternative to conventional paediatric dosage forms. It is recommended that further clinical studies be conducted to determine their effectiveness and safety in real-world paediatric settings.

Keywords: Cefixime, Medicated lollipops, Pediatric drug delivery, *In vitro* dissolution, Stability studies

How to cite this article: Vadivel SA, Sibichanduru E, Saravanan S, Karthik S. Formulation and Evaluation of Cefixime Pediatric Medicated Lollipops. International Journal of Drug Delivery Technology. 2024;14(4):2102-07. doi:10.25258/ijddt.14.4.22

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

The administration of medications in pediatric patients presents unique challenges, primarily due to issues such as taste, dosage form, and compliance. Children often resist taking medicines in conventional forms like tablets and capsules due to their unpalatable flavors or difficulty in swallowing. Thus, pediatric formulations require innovative approaches that can make the medication process more child-friendly while ensuring precise dosing and therapeutic effectiveness. Cefixime, a widely used third-generation cephalosporin antibiotic, plays an essential role in treating Children can contract possible to get respiratory tract infections, urinary tract infections, and otitis media in various ways. However, its bitterness and the need for strict dosing control limit its acceptability and compliance among pediatric patients. Medicated lollipops offer a promising solution to these challenges by creating an attractive, palatable drug delivery system that can make the administration of medications more enjoyable for children. A lollipop format allows for prolonged oral residence time, which can help in the sustained release of cefixime, potentially enhancing its absorption and therapeutic impact. This formulation strategy aligns with recent advancements in pediatric drug delivery, where emphasis is placed on combining efficacy, safety, and convenience. By masking the bitterness of cefixime and incorporating it into a slow-dissolving lollipop base, children are more likely to adhere to their treatment regimen, which is crucial for successful outcomes in bacterial infection management. The formulation of cefixime pediatric medicated lollipops requires careful consideration of factors like flavour masking, texture, uniformity of drug distribution, and stability. Moreover, evaluating the final product's organoleptic properties (taste, texture, and appearance) is essential to ensure it is not only effective but also appealing to children. In this study, we focus on formulating and evaluating of these medicated lollipops, using quality control tests that assess parameters such as drug release profile, physical and chemical stability, microbial safety, and taste-masking efficacy. Research goals include developing an alternative drug delivery system that addresses both therapeutic and patient compliance needs in the pediatric population. By overcoming traditional medication challenges and focusing on a formulation that children are more likely to accept, this study contributes to the growing field of pediatric pharmaceutics and provides valuable insights into improving pediatric drug administration. The findings could open up new pathways for the use of medicated confectioneries as effective vehicles for pediatric drug delivery, supporting better health outcomes and promoting more positive treatment experiences for young patients. Scarlet fever is an illness caused by *Group A Streptococcus* bacteria, which can produce a toxin leading to its characteristic red rash. Although not all people infected with this bacterium develop the scarlet rash, those sensitive to the toxin might experience it alongside symptoms like strep throat. Prompt treatment with

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antibiotics is typically effective.[1,2]. Figure 1 shows the Scarlet Fever

Symptoms of Scarlet Fever

Sore throat: Often very red, the patches may be white or yellowish.

Fever: It is a high temperature, sometimes with chills, of 101°F (38.3°C).The Itchy usually obtains 12-48 hours after the fever starts.

Rash: Red blotches as they develop, they will form tiny pink or red spots similar to sunburns, with a rough texture similar to sandpaper.

An infection of scarlet fever typically causes a rash that Symptoms include earaches, neck pain, elbow pain, inner thighs, groin pain, and chest pain. Face rashes rarely affect the face, but cheeks can blush and mouths can appear pale. This condition is called circumpolar pallor. Tip: Press a glass on the rash to turn it white. Generally, the rash fades within six days. It is possible that the rash is the only sign of milder cases, such as scarlatina.[3, 4]

Figure 2 shows the chemical structure of Cefixime

MATERIALS AND METHODS

Preformulation Studies

Preformulation studies were performed by physical characters and Chemical compatibility study by FT-IR spectroscopy.[5]

Preparation of medicated lollipop

Lollipop prepared by method of congealing and heating (Table 1). As the sugar was dissolved in water, the liquid was heated in a copper vessel for 2 hours while stirring continuously at 160°C. In order to achieve plastic mass, 90°C was lowered until a plastic mass was formed. After adding the drug, the colouring agent, flavouring agent, and taste masking agent, we mixed the material for 30 minutes. We poured the mixture into lollipop moulds, inserted sticks, and allowed them to cool and solidify. Once the lollipops have cooled, remove them from the moulds. Seal wraps of polythene were applied to the lollipops before they were sealed. We prepared all batches of formulations in total.[6-8]

Evaluation of formulated medicated lollipops

General appearance

The characteristics of physical objects were determined visually by observing their shape, colour, and texture.

Thickness

Tests were conducted to determine the thickness of prepared Lollipops using vernier calipers. An average was determined after three tests were conducted.[9]

Hardness

Measurements were made Testing hardness with the Monsanto hardness tester and measured in kg/cm2. Triplicate tests were conducted.[9]

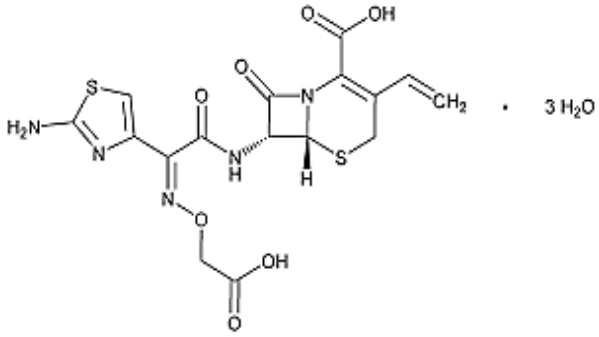

Figure 2: Chemical structure of Cefixime

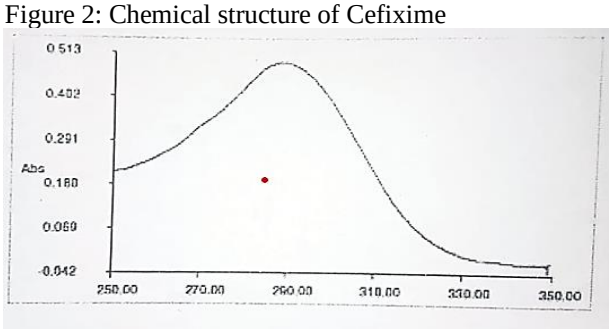

Figure 3: UV-Spectrophotometer for cefixime

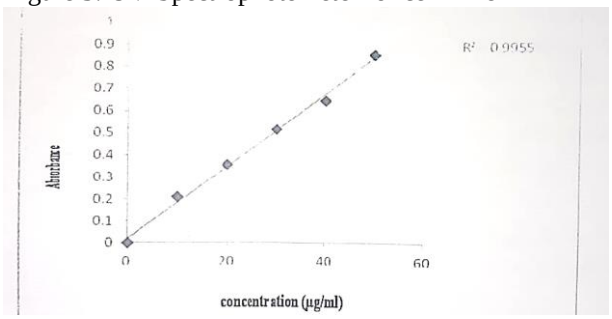

Figure 4: Calibration curve

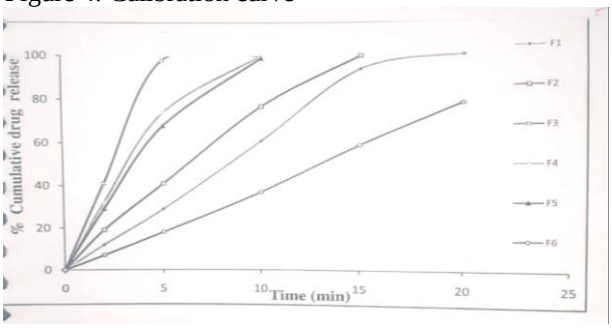

Figure 5: *In-vitro* release studies for different formulation

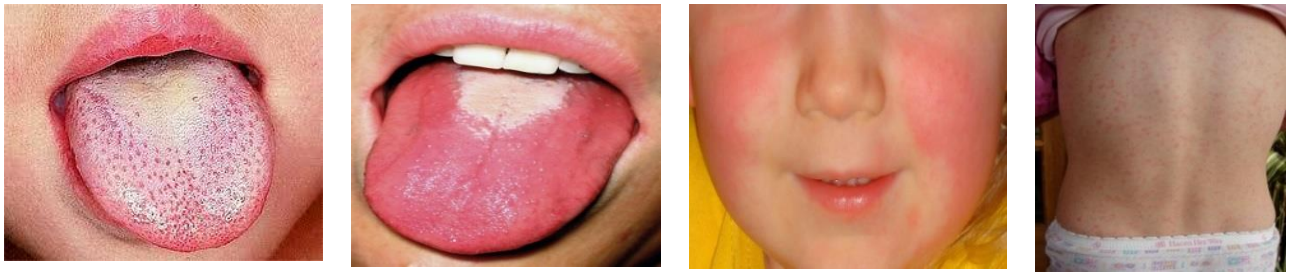

Figure: 1 Scarlet Fever

Table 2: Preformulation studies parameters

S.No.	Parameter	Observation
1	Description	White power
2	Identification	By IR-complies
3	Solubility	Sparingly soluble in water, soluble in ethanol
4	Melting point	218-225^{0}C
5	Assay	99.92% on dried basis (limit: 98%-101%)

Table 3: Absorbance value of cefixime

S.No:	Concentration (ɲg/ml)	Absorbance
1	0	0
2	10	0.211
3	20	0.362
4	30	0.527
5	40	0.656
6	50	0.866

Table 4: FT-IR Interpretation data of cefixime

Principal peaks	Characteristic group	
3317.35cm^{-1}	N-H Stretching	Aromatic amines.
1691.79cm^{-1}	C=C stretching	Saturated hydrocarbon
1741.87cm^{-1}	C=o stretching	Aromatic ketones
1452.52cm^{-1}	C-H bending	Aromatic
694.97cm $^{-1}$	C-Cl stretching	Sharp peaks of halogens

Weight variation

Lollipops were selected for weighing to determine weight variation each one is weighed individually after being randomly selected from the lot. A maximum weight variation is allowed in case of 50 mg is ± 5%.[10]

$$\%\,wt.\,variation \frac{av.wt. - individual\,wt.}{av.wt.} x100$$

Where,

Av. Wt. = average weight

Friability

A Roche friabilator was used to spin 20 lollipops at 25 rpm for four minutes after they were weighed and placed in it. We removed the Lollipops, dedusted them, and weighed them again. Lollipop friability was calculated by[10]

$$\%\,Friability = \frac{initial\,wt. - final\,wt.}{initial\,wt.} x100$$

Drug Content

We selected six lollipops from each batch and transferred them to 100ml volumetric flasks containing 0.IN HCL. Afterwards, 1 ml was taken from each and transferred to test tubes. After filters and dilutions, samples were analysed using UV-double beam spectrophotometers at 261 wavelength to calculate sample mean and standard deviation.

***In-vitro* dissolution study**

A study of *In vitro* release was conducted on all seven formulations. Simulating the mouth conditions is the best way to study release rate. We investigated the release of chemicals *In vitro* using a dissolution apparatus in the present study. As a result of changing the withdrawal time interval, the cumulative release of the drug was calculated. In order to dissolve the solution, we used a modified version of the USP II paddle type dissolution apparatus. We kept the temperature at 37°C and stirred at 100 rpm while maintaining the temperature at 37°C. Sodium phosphate buffer with Dissolution was carried out at pH 6.8. At 5-minute intervals for 25 minutes, fresh fluid was replaced with simulated salivary fluid at the same volume. We diluted each aliquot and analyzed it at 261nm using blanks on a Shimadzu UV-Visible spectrophotometer[8-12]

Stability Studies

Stability is one of the most important parameters to assess when developing formulations to address drug stability at the probable storage conditions. We studied the stability of the tablet formulations at two temperatures, namely 37°C and 45°C, over a period of six months. An adequate number of lollipops (10), packaged in amber-coloured screw-capped bottles, were kept at 37°C in an incubator. A 15-day interval was observed for the collection of samples for the measurement of drug content.[13-17]

Table: 1 Different formulations of lollipop

Ingredients	Formulation (mg)	Formulation (mg)	Formulation (mg)	Formulation (mg)	Formulation (mg)	Formulation (mg)
Cefixime	50	50	50	50	50	50
Sugar	5520	-	-	-	-	-
Sorbitol	-	5520	-	-	-	-
Manitol	-	-	5520	-	-	-
Maltitol	-	-	-	5520	-	-
Lactitol	-	-	-	-	5520	-
Xylitol	-	-	-	-	-	5520
Cream of tartar	100	100	100	100	100	100
Citric acid	50	50	50	50	50	50
Flavouring agent	q.s	q.s	q.s	q.s	q.s	q.s
Colouring agent	q.s	q.s	q.s	q.s	q.s	q.s

RESULT AND DISCUSSION

The present study of medicated lollipop contain Cefixime were formulated as six different formulations using sucrose and five types of polyols. Formulations were evaluated according to the parameters as detailed below, and preformulation studies were conducted on the raw drugs Among these factors are hardness, friability, weight variation, drug content, lollipops' stability, and *In vitro* drug release.

Preformulation study

The preformulation studies for cefixime were done for its physical characters and chemical compatibility by references (table 2). The result were presented the table no and ail parameters were complies with I.P standards.

Determination of uv- spectrophotometer for cefixime

The λ_{max} of cefixime analysed UV- spectrophotometer and it was found 261mm (Figure 3).

Calibration curve for cefixime

For calibrating cefixime, we used UV-Spectrophotometer and the absorbance value was presented in table 3 and figure 4.

Drug-polymer compatibility studies

Molecular properties of pure drugs and polymers, admixture of polymers and drugs used for lollipop preparation were studied by FTIR spectra of the samples were obtained by KBr disc method in the range of 4000 to 600c * m ^ - 1 According to the spectra, there are no drug-drug interactions, nor are there any drug-polymer interactions (table 4).From IR study and above data, it was evident that Cefixime and other excipients were mutually compatible. Since, the IT-IR spectra of drug with the polymer fig shows all the characteristic bands of drugli e 3317 35cm,1691.79cm,1741 87cm 1,1452.52cm-1,694.97cm-1) which are N-H stretching, C-C stretching, C-O stretching. C-H bending, stretching and C-CI stretching respectively). Therefore it can be concluded that there is no interaction occurred in between each of polymers and/or drug.

Evaluation of medicated lollipops

Assay of lollipops

The linear methodology shows good reproducibility, the calibration curve was found to be linear. The amount of cefixime present in the lollipop was calculated by using UV spectrophotometry and According to the results, the following was observed formulations containing Cefixime shows the amount of drug 98.05 + 0.34.

Hardness

Hardness of the all formulation was found to be within the range. The result showed that the hardness of all the tablet formulation was found within the limit and which complies with I.P standard (Table 5).

Thickness

We randomly selected 20 lollipops from the representative sample and measured their thickness with a Vernier calliper using digital Vernier measurement (Table 5).

Friability

An apparatus from Roche was used to determine the friability of the material. There was low friability in all formulations, ranging between 0.3-0.45. There were less than 8% friability values, which indicated that lollipops would be hard and compact.

Weight variation

Despite differences in batch size, all lollipops met the official requirements of uniform weight.

***In-vitro* release studies**

To assess the in-vitro drug release of cefixime medicated lollipops, we used a modified dissolution apparatus using a pH 6.8 phosphate buffer solution for 25 minutes. The results are showed in table 6 and figure 5

The cumulative % of drug release from the formulation Fl and F6 showed 100.05%, 76.11% respectively in 20 mins. The formulations F2 showed 100.09% drug release in 15 mins. The F4 and FS released 100.04%, 99.85% respectively in 10 mins. The F3 showed 98.34% in 5 min. From the all formulations of cefixime medicated lollipops the formulation F2 was found to be best formulation which

Table 5: Physical Evaluation of Medicated Lollipop

Formulation code	Thickness (mm)	Hardness Kg/cm^2	Weight variation (gm)	Friability (%)	Drug content (w/v)
F1	3.76 ± 0.02	8.9±0.2	5.71±0.8	0.13	98.69
F2	3.54±0.05	9.5±0.1	5.71±0.3	0.14	99.26
F3	3.78±0.1	2.2±0.6	5.68±0.6	15.16	98.57
F4	3.85±0.1	5.8±0.7	5.70±0.5	8.95	97.50
F5	3.45±0.7	6.5±0.5	5.73±0.2	3.79	99.83
F6	3.52±0.5	15.2±0.4	5.71±0.3	0.09	99.12

Calculated by averaging three determinations ±SD

Table 6: *In-vitro* release studies for different formulation

Time (min)	Cumulative % Drug release Formulation 1	Formulation 2	Formulation 3	Formulation 4	Formulatin 5	Formulation 6
0	0	0	0	0	0	0
2	12.25±0.32	19.24±0.52	41.57±0.32	32.52±0.12	29.33±0.43	7.34±0.62
5	29.35±0.24	41.33±0.47	98.34±0.42	74.17±0.29	68.48±0.43	18.45±0.72
10	61.17±0.18	77.58±0.82	100.02±0.47	100.04±0.18	99.85±0.52	37.21±0.44
15	94.40±0.52	100.09±0.74	-	-	-	59.73±0.52
20	100.05±0.32	-	-	-	-	78.11±0.75

showed good release and optimum hardness were as the formulation F3, F4 and F5 also showed good release but hardness of lollipop is low as compared with F2 which affect the formulation aspects like packing and transport time.

Stability testing

In the development of formulations, stability testing has become an integral part. A shelf life proposal is determined based on the storage conditions recommended for a drug or dosage form based on the information generated by this tool. Stability studies were conducted to find out whether the quality of the formulation was maintained during storage. The finalized formulation F2 were placed in stability chambers at Room Temperature (RT), 30±2°C /65+5% RH, 40±2°C/75±5% RH and 45+2°C/75±5% RH for about three months. Those Cefixime loaded medicated lollipops have been evaluated for both physical and chemical criteria at the end of first and second month (Table 7 to 10).

CONCLUSION

The formulation of Cefixime medicated lollipops presents a novel and effective approach to overcoming challenges associated with pediatric oral drug delivery. This study demonstrated that the developed lollipops possessed acceptable physical and pharmaceutical properties, including uniform drug content, optimal hardness, and compliance with weight variation standards. Infrared spectroscopy confirmed Ensured the stability of the formulation by ensuring no significant Excipient-drug interactions Cefixime in the formulation. Among the various formulations evaluated, F2 exhibited superior *In vitro* dissolution characteristics, achieving 100.05% cumulative drug release within 15 minutes, highlighting its potential as the most efficient formulation for drug release. Stability studies conducted over three Temperature of 40°C with a relative humidity of 75%, and months at 40°C with a temperature of 2°C indicated that the lollipops maintained their physical integrity and chemical stability, with drug content remaining within specified limits. This

Table 7: Room-temperature stabilities of F2 (25±2^{0}C / 65±5% RH)

S.No	Characteristics	1 month	2 months	3 months
1	Physical appearance	Flat and shaped slightly sticky and brown color.	Flat and shaped slightly sticky and brown color.	Flat and shaped slightly sticky and brown color.
2	Hardness (kg/cm^2)	9.5±0.1	9.5±0.1	9.4±0.9
3	Drug content (mg/ tablet)	99.26±0.34	99.26±0.44	99.26±0.31
4	In-vitro drug release at the end of 15min *± SD	100.09±74	100.06±0.48	100.01±0.81

*Average of 3 determinations

Table 8: Room-temperature stabilities of F2 (30±2^{0}C/ 65±5% RH)

S.no	Characteristics	1 month	2 months	3 months
1	Physical appearance	Flat and shaped slightly sticky and brown color.	Flat and shaped slightly sticky and brown color.	Flat and shaped slightly sticky and brown color.
2	Hardness (kg/cm^2)	9.5±0.1	9.5±0.42	9.4±0.76
3	Drug content (mg/ tablet)	99.26±0.34	99.24±0.49	99.23±0.30
4	In-vitro drug release at the end of 15min *± SD	100.09±0.74	100.07±0.18	100.03±0.21

Table 9: Room-temperature stabilities of F2 (40±2^{0}C/ 75±5% RH)

S.no	Characteristics	1 month	2 months	3 months
1	Physical appearance	Flat and shaped slightly sticky and brown color.	Flat and shaped slightly sticky and brown color.	Flat and shaped slightly sticky and brown color.
2	Hardness (kg/cm^2)	9.5±0.1	8.9±0.92	8.1±0.42
3	Drug content (mg/ tablet)	99.26±0.34	99.25±0.44	99.25±0.31
4	In-vitro drug release at the end of 20min *± SD	100.09±0.74	100.08±0.13	100.04±0.73

*Average of 3 determinants

Table 10: Room-temperature stabilities of F2 (45±2^{0}C /75±5% RH)

S.no	Characteristics	1 month	2 months	3 months
1	Physical appearance	Flat and shaped slightly sticky and brown color.	Flat and shaped slightly sticky and brown color.	Flat and shaped slightly sticky and brown color.
2	Hardness (kg/cm^2)	9.5±0.1	8.3±0.31	7.9±0.24
3	Drug content (mg/ tablet)	99.26±4.34	98.75±0.41	98.25±0.31
4	End-of-life drug release *In vitro* 20min *± SD	100.09±0.74	99.08±0.13	98.54±0.73

*Average of 3 determinants

study concludes that Cefixime medicated lollipops offer an innovative, patient-friendly alternative to conventional pediatric dosage forms by enhancing palatability, improving ease of administration, and potentially increasing patient compliance. These advantages, combined with the reduced dosing frequency associated with the formulation, make it a promising candidate for pediatric use. This dosage form needs to undergo further clinical studies to validate its therapeutic effect and safety in a real-world pediatric population.

REFERENCE

1. Cirri M, Mennini N, Nerli G, Rubia J, Casalone E, Melani F, Maestrelli F, Mura P. Combined use of cyclodextrins and amino acids for the development of cefixime oral solutions for pediatric use. Pharmaceutics. 2021;13(11):1923. doi: 10.3390/pharmaceutics13111923.
2. Jagruti B, Darshit R. Development and in vitro evaluation of medicated lollipop containing cefixime for pediatrics. International Journal of Biology, Pharmacy and Allied Sciences. 2024;13(7):3306-3325. doi: 10.31032/IJBPAS/2024/13.7.8154.
3. Fragkou PC, De Angelis G, Menchinelli G, Can F, Garcia F, Morfin-Sherpa F, Dimopoulou D, Mack E, de Salazar A, Grossi A, Lytras T. ESCMID COVID-19 guidelines: diagnostic testing for SARS-CoV-2. Clinical Microbiology and Infection. 2022 ;28(6):812-822.
4. Brogden RN, Campoli-Richards DM. Cefixime: a review of its antibacterial activity, pharmacokinetic properties and therapeutic potential. Drugs. 1989;38(4):524-50.
5. Patil NS, Patil PN, Patil NL, Patil DR, Jain AS, Shaikh AZ, Tadavi SA. Formulation and evaluation of medicated lollipop. International Journal for Research in Applied Science and Engineering Technology. 2023;11(V):52302. doi: 10.22214/ijraset.2023.52302.
6. Purushotham RK, Kamamia EK, Zakaullah S, Arshiya SA, Ashok KC, Anand C. Medicated lollipops of paracetamol for paediatric patients. World Journal of Pharmaceutical Sciences. 2012;1(3):1226-1234.
7. Kamath J, Jayesh D, Misquith J. Preparation and in-vitro evaluation of levamisole Hydrochloride as a candy based anthelmintic medicated lollipops for pediatrics. International Journal of Pharmaceutical Science and Research. 2012; 3:523-534.
8. Rao KP, Nagoba SN, Vishwanath Reddy VR, Ayshiya SA, Zakaullah S, Kumar CA, Anand C, Saran SV. Medicated lollipops for the treatment of oral thrush in children. 2012; 95-102.
9. Majumdar S, Jogi V. Development of Antifungal Lozenges for Treatment of Oropharyngeal Candidiasis. Indo American Journal of Pharmaceutical Research. 2015;5(1):25-32
10. Phaechamud T, Tuntarawongsa S. Clotrimazole soft lozenges fabricated with melting and mold technique. Research Journal of Pharmaceutical, Biological and Chemical Sc iences. 2010;1(4):579-586.
11. Jagdale S, Gattani M, Bhavsar D, Kuchekar B, Chabukswar A. Formulation and evaluation of chewable tablet of levamisole. International Journal of Pharmaceutical Sciences and Research 2010;1(3):282-289.
12. Esimone CO, Okoye FBC, Odimegwu DC, Nworu CS, Oleghe PO, Ejogha PW. In vitro antimicrobial evaluation of lozenges containing extract of garlic and ginger. International Journal of Health Research. 2010;3(2):105-110.
13. George AE, Davis DR, William WH. Reduction in duration of common colds by zinc gluconate lozenges in a double-blind study. Antimicrobial Agents and Chemotherapy. 1984 ;25(1):20-24.
14. Purushotham RK, Ashok KC, Afshanlaheji, Anilkumar KB, Manjunath P, Baburao NCK. Formulation and evaluation of anti-asthmatic theophylline tablet lozenges. International Journal of Pharmaceutical Sciences and Research. 2011;3(1):125-128.
15. Patel H, Patel N, Patel H. Formulation development and evaluation of the dispersible tablet of cefixime. International Journal Of Modern Pharmaceutical Research. 2012;1(2):45-49.
16. Sayeed A, Mohiuddin MH. Mouth dissolving tablets: An overview. International Journal of Pharmaceutical and Bio-Medical Science. 2011;2(3):171-174.
17. Sharma V, Singh L, Sexena P, Kumar J. Formulation and evaluation of mouth dissolving tablets of cefixime. International Research Journal of Pharmacy. 2011;1(2):171-174.