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Exploring Biomedical Innovations in the Formulation and Assessment of Medicated Hard Candy Lozenges Containing Metoclopramide Hydrochloride

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Abstract

The objective of this study was to formulate and evaluate metoclopramide hydrochloride medicated lozenges for antiemetic action through buccal absorption by incorporating a polymer. All formulations were developed and assessed for in-vitro drug release, physical appearance, weight variation, thickness, hardness, moisture content, mouth-dissolving time, and drug content. The prepared lozenges exhibited uniformity in weight and thickness. The hardness of all formulations ranged between 7.3–15.50 kg/cm², falling within standard limits. The mouth-dissolving time varied from 7:06 to 30:28 minutes, with formulation F10 taking the longest to dissolve. The acceptable moisture content for lozenges should range from 0.5% to 1.5%, and the formulated lozenges meet this criterion. The drug content across all formulations (F1–F10) remained within the acceptable range of 90%–110%. In the in-vitro drug release study, metoclopramide hydrochloride lozenges containing methyl cellulose at concentrations of 0.75%, 0.5%, and 0.25% exhibited the highest drug release within 30 minutes, with formulation F10 achieving 100.6% release. The in-vitro release kinetic study of the optimized formulation (F10) followed a first-order release pattern, with drug release governed by diffusion, dissolution, and a non-Fickian diffusion mechanism. Based on this study, isomalt was successfully utilized as a tooth-friendly sugar substitute in medicated lozenges. Due to its low-caloric value and resistance to plaque formation, it can be safely recommended for diabetic and pediatric patients.

Keywords: Formulation development, evaluation, metoclopramide hydrochloride, hard candy lozenges

INTRODUCTION

Oral drug delivery is the most commonly preferred and straightforward method, as it offers the largest active surface area among all drug delivery systems for administering various medications. This route is extensively utilized for both conventional and novel drug delivery approaches. [1, 2].

Lozenges are solid, medicated dosage forms with added flavor and sweetness, designed to be sucked and held in the mouth or pharynx to alleviate local irritation or treat infections in these areas. They are a widely popular and innovative oral dosage form, often classified as confectionery-based drug delivery products. Lozenges provide an efficient means of delivering drugs either locally or systemically via the oral cavity. Their popularity is largely due to their ease of use, particularly for geriatric and pediatric patients, as well as their

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broad patient acceptance. The development of novel drug delivery systems for existing medications aims to enhance efficacy, bypass first-pass hepatic metabolism, eliminate the need for water intake, improve bioavailability, and reduce dosing frequency while minimizing side effects [3–7].

Oral infections are a widespread public health concern, impacting various parts of the mouth, including the tongue dorsum, lateral sides of the tongue, buccal epithelium, hard and soft palate, as well as supragingival and subgingival plaque on tooth surfaces. [8, 9].

The primary goal of this study is to formulate and evaluate metoclopramide hydrochloride (HCl) lozenges using various sugar bases, plasticizers, and methyl cellulose as a polymer. This formulation is designed to improve bioavailability by avoiding the hepatic first-pass metabolism of the drug.

Metoclopramide HCl is a powerful antiemetic medication used to treat nausea and vomiting, particularly those caused by cancer treatment and pregnancy. Metoclopramide used in the treatment of Gastroparesis by stimulating the stomach activity to hasten the process of gastric emptying. The bioavailability of metoclopramide HCL was about 48%–80% it can be reduced by upto 30% because of first pass metabolism. Hence by formulating metoclopramide HCL as medicated lozenges, favors the buccal absorption which overcomes the drug limitations by avoiding the first pass metabolism. Metoclopramide HCL has melting point 180^{o}C–183^{o}C thus making it an ideal candidate for formulation of lozenges. Molecular weight of the drug is 354.3, which is ideal characteristic for the oral mucosal drug delivery. It is a slightly bitter drug. Taste is masked by formulated as lozenges.

MATERIALS USED

Metoclopramide HCL is supplied by Tablets India Limited, Chennai, ensuring pharmaceutical quality and reliability for therapeutic use.

Isomalt, obtained from TTK Pharma Ltd, Chennai, functions as a multifunctional excipient in pharmaceutical formulations, offering sweetness with lower calorie content.

Sucrose, also from TTK Pharma Ltd, Chennai, functions as a common pharmaceutical excipient, contributing sweetness and aiding in formulation stability.

Liquid glucose, sourced from the same supplier, TTK Pharma Ltd, Chennai, serves as a versatile excipient, providing a source of carbohydrates and aiding in formulation processes. These materials are chosen for their trusted origins and compliance with pharmaceutical standards, supporting various medicinal applications and formulations.

PREFORMULATION STUDIES

Preformulation studies refer to preliminary investigations conducted on drug substances prior to formulation development. These studies aim to assess the physicochemical characteristics of the active pharmaceutical ingredient (API) and examine its compatibility with various excipients. They provide crucial insights into stability, solubility, polymorphism, and degradation pathways of the API, influencing formulation strategies and dosage form selection. By identifying optimal conditions for drug delivery, preformulation studies facilitate the design of effective and safe pharmaceutical products. These investigations are integral in enhancing the overall efficiency and success of drug development processes, ensuring that formulations meet regulatory standards and patient requirements.

Preformulation studies represent the first stage in the systematic development of any formulation. They involve examining the physical and chemical properties of a drug substance both alone and in combination with excipients. These studies primarily emphasize the physicochemical attributes of a new compound that could impact drug performance and the

design of an optimal dosage form. The primary objective of preformulation testing is to generate crucial data that enable formulators to create stable and bioavailable dosage forms, as shown in Table 1.

Table 1. Materials used in the formulations.

S.N.	Chemicals	Suppliers
1.	Metoclopramide HCL	Tablets India Limited, Chennai.
2.	Isomalt	TTK Pharma Ltd, Chennai.
3.	Sucrose	TTK Pharma Ltd, Chennai.
4.	Liquid glucose	TTK Pharma Ltd, Chennai.

Determination of Melting Point of Metoclopramide HCL

The melting point of metoclopramide HCl was determined using an electrical melting point apparatus with the capillary method, as shown in Table 2.

Determination of λ max of Metoclopramide HCL

A solution of metoclopramide HCl in phosphate buffer (pH 6.8) was prepared and analyzed using a spectrophotometer, scanning from 200 to 400 nm to determine the drug's maximum absorption wavelength (λ max).

Table 2. Formulation table.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Metoclopramide HCL (mg)	5	5	5	5	5	5	5	5	5	5
Sucrose	1880	–	–	–	–	–	–	–	–	–
Dextrose	–	1880	–	–	–	–	–	–	–	–
Mannitol	–	–	1880	–	–	–	–	–	–	–
Isomalt	–	–	–	1880	1880	1880	1880	1862	1868	1874
Liquid glucose	500	500	500	500	500	500	500	500	500	500
Citric acid	25	25	25	25	25	25	25	25	25	25
Aspartame	90	90	90	90	90	90	90	90	90	90
Propylene glycol	–	–	–	–	0.1 ml	–	–	–	–	–
PEG 200	–	–	–	–	–	0.1 ml	–	–	–	–
Glycerine	–	–	–	–	–	–	0.1 ml	0.1 ml	0.1 ml	0.1 ml
Menthol	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Methyl cellulose	–	–	–	–	–	–	–	18.5 0.75%	12.5 0.50%	6.25 0.25%
Color	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s
Flavor	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s
Purified water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s
Total (g)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5

DRUG-EXCIPIENT COMPATIBILITY STUDIES

The successful design and development of a dosage form necessitate thorough evaluation of the physical and chemical properties of both the drug substances and the excipients incorporated in the final product. The stability and efficacy of a dosage form largely depend on the appropriate selection of excipients incorporated into the formulation. To ensure the formulation is stable, effective, easy to administer, and safe, the drug and excipients must be compatible. A compatibility study was conducted using Fourier Transform Infrared (FTIR) Spectroscopy, employing the potassium bromide pellet technique within the range of 4000 cm^{-1} to 400 cm^{-1}. The obtained spectra were examined and analyzed

for compatibility assessment.

PREPARATION OF PHOSPHATE BUFFER pH 6.8

A total of 13.609 g of potassium hydrogen orthophosphate was dissolved in 500 ml of distilled water to prepare a 0.2 M solution. Similarly, 4 g of sodium hydroxide was dissolved in 500 ml of water to create a 0.2 M solution. Then, 500 ml of the 0.2 M potassium hydrogen orthophosphate solution was combined with 224 ml of the 0.2 M sodium hydroxide solution and diluted with distilled water to a final volume of 2 liters.

PREPARATION OF CALIBRATION CURVE FOR METOCLOPRAMIDE HCL

A precise amount of 10 mg of metoclopramide HCL was weighed and transferred into a 100 ml volumetric flask. The drug was dissolved in phosphate buffer (pH 6.8), and the volume was brought up to 100 ml to obtain a stock solution with a concentration of 100 μg/ml. From this stock solution, aliquots of 3, 6, 9, 12, 15, and 18 ml were further diluted with phosphate buffer (pH 6.8) to a final volume of 100 ml, resulting in concentrations of 3, 6, 9, 12, 15, and 18 μg/ml. The prepared solutions were then examined at 272 nm using a double-beam UV-visible spectrophotometer.

FORMULATION TABLE FOR METOCLOPRAMIDE HYDROCHLORIDE MEDICATED LOZENGES

Formulation Table for Medicated Lozenges Containing Metoclopramide Hydrochloride provides a detailed outline of the ingredients, and their respective quantities used in the preparation of lozenges. This document serves as a comprehensive guide for pharmacists and manufacturers, specifying the exact formulation steps and proportions required to ensure consistent dosage and efficacy. It includes information on excipients, active ingredients, and the process parameters necessary for producing high-quality lozenges. These formulation tables play a crucial role in pharmaceutical development, ensuring that every batch complies with regulatory standards while providing the intended therapeutic effects safely and effectively.

PREPARATION OF METOCLOPRAMIDE HYDROCHLORIDE HARD CANDY MEDICATED LOZENGES

The Preparation of Metoclopramide Hydrochloride Hard Candy" involves detailed instructions for compounding hard candy infused with the medication. This procedure outlines the specific steps and ingredients needed to ensure precise dosage and uniform distribution of the active ingredient throughout each candy piece. It includes meticulous temperature controls and mixing times to achieve desired consistency and therapeutic efficacy. Such formulations are crucial in pharmaceutical compounding, offering a palatable delivery method for medications while maintaining stability and quality. This preparation method adheres to stringent regulatory guidelines to ensure safety, potency, and consistency in each batch produced.

The lozenges were formulated using the heating and congealing method. A syrupy base was prepared by dissolving the required amount of sugar in water and heating the mixture on a hotplate. The temperature was maintained between 105°C and 110°C until the solution thickened. After 30 minutes of continuous heating, the drug and other excipients (excluding the plasticizer) were manually added and thoroughly mixed. The mixture was further heated for 45 minutes before incorporating the plasticizer. The prepared syrupy base was then poured into pre-cooled, pre-lubricated molds and left undisturbed for 10–15 minutes. Finally, the lozenges were removed from the molds and allowed to air dry.

RESULTS AND DISCUSSION

Preformulation Studies

Preformulation studies involve initial assessments of drug substances before the formulation development process. These studies primarily examine the physicochemical characteristics of the active pharmaceutical ingredient (API) and assess its compatibility with various excipients. They provide crucial insights into stability, solubility, polymorphism, and degradation pathways of the API, influencing formulation strategies and dosage form selection. By identifying optimal conditions for drug delivery, preformulation studies facilitate the design of effective and safe pharmaceutical products. These investigations are integral in enhancing the overall efficiency and success of drug development processes, ensuring that formulations meet regulatory standards and patient requirements.

CHARACTERIZATION OF THE DRUG

Melting Point of Metoclopramide HCL

Melting point was measured by the capillary method, and it was found to be 182ºC.

Determination of λ Max of Metoclopramide HCL

The maximum absorbance of the metoclopramide HCL was studied and found to be 272 nm. Hence, the wavelength of 272 nm was selected for the analysis of the drug in dissolution media as shown in Figure 1.

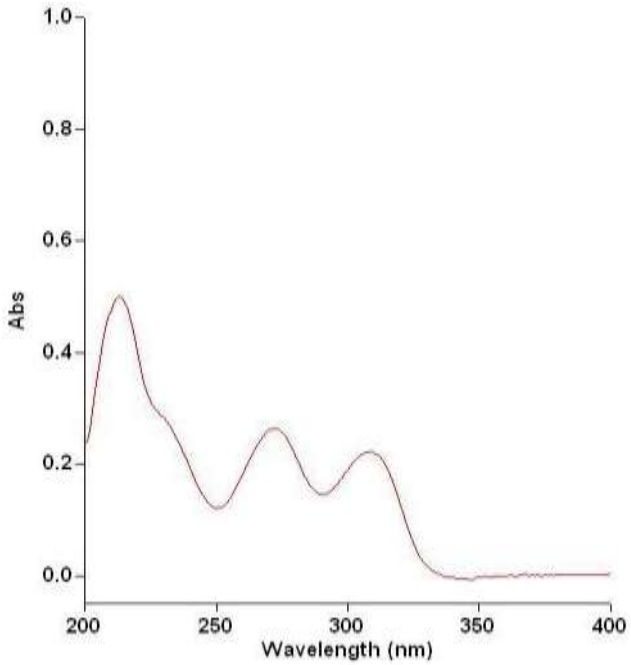

Figure 1. The UV spectrum of metoclopramide HCL in phosphate buffer 6.8.

DRUG-EXCIPIENT COMPATIBILITY STUDY

The excipient study was performed to assess the compatibility between the drug and excipients.

Physical compatibility was observed visually. The study indicates that the drug and excipients are physically compatible, as no color change was observed. The selected excipients were found to be suitable for formulation, as shown in Table 3.

CHEMICAL COMPATIBILITY STUDY

Observation

There is no disappearance of characteristic peaks of drug in FT-IR spectra as shown in Figure 2 and Table 4.

DATA FOR CALIBRATION CURVE

It was found that the solutions metoclopramide HCL in phosphate buffer pH as shown in Figure 3.

Table 3. Physical compatibility of drug and excipients.

S.N.	Drug + Excipients	Description and Condition	Room Temperature and 40°C/75% RH in Days		
			10th	*20th*	*30th*
1.	Metoclopramide HCL	White crystalline powder	NC	NC	NC
2.	Sucrose	White crystalline powder	NC	NC	NC
3.	Mannitol	White crystalline powder	NC	NC	NC
4.	Dextrose	White powder	NC	NC	NC
5.	Isomalt	White powder	NC	NC	NC
6.	Citric Acid	White crystalline powder	NC	NC	NC
7.	Aspartame	White powder	NC	NC	NC
8.	Methyl cellulose	White powder	NC	NC	NC

Note: NC: No change.

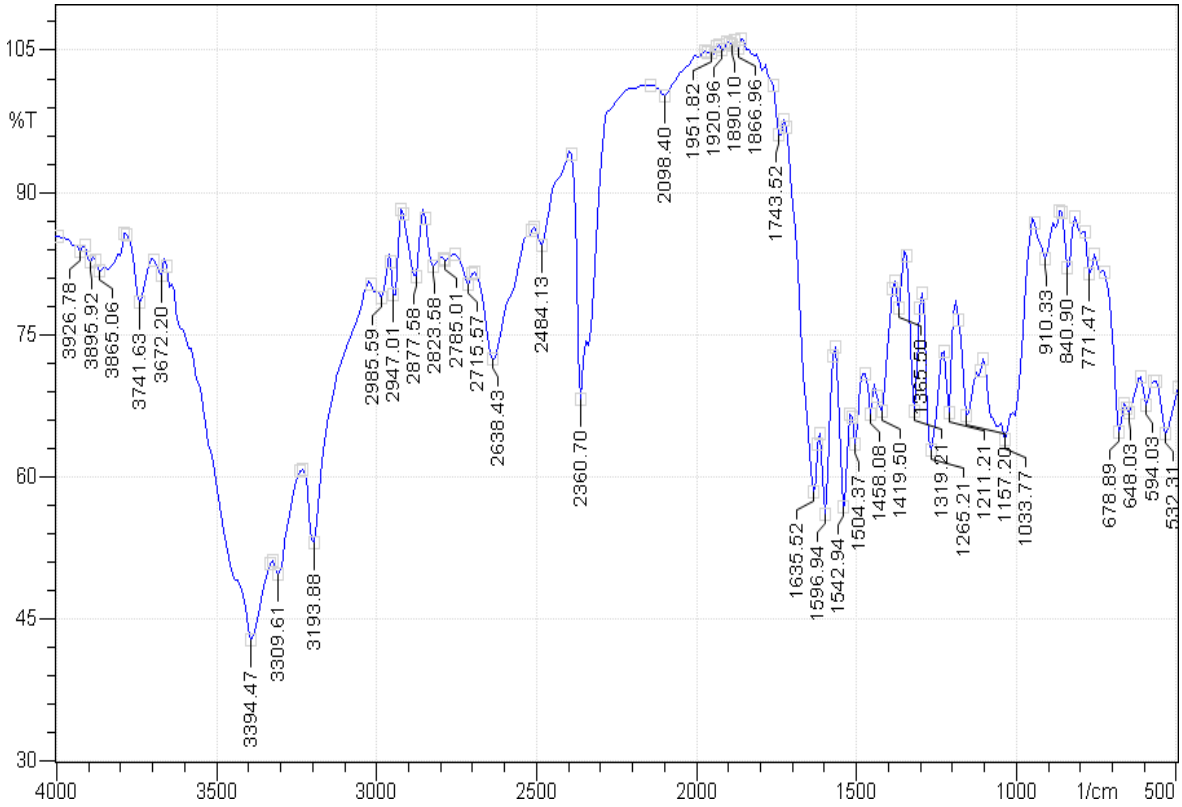

Figure 2. IR for the optimized formulation.

Table 4. FTIR spectral interpretation of the optimized formulation.

S.N.	Functional Group	Characteristic Peak		Observed Peak	
		Stretching	*Bending*	*Stretching*	*Bending*
1.	Ar–NH_2	3500–3350	–	3394.4	–
2.	CO–NH	1700–1500	–	1635.5	–
3.	Ar–C = C	1600–1400	–	1596.9	–
4.	C–O–C	1250–1050	–	1265.2	–
5.	$C–Cl_3$	800–600	–	678.8	–

Hence, there is no interaction.

6.8 showed linearity $R^2 = 0.9999$ in absorbance at concentrations of 3–18 µg/ml and obey Beer–Lambert's law as seen in Table 5.

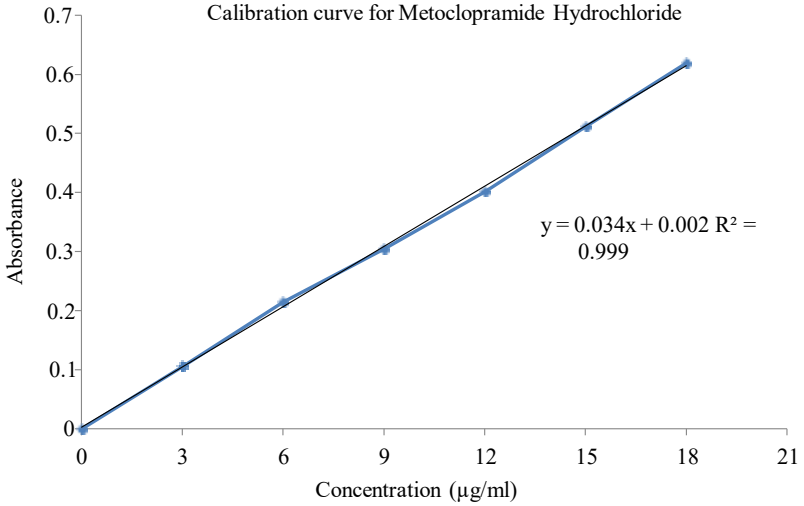

Figure 3. Calibration curve for metoclopramide HCL.

Table 5. Concentration and absorbance of metoclopramide HCL.

Concentration (µg/ml)	Absorbance at λ 272 nm
0	0
3	0.106 ± 0.005
6	0.215 ± 0.005
9	0.305 ± 0.003
12	0.402 ± 0.005
15	0.512 ± 0.004
18	0.620 ± 0.005
R^2	0.9995

Note: n = 3.

PHYSICAL APPEARANCE OF METOCLOPRAMIDE HCL MEDICATED LOZENGES

The physical appearance evaluation revealed that all formulations had a translucent and smooth texture. However, formulations F1, F5, and F6 displayed a mildly thick and adhesive texture. The remaining formulations were found to be well-developed and acceptable, as presented in Table 6.

Table 6. Physical appearance of formulated lozenges.

S.N.	F Code	Clarity	Texture	Consistency	Stickiness
1.	F1	Translucent	Smooth	Slightly thick	Sticky
2.	F2	Translucent	Smooth	Thick	Non-sticky
3.	F3	Translucent	Smooth	Thick	Non-sticky
4.	F4	Translucent	Smooth	Thick	Non-sticky
5.	F5	Translucent	Smooth	Slightly thick	Sticky
6.	F6	Translucent	Smooth	Slightly thick	Sticky
7.	F7	Translucent	Smooth	Thick	Non-sticky
8.	F8	Translucent	Smooth	Thick	Non-sticky
9.	F9	Translucent	Smooth	Thick	Non-sticky
10.	F10	Translucent	Smooth	Thick	Non-sticky

WEIGHT VARIATION OF METOCLOPRAMIDE HCL HARD CANDY LOZENGES

The average weight of 20 lozenges was taken to determine weight variation from each formulated lozenge. There was no specified deviation in the weight of lozenges, comparing each formulation. This indicates the uniform weight of the prepared lozenges as seen in Table 7.

Table 7. Weight variation of formulated medicated lozenges.

S.N.	Formulation Code	Weight of Lozenges
1.	F1	2.5035 ± 0.032
2.	F2	2.493 ± 0.039
3.	F3	2.488 ± 0.059
4.	F4	2.515 ± 0.023
5.	F5	2.507 ± 0.030
6.	F6	2.508 ± 0.036
7.	F7	2.518 ± 0.041
8.	F8	2.511 ± 0.038
9.	F9	2.519 ± 0.040
10.	F10	2.503 ± 0.029

Note: Mean ± SD (n = 20).

HARDNESS OF MEDICATED LOZENGES

The hardness of all formulated lozenges was found within the range of 7.3–15.50 kg/cm^2. Among the 10 formulations of lozenges, the lowest value for hardness was noted for F3 (i.e., 7.3 kg/cm^2) and the highest, that is, 15.50 kg/cm^2 for F9. The hardness of the lozenges is due to the presence of methyl cellulose as seen in Table 8.

Table 8. Hardness of formulated medicated lozenges mean ± SD (n = 3).

S.N.	Formulation Code	Hardness of Lozenges (kg/cm^2)
1.	F1	10.5 ± 0.57
2.	F2	10.75 ± 0.92
3.	F3	7.3 ± 0.42
4.	F4	13.6 ± 0.64
5.	F5	10.65 ± 0.57
6.	F6	9.65 ± 0.56
7.	F7	15.25 ± 0.63
8.	F8	15.45 ± 0.43
9.	F9	15.50 ± 0.74
10.	F10	15.30 ± 0.74

THICKNESS OF MEDICATED LOZENGES

Thickness of the lozenges was found to be in the uniform range of 12–12.26 mm as seen in Table 9.

MOUTH DISSOLVING TIME OF MEDICATED LOZENGES

The mouth dissolving time of the medicated lozenges was observed to range between 7:06 and 30:28 minutes. The addition of plasticizer increases the mouth dissolving time of the formulations. F10 formulation shows the highest mouth dissolving time as seen in Table 10.

MOISTURE CONTENT OF MEDICATED LOZENGES

Moisture content determination is a critical parameter of lozenges quality. It affects the manufacturing and packaging of lozenges. The acceptable moisture content should fall within the range of 0.5% to 1.5%.

The results showed that the moisture content in the prepared lozenges ranged between 0.5% and 1.5%, which falls within the standard limits, as presented in Table 11.

DRUG CONTENT UNIFORMITY OF METOCLOPRAMIDE HCL MEDICATED LOZENGES

The drug content of all lozenges (F1–F10) is within 90% to 110% as per specification when compared with the metoclopramide HCL tablets (IP 2018), Volume II) as seen in Table 12.

Table 9. Thickness of formulated medicated lozenges.

S.N.	Formulation Code	Thickness of Lozenges (mm)
1.	F1	12.25 ± 0.051
2.	F2	12.23 ± 0.044
3.	F3	12.02 ± 0.043
4.	F4	12.24 ± 0.054
5.	F5	12.24 ± 0.057
6.	F6	12.25 ± 0.054
7.	F7	12.26 ± 0.054
8.	F8	12.25 ± 0.054
9.	F9	12.24 ± 0.041
10.	F10	12.24 ± 0.054

Table 10. Mouth dissolving time of the formulated medicated lozenges.

Formulation Code	Mouth Dissolving Time (mins)	Average
F1	10:58	10.16 ± 0.51
	10:32	
	9:59	
F2	11:02	11.00 ± 0.3
	10:52	
	11:48	
F3	7:16	7.06 ± 0.43
	7:54	
	6:49	
F4	12:53	12:50 ± 0.19
	12:17	
	12:08	
F5	15:42	15:61 ± 0.45
	16:14	
	15:29	
F6	12:08	13.47 ± 1.25
	13:23	
	15:12	
F7	16:48	16:65 ± 0.36
	17:16	
	16:33	
F8	25:26	24:20 ± 0.56
	24:02	
	22:14	
F9	28.26	29:05 ± 0.31
	27.58	
	30.12	

F10	30:25	30:28 ± 0.75
	29:52	
	31:08	

Table 11. Moisture content of formulated medicated lozenges.

S.N.	Formulation Code	Moisture Content of Lozenges (%)
1.	F1	1.19
2.	F2	1.44
3.	F3	2.10
4.	F4	1.02
5.	F5	1.15
6.	F6	0.94
7.	F7	0.69
8.	F8	0.93
9.	F9	0.84
10.	F10	0.83

Table 12. Percentage drug content uniformity of formulated medicated lozenges.

Formulation Code	Drug Content (%)
F1	93.13 ± 2.32
F2	91.43 ± 3.31
F3	94.84 ± 3.85
F4	98.24 ± 3.5
F5	90.22 ± 2.50
F6	95.15 ± 2.65
F7	92.38 ± 3.52
F8	95.29 ± 2.53
F9	97.60 ± 2.96
F10	99.68 ± 1.50

Note: Mean ± SD (n = 3).

FORMULATED METOCLOPRAMIDE HCL MEDICATED LOZENGES

In-vitro Dissolution Study of Formulated Medicated Lozenges of Metoclopramide HCL

The cumulative drug release for formulation F1, which contains sucrose as the sugar base, reached 99.4% in 15 minutes. Meanwhile, formulations F2 and F3, formulated with dextrose and mannitol as bases, showed drug release of 92.4% and 96.8%, respectively, within 10 minutes, as presented in Table 13.

In the F4 formulation, which used isomalt as the sugar base, drug release reached 101% within 15 minutes. The inclusion of plasticizers in formulations F5, F6, and F7 resulted in a prolonged drug release time. Formulation F5 achieved a release rate of 100.4% in 20 minutes, while F6 exhibited a cumulative drug release of 97.7% at 15 minutes. Meanwhile, F7 showed a drug release of 99.6% in 25 minutes, as illustrated in Figure 4.

Formulations F8, F9, and F10, containing methylcellulose as a polymer at concentrations of 0.75%, 0.5%, and 0.25%, respectively, exhibited cumulative drug release of metoclopramide HCl at 95.02%, 98.6%, and 100.6% within 30 minutes. As a result, formulation F10, containing 0.25% methylcellulose and achieving 100.6% drug release within 30 minutes, was determined to be the optimized formulation.

In-vitro Release Kinetics

The drug release followed a first-order model, as indicated by the R2R^2R2 value being closer to 1 compared to the R2R^2R2 value of the zero-order equation.

The slope of the regression line from the Higuchi plot (R^2 = 0.949) and Hixon–Crowell plot R^2 = (0.981), which indicates the rate of drug release follows both diffusion and dissolution mechanism as seen in Table 14.

Figure 4. Optimized formulation of medicated lozenges.

Table 13. *In-vitro* drug release study of medicated lozenges.

Time (min.)	Percentage Drug Release (%)									
	F1	***F2***	***F3***	***F4***	***F5***	***F6***	***F7***	***F8***	***F9***	***F10***
0	0	0	0	0	0	0	0	0	0	0
5	53	73.2	84.5	71.5	51.5	63	23	23	31.4	25.5
10	74.2	92.4	96.38	96.86	88.06	82.02	41.92	33.8	40.2	38.4
15	99.4	–	–	101.1	96.5	97.7	79.4	51.48	62.2	71
20	–	–	–	–	100.14	–	92.14	80.6	82.0	83.6
25	–	–	–	–	–	–	99.6	88.6	94.2	91.4
30	–	–	–	–	–	–	–	95.02	98.6	100.6

The n-value, an exponent of Korsemeyer-Peppas equation was 0.815 indicating that mass transfers follows the non-Fickian diffusion.

Thus, the release kinetics of the optimized formulation showed first order release with non-Fickian diffusion as seen in Table 15.

Table 14. *In-vitro* release kinetics of optimized formulation.

Time in Mins	Square Root of Time	Log Time	% Cumulative Drug Release	% Cumulative Drug Remaining	Log % Cumulative Drug Remaining	Log % Cumulative Drug Release	Cube Root of % Drug Remaining
0	0	∞	0	100	2	∞	4.64159
5	2.23607	0.69897	25.5	74.5	1.87216	1.40654	4.20777
10	3.16228	1	38.4	61.6	1.78958	1.58433	3.94936
15	3.87298	1.17609	71	29	1.4624	1.85126	3.07232
20	4.47214	1.30103	83.6	16.4	1.21484	1.92221	2.54067

25	5	1.39794	91.4	8.6	0.9345	1.96095	2.0488

STABILITY STUDIES

The optimized formulations underwent stability testing at 45ºC and 75% relative humidity for one month. Following the stability studies, no alterations were observed in the physicochemical properties. Additionally, formulation F10 exhibited no significant changes in its release kinetics, as shown in Table 16.

Table 15. The summarized data of the *in-vitro* release kinetics.

S.N.	*Data Fitted in*	*X-axis*	*Y-axis*	*Slope*	*Intercept*	R^2	*Linear Equation*
1.	Zero-order equation	Time in hours	Cumulative % drug release	3.42	9.757	0.956	y = 3.42x + 7.342
2.	First-order equation	Time in hours	Log cumulative drug remaining	0.043	2.090	0.963	y = –0.043x + 2.090
3.	Higuchi	Square root of time	Cumulative % drug release	19.57	9.099	0.949	y = 19.57x – 9.099
4.	Hixson-Crowell	Time in hours	Cube root of drug remaining	0.107	4.756	0.981	y = –0.107x + 4.756
5.	Korsemeyer-Peppas equation	Log time	Log cumulative % dug released	0.815	0.829	0.965	y = 0.815x + 0.829

Table 16. Evaluation parameters after the stability studies.

Evaluation Parameter	Optimized Formulation (F10)	After Stability Study of 1 Month
Weight variation	2.503 ± 0.0290	2.507 ± 0.030
Hardness	15.30 ± 0.74	15 ± 0.08
Thickness	12.26 ± 0.054	12.18 ± 0.16
Moisture content	0.83%	0.69%
Mouth dissolving Time	30:28 ± 0.75	29:61 ± 0.98
Content uniformity	99.68% ± 1.50	96.48 ± 1.20
Drug release	100.6%	99.2%

SUMMARY AND CONCLUSION

This study focused on formulating and evaluating metoclopramide HCl medicated lozenges to achieve antiemetic effects through buccal absorption with the incorporation of a polymer.

1. The study on physical compatibility verified that the drug and excipients were well-suited for use together.
2. Chemical compatibility study was performed using FT-IR spectroscopy and FT-IR studies revealed that there was no change in major peaks, thus confirming no interaction between the drug and excipients.
3. 20% of liquid glucose is used in the formulation to improve appearance, smoothness, and prevent the crystallization of the sugar base.
4. After formulating batches for sugar selection (F1–F4), the observations were recorded. While mannitol dissolved easily in water, the formulated mass adhered to the beaker walls during heating, preventing the formation of a thick, viscous mass. Batches prepared with dextrose and sucrose exhibited sugar recrystallization. The batch containing isomalt resulted in hard candy-like lozenges; however, the appearance was not satisfactory. Due to these physical appearance issues, the decision was made to incorporate a plasticizer in subsequent formulations.
5. Formulations were prepared by incorporating a plasticizer, that is, PG and PEG 200 showed soft lozenges while those formulated with glycerine formed hard candy lozenges after keeping aside for half an hour. Also, formulations with PG, PEG 200 was in sticky nature. So, glycerine was selected for further batches and its quantity was varied to check the effect on the quality of

lozenges.

6. With lower concentration of glycerine, the lozenges remained as hard candy type with good appearance. Further addition of methylcellulose increased the buccal retention time.
7. All formulations were designed and evaluated based on in-vitro drug release, physical characteristics, weight consistency, thickness, hardness, moisture levels, mouth dissolving time, and drug content.
8. The prepared lozenges exhibited consistency in both weight and thickness.
9. The hardness of all the developed lozenges was measured within the acceptable range of 7.3–15.50 kg/cm².
10. The in-vitro drug release study revealed that metoclopramide HCl lozenges formulated with methyl cellulose at concentrations of 0.75%, 0.5%, and 0.25% achieved maximum drug release within 30 minutes. Among these, formulation F10 exhibited the highest drug release, reaching 100.6%.
11. The in-vitro release kinetics for the optimized formulation (F10) adhered to a first-order model. The dosage form's release was governed by both diffusion and dissolution processes, along with a non-Fickian (anomalous) diffusion mechanism.
12. Metoclopramide lozenges were formulated using isomalt as a base, allowing for slow dissolution in the mouth. This approach helps overcome dysphagia, a common issue among pediatric and geriatric patients, as well as individuals experiencing nausea (such as cancer patients) and those who have difficulty swallowing tablets.
13. The study's results indicate that isomalt can be successfully employed as a tooth-friendly alternative to sugar in the formulation of medicated lozenges. Due to its low-caloric nature and resistance to plaque formation, it is a safe option for both diabetic and pediatric patients.
14. Candy-based medicated lozenges are identified as a promising alternative dosage form, offering benefits such as improved patient compliance, ease of administration, and enhanced comfort. Additionally, they provide advantages like a lower required dose, rapid onset of action, reduced dosing frequency, and cost-effectiveness.

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