WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 22, 834-847. Research Article ISSN 2277–7105

DEVELOPMENT, PREPARATION AND IN-VITRO CHARACTERIZATION OF MUCOADHESIVE BUCCAL TABLETS OF ETHAMSYLATE USING BIODEGRADABLE POLYMERS

Sudhir Priyadarshi* and Shaffi Khurana Tangri

School of Pharmaceutical Sciences, Shri Guru Ram Rai University, Dehradun, Uttarakhand, India-248001.

Article Received on
27 October 2023,

Revised on 17 Nov. 2023,
Accepted on 07 Dec. 2023

DOI: 10.20959/wjpr202322-30150

***Corresponding Author**
Sudhir Priyadarshi
School of Pharmaceutical Sciences, Shri Guru Ram Rai University, Dehradun, Uttarakhand, India-248001.

ABSTRACT

The buccal route has various advantages, including greater compliance to patient, avoiding GIT, and preventing the hepatic First pass action. The goals are to develop a mucoadhesive buccal tablet containing Ethamsylate and appropriate excipients, and then to assess the goods through standard methodologies. As well as in vitro experiments. The substances were tested for compatibility using Fourier Transform Infrared Spectroscopy, and the results revealed no interaction. Ethamsylate buccal tablet was made in Five Formulations among which Formulation F4 found to be most Stable and Effective. The thickness and diameter of the tablets are 5.83mm to 6.93mm and 12.03mm to 12.11mm, respectively. All tablets are within +/- 5% of the standard. The hardness of tablets ranges from 6.5kg to 8.5kg, with a maximum friabilation of 0.75%. All tablets decomposed within 4 hours, according to the disintegration test. The content homogeneity of tablets was found to be between 85% and 115%. The weight of the tablet is within the ±5% range. The tablet's surface pH is near to salivary pH, This means it will not cause discomfort to the buccal mucosa. The pH remained unchanged also the size after being exposed to stability experiments in human saliva. Drug release trials after 8 hours found a range of 68.17% to 80.83%. The results are still within acceptable limits after three months of being subjected to 40°C and 75% RH. According to the findings, the formulation has the potential to be a mucoadhesive buccal tablet and also This research can help to build up patient compliance to uncooperative or unconscious Patient.

KEYWORDS: Ethamsylate, Buccal Tablets, Mucoadhesion, SCMC, HPMC K4M.

INTRODUCTION

The oral method for administration of drugs distribution is the ever accepted and broadly acknowledged approach for both patients and healthcare practitioners to give therapeutically active drugs. The advantages of oral administration are ease of use, low cost, drug stability, and precise dose.[1]

Regardless of its advantages, oral drug delivery is restricted due to hepatic first pass effect (the removal of a medicine through the liver before it enters the systemic system) and enzyme breakdown throughout the gastrointestinal tract (GIT).[2, 3] Over the years, researchers in drug development have focused on various forms of administration in order to improve pharmaceutical products while avoiding the limits of the oral way of administration. Because of the benefits it provides in overcoming the difficulties connected with oral administration, The buccal route is a great replacement to the oral route.[12] It avoids the GI tract, hepatic first pass action, and drug decline into the GI tract.[4] The buccal route has been shown to be effective for both local and systemic effects.[9] Low permeability is one of the downsides of the buccal route. The buccal membrane has a shorter persistence period than the sublingual membrane due to mechanical stress and swallowing,[13] and the medication is diluted due to continual saliva flow in the mouth. Nonetheless, the benefits and current advances in medication distribution would exceed the drawbacks.[5, 6] Mucoadhesive dose formulations have grown in favor as a means of overcoming the limitations of the buccal route of administration. By keeping the medication dosage form near with the absorption site, mucoadhesion has the possibility to improve drug delivery system localization, such as the buccal cavity.[8] Drug transport into buccal cavity mucosa, including sublingual, buccal and gingival mucosa, as well as the eyes, nose, rectum, and vagina, has been explored using mucoadhesive formulations. The buccal mucosa has various advantages over other approaches, including high immersion, availability, simple delivery equipments, minimal drug declination, and the possibility to combine medications as a regulated delivery system.[14] Ethamsylate is a common anti-hemorrhagic drug that has the side effect of causing GI discomfort. A mucoadhesive buccal tablet can help overcome the drawbacks of oral administration of Ethamsylate, such as GI discomfort, ulceration, and restricted absorption.

METHOD AND MATERIAL

Materials

Ethamsylate (Gift Sample) purchased from Windlas Biotech Limited, Sodium Alginate was obtained from S.D. Fine Chem. Ltd. in Mumbai, and Hydroxypropyl Methyl Cellulose K4M from Yarrow Chem Products in Mumbai. S.D. Fine Chem. Ltd, Mumbai, provided the Sodium Carboxy Methyl Cellulose. Loba Chemie Pvt Ltd, Mumbai, supplied the magnesium stearate.

Weight Variation

To investigate weight fluctuation, 20 compressed tablets in Every formulation was weighed independently utilizing a digital scale and tested in accordance with the approved USP protocol. The USP limit allows for a weight fluctuation of 5%. Individual tablet weights were within USP standards.[7]

Drug content

The drug content homogeneity of the produced Ethamsylate buccal tablets was assessed in compliance with IP 1996 standards. The chemical was extracted in water after five tablets were individually weighed. The medication content was determined according to the protocol. Water was used to extract a properly weighed quantity of a powdered Ethamsylate granules (500 mg), and the resultant solution was clarified through a 0.45 membrane. The absorbance at 300 nm was calculated after appropriate dilution.[7]

Diameter and Thickness

Uniform Thickness is the product of uniform force of compression and die fill volume. Three buccal tablets were obtained from each batch and measured using a vernier calliper. Similarly, three pills were ingested and their diameters were measured with a vernier.[7]

Hardness

The Monsanto Hardness Tester was utilized to assess the hardness of three tablets taken from every formulation, and an average was produced.[7, 1]

Friability

The Friability of 10 tablets was measured for each formulation using the Roche friabilator.[1]

In-vitro Drug release

The in-vitro dissolving experiments was performed out at a speed of 75 rpm utilizing USP equipment type II. The phosphate buffer of pH 6.8 dissolving media (900 ml) was held at 37°C ± 0.5°C. The dissolution medium was filled with 500 mg Ethamsylate tablets, and The paddle stirrer was set at 75 revolutions per minute. 5ml aliquots of dissolving material were withdrawn at regular intervals, and The removed volume was replenished with new dissolving medium. The drug release profile was measured using a diode array UV-visible spectrophotometer at 300 nm at different intervals of time (1h, 2h, 3h, 4h, 5h, 6h, 7h, and 8h). The dissolved Ethamsylate percentage was calculated and plotted versus time at various time intervals.[10]

FTIR compatibility

A determined dose of the medicine (100 mg) was completely blended with 100mg of potassium bromide (dry at 40° to 50° C), and then crushed in a hydraulic press at a pressure of 10 tones to create a pellet, This was then scanned with an FT-IR 410 PC spectrophotometer from 4000 to 400-1cm. Polymers and formulations were treated in the same way. The IR spectra of ethamsylate were compared to that of the formulation.[11]

RESULTS AND DISCUSSION

Studies on Pre-Formulation

Pre-formulation examination is the basic step in logical process of developing dosage types of pharmaceutical substances. Pre-formulation research is a method of improving medication distribution by examining Excipient physicochemical properties which could influence pharmacological performance, as well as the development of an efficient, steady, and safe dose form. It serves as an approach for integrating pharmaceutical excipients with drugs in dosage form.

Determination of λmax

Ethamsylate was dissolved in Distilled Water and diluted before being scanned in a UV visible spectrophotometer for maximal absorbance (Carry Win) in the 200 to 400 nm range, which was found to be 300nm.

Solubility

The shake flask method was used to assess the solubility of Ethamsylate in distilled water, ethanol, methanol, acetone, chloroform, and phosphate buffer of pH 6.8. until the solution is

saturated, a sufficient amount of Ethamsylate has been added into each vial contains 10 mL of the chosen solvent. For 48 hours, the mixtures were mechanically agitated in an isothermal shaker at 25°C ± 10°C before they were passed through the Watmann's filter paper. Absorbance is determined with a UV-Visible Spectrophotometer. The drug content is analyzed with the help of the standard graph.

Procedure for Standard Graph of Ethamsylate

Stock preparation In a standard flask, 50 mg of pure medication (Ethamsylate-API) is produced in a volume of 50ml after being dissolved in distilled water. To make the stock solution 100µg/ml, In a standard flask of 50ml, then 10 ml of the drug solution is extracted and produced upto 100 ml with Distilled water, in a standard flask of 100ml. Pipette out 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, and 5.0 ml of this solution, which was placed into a sequence of 10 ml volumetric flasks after being labeled to 10 ml with distilled water to reach concentrations of 5, 10, 15, 20, 25, 30, 35, 40, 45, and 50 µg/ml. In addition, a blank was constructed. At 300nm, The absorbance was determined, and a standard graph of concentrations (µg/ml) vs. absorbance (nm) was created. Table 1 as well as Figure 1 illustrate the results.

Table 1: Concentration and Absorbance of Ethamsylate.

Concentration (µg/ml)	Absorbance(nm)
5	0.0952
10	0.1656
15	0.2506
20	0.3358
25	0.4113
30	0.4788
35	0.5768
40	0.6649
45	0.7187
50	0.7856

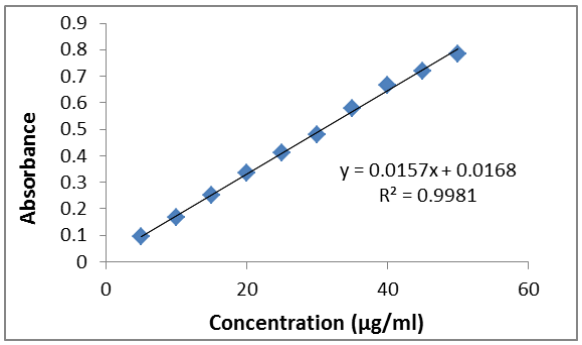

Figure 1: Concentration VS Absorbance Graph of Ethamsylate.

FT-IR compatibility research

FTIR was used to test the drug's compatibility (API) as well as polymers, both singly and in combination. The results were checked for incompatibility. Compatibility is one of the criteria to consider while selecting acceptable polymers or vehicles for pharmaceutical formulation. In the current study, Infrared spectroscopy (IR) was used to determine whether Ethamsylate and the polymers (Sodium Alginate, Hydroxypropyl Methyl Cellulose K4M, Sodium Carboxy Methyl Cellulose, and Magnesium Stearate) could interact chemically.

Spectrum analysis in the IR

A weighed portion of the medication (100mg) was thoroughly mixed with 100mg of potassium bromide (dried at 40° to 50° C), followed by compacted in a hydraulic press under 10 tone pressure to generate a pellet, which was then scanned with an FT-IR 410 PC spectrophotometer from 4000 - 400-1cm. Polymers and formulations were treated in the same way. The IR spectra of ethamylate were compared to those of polymers.

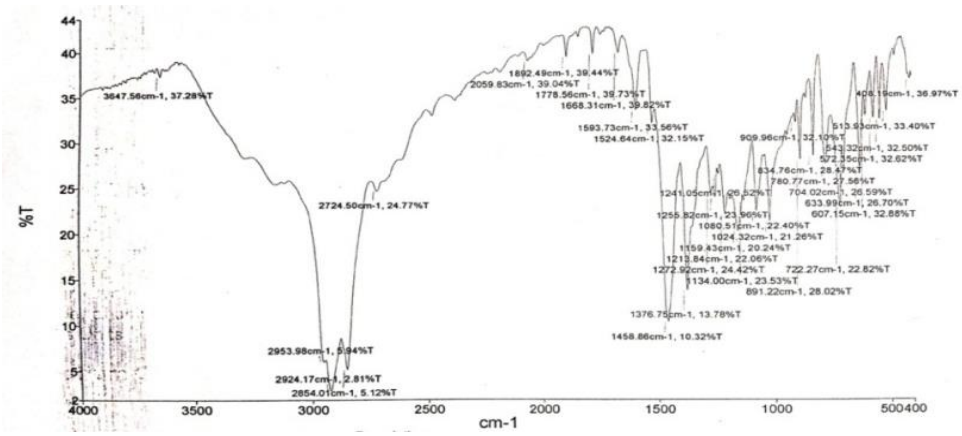

Figure 1: IR spectrum of Ethamsylate(API).

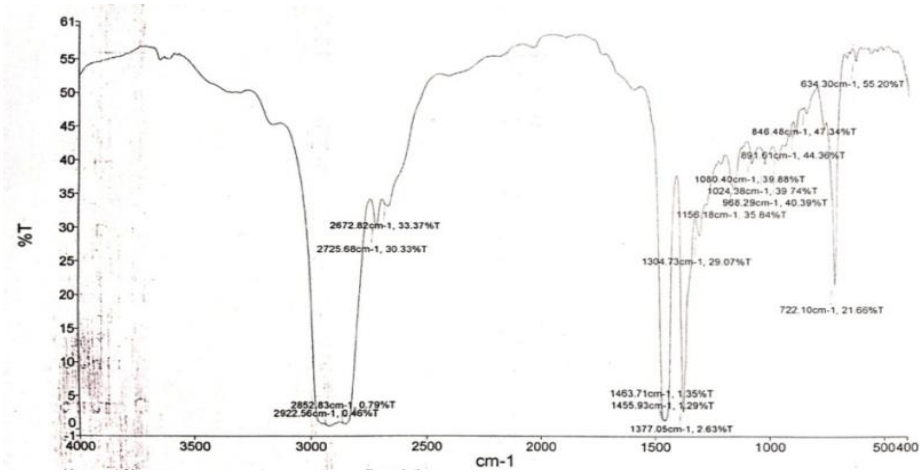

Figure 2: IR Spectrum of Ethamsylate with Sodium Alginate.

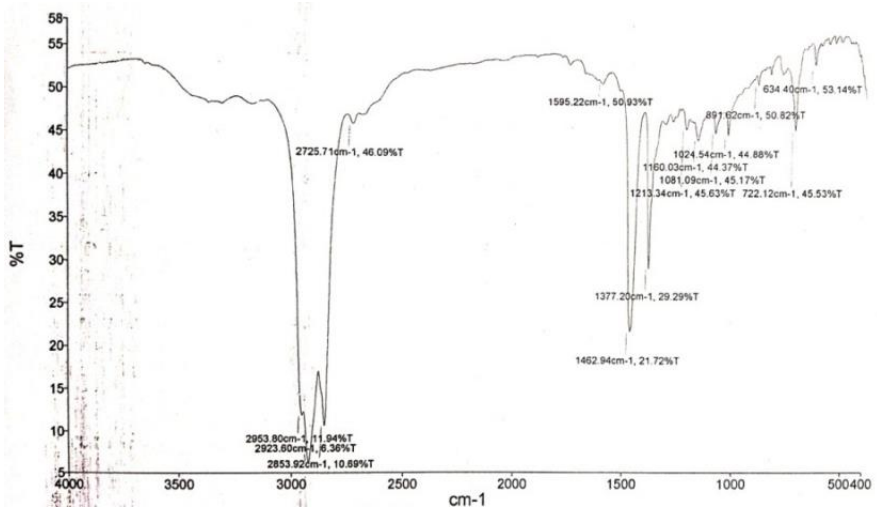

Figure 3: IR Spectrum of Ethamsylate and HPMC K4M.

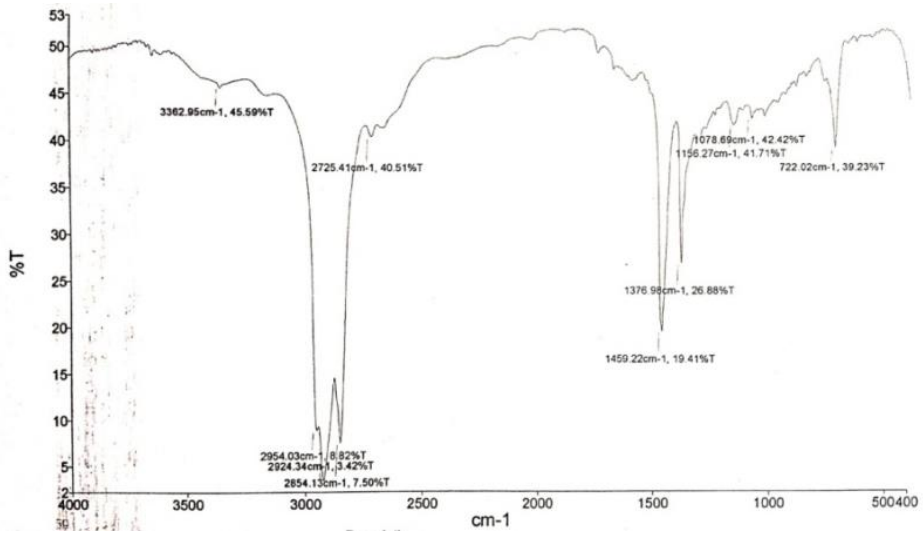

Figure 4: IR Spectrum of Ethamsylate With SCMC.

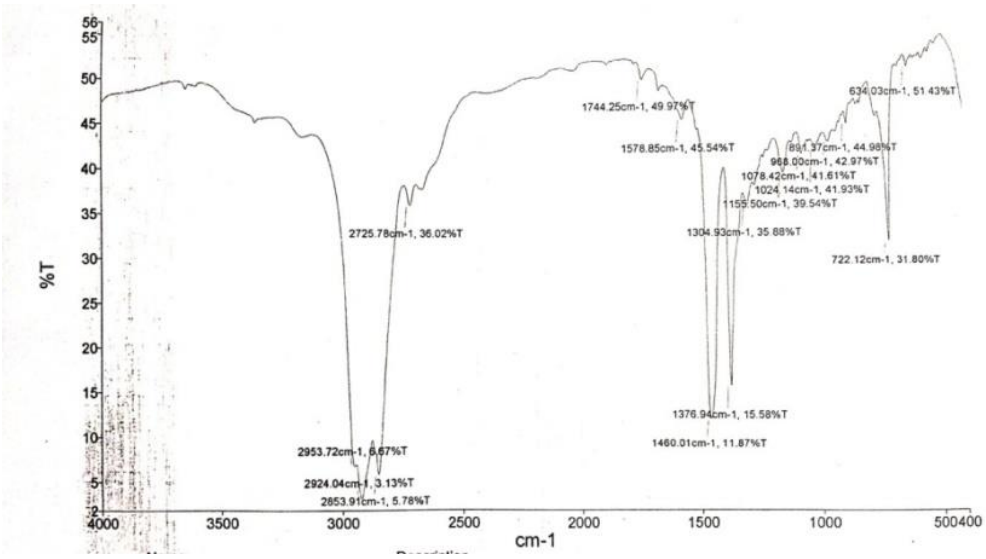

Figure 5: IR Spectrum of Ethamsylate and Magnesium Stearate.

Table 2: FTIR analysis of drugs and excipient compatibility.

Functional group	Wave number (cm^{-1})					
	Standard peaks	Pure drug	Sodium Alginate	HPMC K4M	SCMC	Magnesium Stearate
Aliphatic C-H stretch	3300-2500	2854.01	2852.83	2853.92	2854.13	2853
C-H bend	1470-1450	1458.86	1455.93	1462.94	1459.22	1460.01
C-H stretch	1300-1000	1272.92	1156.18	1213.34	1156.27	1155.50

Procedure For Preparation of Ethamsylate

The direct compression approach was used to create the mucoadhesive buccal tablet. Ethamsylate-compatible excipients were employed. All ingredients were sieved using a mesh sieve that had a mesh size of 60. The formulation's specified quantity was chosen and properly blended with a blender. To make the tablet, the mixed powder was compressed using a compression machine. Direct compression was used to make two batches of the best formulation.

Table I shows the preparation of five formulations of a mucoadhesive buccal tablet. Formula 4 was chosen among the formulations because it did not display any of the difficulties seen in other formulations like Capping, lamination, and medication release.

In Formulas 1, 2, 3, and 5, when the tablets were separated into layers, capping, adhering, and lamination were observed. This could be caused by trapped air within the tablet or due to the tablet's composition. The drug release characteristics of Formulas 1 and 2 varied with time, indicating the compositions are unstable. Only Formulation 4 indicated at least 80% drug release, and Table 6 details the physicochemical properties of the produced tablet.

Table 3: Formulation of mucoadhesive buccal tablet for Ethamsylate.

Ingredients	Formulation				
	F1 in mg	F2 in mg	F3 in mg	F4 in mg	F5 in mg
Ethamsylate	500	500	500	500	500
Sodium Alginate	35	35	35	35	35
HPMC K4M	70	56	42	28	14
SCMC	83	97	111	125	139
Magnesium Stearate	7	7	7	7	7
Total weight	695	695	695	695	695
Problems Experienced	Lamination, Capping, Drug Release	Lamination, Capping, Drug Release	Lamination, Capping	Problems Not Found	Sticking

Figure 7: Appearance of Ethamsylate Tablets.

Weight variation

To investigate weight variance, 20 tablets from every formulation were weighted with an Digital weighing balance and analyzed by utilizing the approved USP technique. The USP limit allows for a weight fluctuation of ±5%. The individual tablet weights were under the USP limits. Table 4 displays the results.

Table 4: Formulated Ethamsylate buccal Tablets Weight Variation.

Formulation	Wt of 20 tabs (mg) Range	Average weight (mg)	Limit range (±7.5%)
F1	667-680	673.5	622.987-724.012
F2	675-689	682	630.850-733.150
F3	673-690	681.5	630.387-732.612
F4	676-698	687	635.475-738.525
F5	679-682	680.5	629.462-731.537

Drug content

The drug content homogeneity of the produced Ethamsylate buccal tablets was assessed in compliance with IP 1996 standards. The chemical was extracted in water after five tablets were individually weighed. The medicine content was calculated in accordance with the protocol. After extracting a suitably weighed quantity of powdered Ethamsylate granules (500 mg) with water, the resulting solution was passed through a 0.45mm membrane. The absorbance at 300 nm was measured after appropriate dilution. The results are shown in Table 5.

Table 5: Percent Purity of Five Formulation.

Formulation	Absorbance (300nm)	Amount of Ethamsylate content per buccal tablet	
		Amt (in mg)	Percentage Purity
F1	0.284	496.703	99.34
F2	0.273	489.713	97.94
F3	0.278	479.083	95.81
F4	0.291	499.198	99.83
F5	0.283	488.816	97.76

Thickness and Diameter

Uniform thickness is achieved through uniform force of compression and die fill volume. Three buccal tablets were obtained from each batch and tested using a Vernier Calliper. Table 12 shows the results of the standard deviation calculation. Similarly, three tablets were eaten and their diameters were measured using a vernier; the results are shown in Table 6.

Hardness

The hardness of three tablets from each formulation was evaluated using the Monsanto hardness tester, and the average was analyzed and documented in Table 6.

Friability

The friability of 10 tablets was assessed from every formulation using the Roche friabilator Table 6.

Table 6: Thickness, hardness, % friability and Diameter of various formulated Ethamsylate buccal tablets.

Sl. No.	Formulations	Thickness (mm)	Diameter (mm)	Hardness (kg/cm^2)	Friability (%)
1	F1	6.42 ± 0.2	12.06 ± 0.004	7.5 ± 0.14	0.75
2	F2	6.93 ± 0.1	12.03 ± 0.007	6.5 ± 0.09	0.69
3	F3	6.14 ± 0.3	12.11 ± 0.001	8.5 ± 0.11	0.40
4	F4	6.25 ± 0.1	12.05 ± 0.007	7.5 ± 0.13	0.48
5	F5	5.83 ± 0.3	12.07 ± 0.003	6.5 ± 0.18	0.13

Studies on Drug Release in Vitro

The in-vitro dissolution experiments were carried out at 75 rpm utilizing USP equipment type II. The phosphate buffer of pH 6.8 dissolving media (900 ml) was held at 37°C ± 0.5°C. The dissolution medium was filled with 500 mg Ethamsylate tablets, and The paddle stirrer was set at 75 revolutions per minute. At regular intervals, 5ml aliquots of dissolving solution were taken, and the volume removed was replenished with fresh dissolution medium. Drug release was measured with the help of UV-visible spectrophotometer set to 300 nm at various

intervals of Time (1hr, 2hr, 3hr, 4hr, 5hr, 6hr, 7hr, and 8hr). The amount of Ethamsylate dissolved was determined and plotted against time at various time intervals. The outcomes are shown below.

Table 7: Dissolution behaviour of buccal formulations F1, F2, F3, F4 and F5 at pH 6.8 with time.

Time (hr)	F1 Cumulative % release	F2 Cumulative % release	F3 Cumulative % release	F4 Cumulative % release	F5 Cumulative % release
1	29.17± 0.39	18.33 ± 0.12	29.00 ± 0.33	35.00 ± 0.45	18.33 ± 0.48
2	35.00 ± 0.74	30.00 ± 0.54	31.00 ± 0.65	62.50 ± 0.51	20.83 ± 0.89
3	40.00 ± 0.46	36.25 ±0.09	39.00 ± 0.58	70.00 ± 1.52	31.66 ± 0.73
4	44.17 ± 0.62	37.67 ±0.86	49.00 ± 0.42	71.67 ± 1.09	32.50 ± 0.33
5	45.83 ± 0.86	44.50 ±1.08	55.50 ± 0.96	73.33 ± 0.86	34.17 ± 0.65
6	48.33 ± 1.2	47.08 ±0.56	64.50 ± 1.21	75.83 ± 0.77	39.17 ± 0.33
7	50.83 ± 0.78	52.83 ±0.78	71.50 ± 1.10	78.33 ± 0.64	62.50 ± 0.55
8	73.33 ± 1.34	68.33 ±1.21	79.00 ± 0.52	80.83 ± 0.93	68.17 ± 0.68

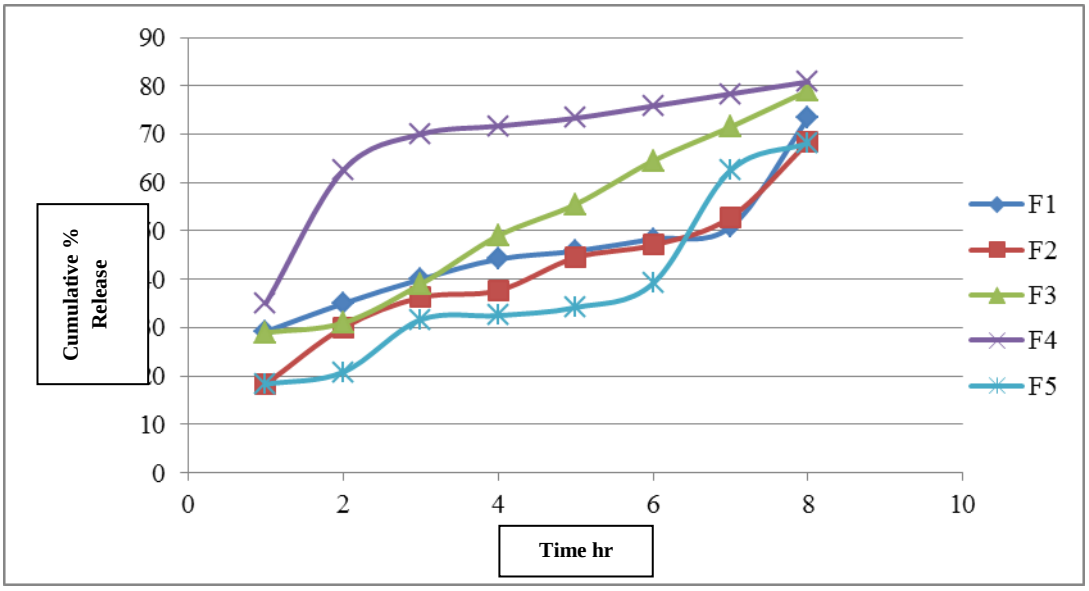

Figure 8: Graph comparing the in vitro dissolution of Ethamsylate buccal Tablets F1, F2, F3, F4, and F5.

Stability Studies

The buccal tablets went through to a three-month short-term stability test, which entailed keeping the formulation at 40° Celsius and 75% relative humidity. The stability testing demonstrated no statistically significant variations in physiological attributes, drug content, or in vitro release of drugs rate.

Table 12: Stability data of F4 Buccal Tablets.

Stability period	40°C / 75% RH			
	Hardness Mean ± SD	% Friability Mean ± SD	% Drug content Mean ± SD	Drug release 8 hr
Initial	7.50 ± 0.13	0.48±0.01	99.83±0.532	79.00
1 month	7.37 ± 0.49	0.52±0.03	99.35±0.751	75.42
2 month	6.41 ± 0.49	0.56±0.06	98.96±0.792	74.73
3 month	5.33 ± 0.60	0.73±0.03	96.94±0.921	74.38

SUMMARY AND CONCLUSION

Drug distribution via the oral cavity might be buccal, sublingual or local. Sublingual and buccal medication administration are the two most effective methods of drug delivery inside the mouth cavity. The buccal medication delivery method was chosen over the sublingual drug delivery system as it is more suited for oral transmucosal administration. Buccal administration of systemic transmucosal medication is preferred. The buccal mucosa is a preferable place for medications employed in oral mucosal drug administration because it has an extensive network of smooth muscle and mucosa that is relatively immovable. As a result, the buccal mucosa has become more dense, allowing less permeable molecules and possibly peptide medicines to enter.

Using different bioadhesive polymers like those SA, HPMC K4M, SCMC, and MS, the current study used direct compression methods to create five distinct buccal formulations containing Ethamsylate. The physicochemical properties, in vitro drug release, and the in vitro dissolution profile of all five formulations were investigated. From the findings of this study, we find that F4 (Content: Ethamsylate 500mg, Sodium Alginate 35mg, HPMC K4M 28mg, SCMC 125mg, Magnesium Stearate 7mg) have been discovered to be suitable buccal tablets, with the greatest percentages of release of 80.83 ± 0.93% and 87.0 ± 1.03%, respectively, and we also discovered that the suitable bioadhesive vehicles were HPMC K4M and SCMC, because of their great wettability to the buccal mucosal membrane. Here HPMC K4M used as a binder due to which the formulation play sustained release action also by increasing HPMC K4M the disintegration time increases so for counteract the sustained release action SCMC has been used as it is disintegrating agent due to which an immediate release can form to match the dissolution time as SCMC has tendency to disintegrate rapidly due to which increasing the SCMC quantity decreases Disintegration time. Sodium alginate is used as a Diluent while Magnesium Stearate is used as Lubricant. In for the purpose to optimize the buccal delivery method, in vivo permeability analyses can be done. Animal

models can be used to study medication transport through buccal tissues. Buccal cultures of cells have been used as models in vitro for medication penetration and metabolic activity in the mouth. Beckett and Triggs pioneered in vivo ways for measuring drug absorption kinetics with the buccal absorption test. The downsides of this approach include the drug being diluted by saliva, mistakenly ingesting a small amount of the sample solution, and having difficulty in precisely localizing the drug solution. The plasma concentration vs. time profile is then applicable to calculate pharmacokinetic characteristics like bioavailability.

The buccal mucosa has various benefits for effective medication distribution. The mucosa is adequately drained, and the digestive tract prevents first pass metabolism and presystemic excretion. The location looks to be appropriate for a retentive delivery and is acceptable to the patient. The permeability and local conditions of the mucosa can be adjusted and altered to allow pharmacological penetration with the right dosage form with design and formulation. Buccal drug administration is an exciting area of study that aims to give systemic dispersion of medications that are ineffectual when taken orally, as well as a non-invasive delivery strategy for active peptide and protein therapeutic agents. Bioadhesive assays, animal models, and in vivo drug release might all be used to analyze the efficacy of Ethamsylate produced buccal tablets.

REFERENCE

1. Velmurugan S, Srinivas P. Formulation and in vitro evaluation of losartan potassium mucoadhesive buccal tablets. Asian J Pharm Clin Res., 2013; 6(3): 125-130.
2. Le J. Drug Administration [Internet]. Kenilworth NJ USA: Merck Sharp & Dohme Corp; 2016 [cited 2016 Nov 8]. Available from: http://www.msdmanuals.com/home/drugs/administration-and-kinetics-of-drugs/drug administration.
3. Shepherd M. Administration of drugs: oral route. Nursing Times, 2011; 107(32): 18.
4. Chinna RP, Chaitanya KSC, Madhusudan RY. A review on bioadhesive buccal drug delivery systems: current status of formulation and evaluation methods J. Pharm Sci., 2011; 19(6): 385-403.
5. Russo E, Selmin F, Baldassari S, Parodi B. A focus on mucoadhesive polymers and their application in buccal dosage forms. J Drug Deliv Sci Tec., 2016; 32(Part B): 113-125.
6. Salamat-Miller N, Chittchang M, Johnston T. The use of mucoadhesive polymers in buccal drug delivery. Adv Drug Deliv Rev., 2005; 57(11): 1666-1691.

7. Fatima S, Panda N, Reddy AV, Fatima S. Buccal mucoadhesive tablets of sumatriptan succinate for treatment of sustainable migraine: design, formulation and in vitro evaluation. Int J Pharm Res., 2015; 4(30): 114-126.
8. Semalty M, Semalty A, Kumar G. Formulation and characterization of mucoadhesive buccal films of glipizide. Indian J Pharm Sci., 2008; 70(1): 43-48.9. Raghavendra Rao NG, Shravani B, Reddy MS. Overview on buccal drug delivery systems. J Pharm Sci Res., 2013; 5(4): 80-88.
9. Shojaei, A. H., & Sadeghi, F. Buccal mucosa as a route for systemic drug delivery: A review. Journal of Pharmacy and Pharmaceutical Sciences, 2008; 11(1): 15-30.
10. Vikram A, Firoz S, Kishore D, Chandra Mouli Y, Venkataramudu T. Formulation and evaluation of mefenamic acid tablets by using modified starch. Asian J Pharm Sci Tec., 2012; 2(2): 46-53.
11. Yadav Deepak R, Ayyappan T, Shanmugam S, Sundaramoorthy K, Vetrichelvan T. Development and in-vitro evaluation of buccoadhesive metoclopramide hydrochloride tablet formulations. Int J PharmTech Res., 2011; 3(1): 516-525.
12. Advances in Nanoparticulate Drug Delivery Approaches for Sublingual and Buccal Administration (2023), by Sanjoy Kumar Bera, Dwaipayan Mondal, and Amitabha Ghosh, published in Pharmaceutics.
13. Biopharmaceutical considerations for sublingual and buccal drug delivery (2017), by Anchal Patel, Smita Patel, and Ashwin Patel, published in Pharmaceutics.
14. Buccal Mucosa as a Potential Route for Drug Delivery (2020), by Pratik Patel, Amit Patel, and Ashwin Patel, published in Pharmaceutics.