Section A-Research paper

FORMULATION AND EVALUATION OF RIVAROXABAN BUCCAL TABLETS

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ABSTRACT

Background: This study aims to explore the potential of tablets in enhancing the buccal delivery of rivaroxaban. Materials and Methods: Buccal tablets formulations of rivaroxaban were prepared using different concentrations of Carbopol-934 as a polymer.Hydroxypropyl methyl cellulose is used as adhision for the preparation of buccal tablets. Microcrystalline cellulose 200, Aerosil, Talcum and magnesium stearate were also used in the formulation. The formulated buccal tablet was evaluated by different parameters such weight variation, hardness, dimension, friability, dissolution, swelling index, drug content and compatibility study.

Result: All the prepared formulations showed acceptable weight variation, hardness, friability. But dissolution study, assay and swelling property was not acceptable for the formulations. After studying the evaluation parameters, the formulation F3 showed consistent release of the drug form buccal tablets in which all the parameters is within the range.It might be due to the proper concentration of the carbopol 934 and the Hydroxypropyl methyl cellulose.

Conclusion: From this study we can conclude that the formulation B3 shows the better results as compared with the others. It shows good drug content, better dissolution rate and swelling property.

Keywords: Buccal Tablets, Rivaroxaban, Swelling Index

1. Background[4]

An alternate drug delivery method, buccal delivery has a number of benefits over the oral route. Due to the high vascularity of the buccal mucosa and the direct blood flow into the jugular vein, medicines taken through the buccal mucosa avoid the gastrointestinal system and the hepatic first-pass effect. The mouth's mucosa resembles skin more morphologically and differs greatly from the other areas of the gastrointestinal system. The oral mucosa does not exhibit the good permeability that the intestine shows, despite the fact that skin permeability is typically perceived as being low.

For many years, this medication have been topically used to the oral mucosa. However, there has recently been interest in using the oral cavity as a route for administering medications to the body's circulatory system. Despite the epithelium's generally low permeability, there are a number of benefits to using this method of administration. First-pass metabolism avoidance, simplicity of access to the delivery location, and the possibility of sustained drug delivery, primarily through the buccal tissues, are among these.For the systemic administration of medications, buccal delivery is regarded as a significant substitute to the oral route since it is the most practical, simple, and secure mode of administration.

1.1 **Anatomy of Buccal mucosa [5]:**

The buccal mucosa is the pink colored, moist lining of the inner cheek. It is composed of several layers of tissue, including:

Epithelium: The outermost layer of the buccal mucosa is composed of

stratified squamous epithelium. This layer is responsible for protecting the underlying tissue from physical and chemical damage.

Lamina propria: The layer benath the epithelium is the lamina propria which is made up of loose connective tissue. This layer contains blood vessels, nerve and lympathic vessels, as well as various types of cells involved in immune defense.

Submucosa: The submucosa is a layer of connective tissue that lies beneath the lamina propria. It contains larger blood vessels and nerve as well as glands that secrete saliva,

Muscle layer: The muscle layer of the buccal mucosa consists buccinator muscle, which is responsible for moving food around the mouth during chewing.

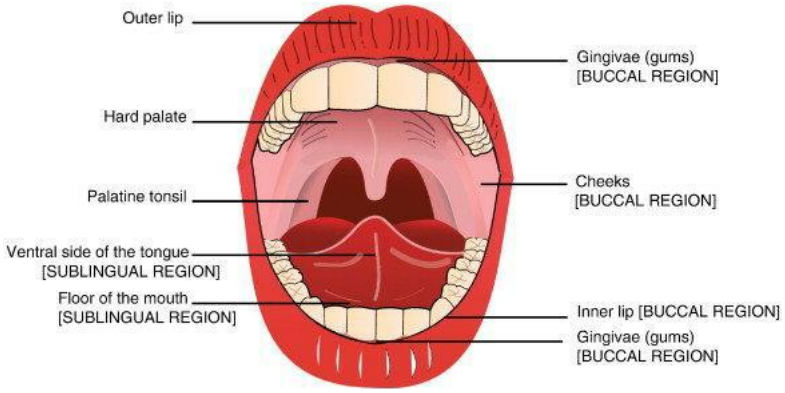

Figure1.1: Different anatomical region of buccal cavity

1.2 Characteristics of an Ideal Buccoadhesive System[1]:

The following properties should be present in an ideal buccal adhesive system:

- Easily attachment to the buccal mucosa and adequate mechanical strength.
- Drug release is monitered.
- Enhances the amount and rate of medication absorption.
- With good patient compliance.
- Should not encourage the development of secondary diseases such dental caries.
- Have wide range of safety with both systematically and locally.

1.3 Some advantages of Buccal Drug Delivery System[1]:

Drug administration through the buccal mucosa has a number of specific benefits:

- The buccal mucosa is robust as compared to other mucosal tissues, blood supply is abundant, and it is more permeable.
- Prevent the drugs from getting into contact with the gastrointestinal fluids and avoid the first-pass metabolism.

- Easy access to the membrane facilitates simple application, localization, and removal of the delivery system.
- Enhance the performance of many drugs, due to their extended period of contact with the mucosa.
- High level of patient acceptance in comparison to other non-oral medication means of administration.
- Due to adhesion and close contact, the formulation remains at the delivery site for a longer period of time, enhancing API bioavailability while requiring lower API doses for disease therapy.
- Buccal drug delivery avoids oral drug delivery from being affected by unfavorable environmental factors.

1.4 Disadvantages of Buccal Drug Delivery System[1]:

- The most important challenges of buccal administration are:
- Only a small portion of the mouth cavity's membranes, 170 cm2, which includes the buccal membrane and other non-keratinized tissues, is available for medication absorption.
- The mucosa's barrier characteristics.
- Continuous release of saliva (0.5-2 l/day) causes the medicine to be diluted as the result.
- If the delivery system is unexpectedly swallowedthere is a risk of choking.
- The loss of a medicine that has been dissolved or suspended in saliva could also result in the dosage form being unintentionally removed.

1.2 Rivaroxaban

Rivaroxaban is the most frequently used anticoagulant which is also the first direct factor Xa inhibitor. Oral anticoagulants without vitamin K are another name for it. However, in the event of a serious bleed, there is no antidote available [3].

Anticoagulants are administered to stop blood from clotting or to stop already-formed clots from enlarging. Clots can prevent blood from getting to the brain or the heart muscle. A heart attack or stroke is brought on by these. Rivaroxaban, which is an oral oxazolidinone-based anticoagulant, is used to prevent venous thromboembolism in grown up patients followingcomplete hip replacement surgery or knee replacement surgery. Rivaroxaban is a powerful, selective direct inhibitor of factor Xa[3].

Rivaroxaban (Figure 1.2) is a tiny molecule having molecular mass of 436 g mol-1 and is a significant plasma protein binding (92–95%) in humans. The major binding componentserum albumin[3].

1.3 DRUG PROFILE

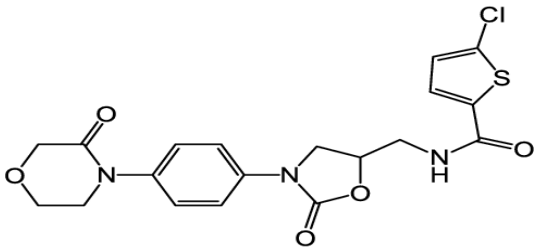

Figure 1.2: Chemical structure of Rivaroxaban

Table 1.1: Data of Rivaroxaban

Chemical Formula	C19H18ClN3O5S
Molecular Mass	432.882
Solubility	It basically cannot dissolve in water
Category	Anticoagulents
Description	It is a white to yellowish powder with no odor, no hygroscopic properties and chirality (S)-enantiomer.
BCS Classification	Class II (High permeability low solubility)

1.3.1 Rivaroxaban Mechanism of Action[23]:

In terms of hemostasis, an activated factor X (Xa) is where the intrinsic and extrinsic coagulation pathways meet. Prothrombin is directly changed into thrombin through the prothrombinase complex, which results in the development of fibrin clots and platelet activation. However, factor X activity can be considerably reduced without having an impact on hemostasis. In order to avoid thrombosis without causing systemic hypocoagulation or unwanted bleeding consequences, factor X is a suitable target.A greater understanding of coagulation routes has come forth as a result of from ongoing scientific research, which has also shown the creation of various new parenterally or orally active drugs which particurlarly target individual blood coagulation components. Rivaroxaban reversibly inhibits prothrombinase activity and free and clot-bound Factor Xa, thus preventing the production of thrombin. Additionally, rivaroxaban raises the permeability and degradability of clots.

1.4 Literature Review

1. Kaul et al.,describes the Buccal drug delivery. Buccal drug delivery has attracted a lot of interest and momentum since it provides outstanding benefits. Recent years have seen a substantial increase in interest in the buccal route for systemic drug delivery employing mucoadhesive polymers to significantly enhance the efficacy of numerous medicines. This review article provides a general overview of buccal drug delivery systems, including information on the oral mucosa, formulation considerations for buccal drug delivery systems, theories and mechanisms underlying mucoadhesion, various mucoadhesive formulations for buccal drug delivery, and active ingredients administered buccally.

2. In several countries, rivaroxaban is approved when combined with other DOACs like apixaban and dabigatran for the prevention of recurrent pulmonary embolism (PE), deep vein thrombosis (DVT), and PE in adult patients having hip or knee replacement surgery. It is also approved for the prevention of stroke and systemic embolism with non-valvular Atrial fibrillation (AF). The most frequent reason for prescribing a DOAC in patients with AF was by far the avoidance of stroke.

3. Formulation and In vitro evalauation of Rivaroxaban Immeiate release Tablets: A strategy for increasing oral bioavailability through solid dispersion.

4. Gopalraoet al.,updated review of Formulation and Evaluation of Buccal Tablets. Sodium alginate, chitosan, HPMC K4M, and other mucoadhesives were used to create buccal tablets utilizing the direct compression method. Numerous criteria were measured, including hardness, thickness, weight uniformity, friability, swelling index, homogeneity of the drug content, pH, and drug-excipient interactions as well as an in-vitro drug release research.

5. Patel et al., developed and Evaluatedabioadhisive buccal medication delivery forRipaglinide Tablets. Buccal tablets have been developed by use of ethyl cellulose as an

impermeable baking layer, cytosan as a bioadhesive polymer, and HPMC K15M as a sustain release polymer. Weight variation, hardness, thickness, surface pH, friability, mucoadhesive strength, swelling index, in vitro drug release, ex vivo mucodhesion time, and ex vivo drug permeation had been tested for the tablets.

6. Thomas, et al., have described about Rivaroxaban: An oral factorXa inhibitor. This article discusses the pharmacology, effectiveness, and rivaroxaban's tolerability for VTE prevention in nonvalvular AF patients after orthopedic surgery, adjunctive therapy in patients with ACS, and VTE treatment.

7. Barpete, et al., create a formula in the design of a buccal patch with a prolonged residence duration for the purpose of resolving the osteoporosis issue in infected teeth. Patients have the option to change the delivery schedule or stop it altogether in an emergency. The buccal drug delivery devices make it simple to provide medication to the buccal cavity.

8. Koirala Set al.,discuss the formulation as well as evaluation of aceclofenac buccal mucoadhesive tablets. The objective of this project was to create and analyze aceclofenac buccal mucoadhesive tablets using various ratios of the three polymers carbopol 934, hydroxypropyl methylcellulose, and sodium carboxymethylcellulose. The direct compression method was used to create 12 batches of buccoadhesiveaceclofenac. After that, physicochemical characteristics as hardness, dimension, weight variation,surface pH, drug content, friability, swelling index, and ex vivo mucoadhesion have been evaluated for the compressed tablets. [2].

9. KL, et al.,has worked on formulation and evaluation of buccal mefenamic acid tablet that adheres to mucous membranes, Journal of Pharmaceutical Sciences in Brazil. The buccal route of administration has various benefits, including increased patient compliance and avoiding the GIT and first pass effect on the liver.

10. Buccal medication delivery as described by Rossi S et al.: a challenge already won?The barrier properties of the mucosa and the limited absorption surface are the main problems that medications encounter when administered orally. The effective physiological

clearance processes of the oral cavity that move the formulation away from the absorption site are the other difficulties that must be taken into consideration.

11. Buccal drug delivery system,Drug development and industrial pharmacy have been explained by Hao J et al.,Because it is simple to administer, the oral cavity is a desirable location for drug delivery because it prevents drug degradation in the gastrointestinal tract and first-pass metabolism. In order to impact local or systemic pharmacological actions, buccal drug delivery specifically refers to the distribution of medications within or through buccal mucosa. This review provides a concise overview of the benefits and drawbacks of buccal drug delivery, the anatomical makeup of the oral mucosa, and the methodology for evaluating buccal drug delivery systems, with a focus on physiology, pharmacology, pathology, and formulation design in line with recent advancements in buccal delivery systems.

12. "A Review on Rivaroxaban: A Prominent Oral Anti-coagulant Agent" was discussed by Iram et al. Oxazolidinone-based oral anticoagulant rivaroxaban (Xarelto®). In addition to strongly selectively blocking free factor Xa, it also inhibits prothrombinase-bound and clot-associated factor Xa in a concentration-dependent manner. In adult patients who have undergone total hip or total knee replacement surgery, it is used to prevent venous thromboembolism (VTE). It is a strong, specific direct inhibitor factorXa. The drug is converted in the liver to inactive metabolites, half of which are eliminated through the kidneys and the other half through the feces. [3].

2. AIMS AND OBJECTIVES

2.1 General objectives:

- To formulate and evaluate the buccal tablets containing Rivaroxaban.

2.2 Specific Objective:

- To select the suitable components for the formulation.
- To evaluate the required parameters
- Established the formulation process with formula.
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3. MATERIALS AND METHODOLOGY

3.1 Materials used

The materials used for the preparation of rivaroxaban buccal tablets are provided below:

Table 3.1: List of materials required

S.No.	Materials	Source
1	Rivaroxaban	Gift from 'Divine Healthcare Pvt. Ltd. Chitwan, Nepal
2	Lactose Anhudrous	
3	Microcrystalline cellulose 101	
4	Hydroxypropyl Methylcellulose	
5	Sodium Lauryl Sulphate	
6	Crosscarmellose Sodium	
7	Magnesium Stearate	
8	Methylene Chloride	
9	Isopropyl Alcohol	

3.2 Equipment used

The equipment used is listed below:

Table 3.2: List of equipment required

S. No.	Equipments
1	Electronic balance
2	pH Meter
3	HPLC
4	FTIR
5	Dissolution Test Apparatus
6	Disintegration Test Apparatus
7	Hardness Tester
8	Vernier Caliper
9	Friability Tester
10	Manufacturing Container
11	Compression Machine

3.3 Methodology

3.3.1 Formulation of Rivaroxaban Buccal Tablets.

Buccal tablets containing Rivaroxabanisformulated by direct compression process in whichdifferent concentrations with different polymer gradeswas used. All the required powders were accurately weighed and passed through 60 mesh sieve .Firstly, Rivaroxaban and carbopol was mixed thoroughly in a separate container and hydroxypropyl methylcellulose, talc and aerosol were mixed in another container. After proper mixing both the samples were mixed with geometric mixing. Then again the above mixed sample was mixed with MCCP 200 and finally lubricated with Magnesium stearate. Then the granules were compressed. The detail of composition of each formulation is given in the below table.

Figure 3.1: Flow chart of buccal tablets preparation.

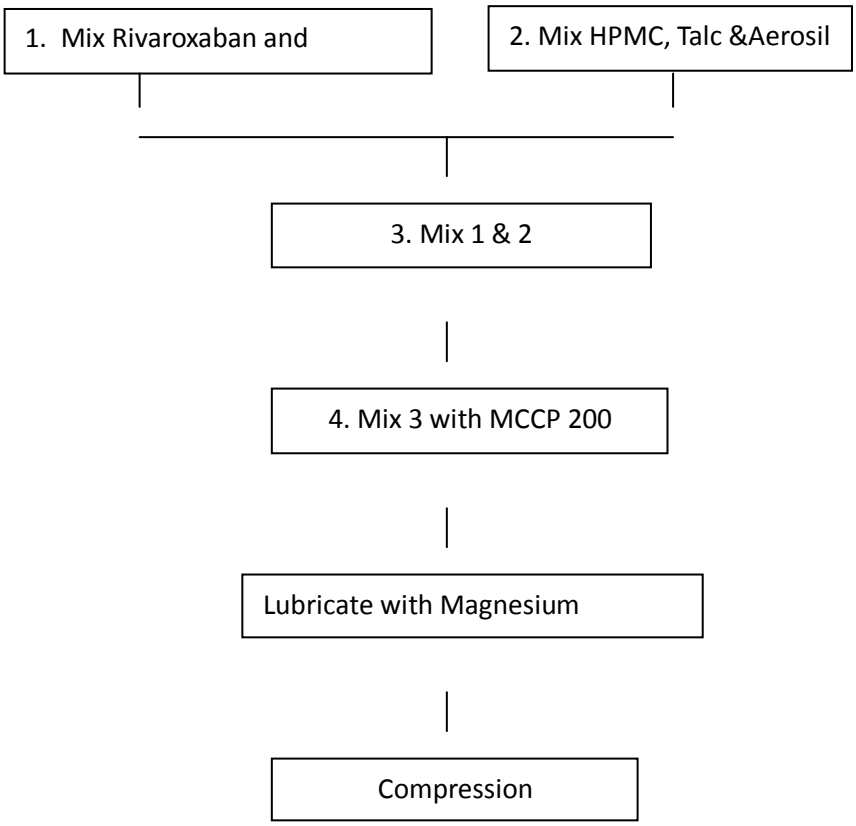


Table 3.3: Formula of different formulation of Rivaroxaban Buccal Tablets.

Composition	**B1(mg)**	**B2 (mg)**	**B3(mg)**	**B4 (mg)**	**B5(mg)**	**B6 (mg)**	**B7(mg)**
Rivaroxaban	20	20	20	20	20	20	20
Carbopol 934	15	37	11.5	5	15	20	30.5
Hydroxypropyl methyl cellulose	28.5	8	32	42	25	17.5	12.5
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Aerosil	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Microcrystalline cellulose powder 200	32	30.5	32	28.5	35.5	38	32.5

Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Total(mg)	**100 mg**	**100 mg**	**100 mg**	**100 mg**	**100 mg**	**100 mg**	**100 mg**

3.4 Evaluation of prepared rivaroxaban 20mg buccal tablets

Both the physical and chemical parameters were used for the evaluation of rivaroxaban buccal tablets. The parameters are listed below.

3.4.1 Weight variation: Take20 tablets randomly and weight the tablets individually.

3.4.2 Uniformity of weight: After determination of average weight, select Lowest weight and Highest weight of tablets among them and calculate the variation from given formula. Only two of the individual weights deviate from the average weight by ±7.5 %. The limit is set as per Indian Pharmacopoeia 2022.

3.4.3 Dimension: Measure thedimension of the tablets.

3.4.4 Hardness: Take 6 tablets in clean and container and place one by one in hardness tester and measure the hardness of tablets.

3.4.5 Disintegration Time: Place one tablet into each of 6 tubes of Basket-rack assembly of Disintegration Tester, suspend the assembly in the beaker which contain 900 ml of water heated at 37 °C and operate the apparatus.

3.4.6 Friability Test: Take the tablet weight containing 6.5 g. Note the weight and place the tablet in Friability test Apparatus and rotate the apparatus for 4 minutes at the speed of 25 rotations per minute. Note the final weight and calculate.

Calculation: $\frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \text{X } 100$

3.4.7 Compatibility Study: To study the drug compatibililty, infrared spectroscopy is used. The FTIR spectrophotometer is used to generate the specturm at wavelength region between 4000 to 400 cm^{-1}. The tablet is crushed in the fine powder and the spectrum is obtained by placing the sample in the light path.

3.4.8 Swelling Test[8]: Take 20 tablets randomly and individually weight(W1) the tablets and place separetely in petridishes having 5 ml phosphate buffer of pH6.8. Remove the tablets from the petridish at intervals of 1, 2, 4, and 8 hours. You should also use filter paper to drain any extra water. The swollen tablet (W2)is weighed and the percentage hydration is calculated using the following formula:

Swelling index = $[(W_2 - W_1)/W_1] \times 100$

3.4.9 Dissolution: Method is as per British Pharmacopoeia

Medium:	900 ml of dissolution medium was used by dissolving 29.9g of sodium acetate, 16.6 ml of glacial acetic acid and 40g of sodium dodecyl sulphate in water, then diluting to 10L with the same solvent.Using glacial acetic acid or sodium hydroxide solution, bring pH to 4.5.
Apparatus:	Paddle (Apparatus 2)
Speed:	75 RPM
Time:	45 minutes
Temperature:	37±0.5˚C

Test Solution: Samples withdraw immediately from the dissolution vessel and filtered.

Reference solution: Weight 28.0 mg of Rivaroxaban RS in 50 ml volumetric flask and dissolve in acetonitrile and dilute to 50 ml with the same solvent. Further dilute 1 ml of the above solution to 25 ml with dissolution media and mix well. Filter the solution.

Table 3.4: Chromatographic Condition for dissolution profile

Column	C18, 25 cm x 4 mm,
Flow rate	1.0 ml per minute
Auto sampler temperature	10°C
Wavelength	250 nm
Injection volume	10 µl
Mobile phase	Acetonitrile : Water (40:60 V/V)

Inject Reference solution and the test solution.

Calculation:

$$\frac{Asp}{Astd} * \frac{Wstd}{50} * \frac{1}{25} * \frac{900}{20} * P$$

Where,

Wstd: Wt of standard taken

Asp: Absorbance of sample

Astd: Absorbance of standard

P: Potency of standard (As is basis)

3.4.10 Drug Content: As per British Pharmacopoeia 2022

Table 3.5: Chromatographic conditions for Drug content

Column	C18, 25 cm x 4 mm,
Flow rate	1.0 ml per minute
Column temperature	45°C
Wavelength	250 nm
Injection volume	5 µl
Mobile phase	A. Acetonitrile : Solution A(8:92) v/v B. Acetonitrile

Solution A:

Dilute 0.67 ml of phosphoric acid to 1000 ml with water.

Preparation of sample solution:

Weigh accurately about 400 mg (80mg) of test sample in 100 ml volumetric flask. Add 60 ml of the solvent mixture and sonicate for 15 minutes and make up the volume to 100 ml with the same solvent mixture. Further dilute 5 ml of the above sample in 20 ml volumetric flask and dilute with the same solvent mixture. Filter the sample through 0.2µm filter.

Preparation of standard solution:

Weigh accurately 20 mg of Rivaroxaban Working Standard and dissolve in 100 ml of water. Filter it through 0.2µm filter. (The resulting solution concentration is 0.2 mg/ml.)

Procedure:

- Inject blank solution and check for interference, if any.
- Inject reference solution; the test is not valid unless the relative standard deviation for replicate injection is less than 1.0%.
- Inject blank solution.
- Inject 2 consecutive test solutions.
- Inject bracketing reference solution.

Calculation:

$$\frac{Asp}{Astd} * \frac{Wstd}{100} * \frac{100}{Wsp} * \frac{5}{20} * \frac{P}{100} * \text{Avg. wt of 20 tablets} * 100$$

Where,

Sp = sample Std = standard

Wsp = Weight of sample Wstd = Weight of standard

P = Potency of standard

4. RESULTS

4.1 Evaluation of the properties of tablet:

4.1.1 Weight variation, dimension, hardness, friability of the tablets analysed in the Quality Control Laboratory for the 7 batches are illustrated in the table 1 given below.

Table 4.1: Results of different evaluation parameters of Rivaroxaban Buccal Tablets

Batch	Wt. Variation (mg ± SD)	Diameter	Thickness (mm ± SD)	Hardness (Kg/cm^2 ± SD)	Friability (%)	Drug Content (%)
B1	101.7 ±2.22	6	3.58±0.03	5.94±0.75	0.09	91.22
B2	98.67± 3.91	6	3.60±0.10	7.46±1.67	0.47	98.78
B3	100.74±3.02	6	3.60±0.08	6.66±0.96	0.17	98.29
B4	101.08±3.25	6	3.63±0.15	8.30±1.46	0.2	97.97
B5	99.30 ± 2.13	6	3.62±0.09	7.47±2.08	0.4	98.69
B6	102.02±2.48	6	3.60±0.05	6.37±1.40	0.24	91.83
B7	102.17±4.39	6	3.60±0.10	7.70±1.53	0.51	98.87

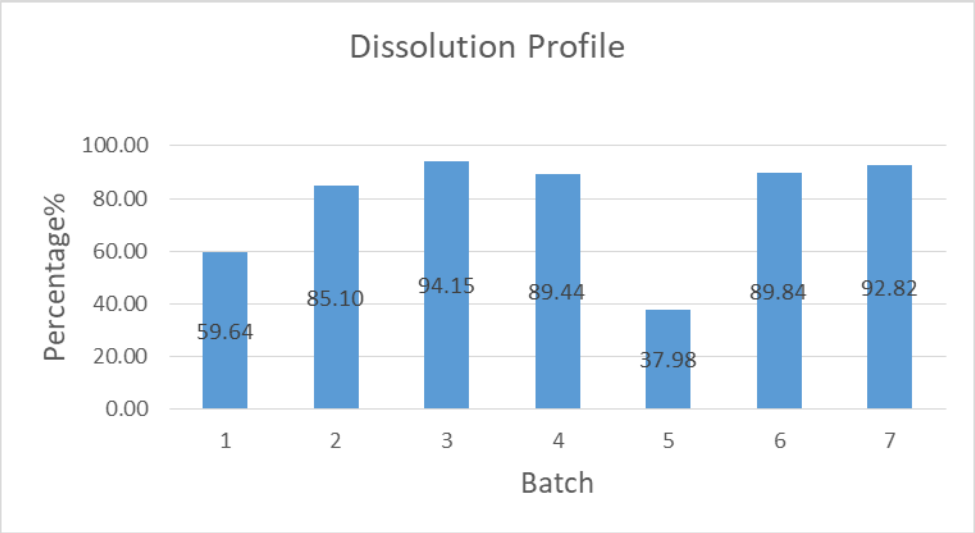
The diameter of the tablets of all the batches were found to be uniform i.e 6 mm. Likewise the thickness of the tablets were almost the same of all the batches which were found to be from 3.58 ± 0.03 to 3.63 ± 0.15. The hardness of the tablets were found to be 5.94± 0.75 to 8.30 ± 1.46 of all the batches which is as per limit as per sigma rule. Similarly the friability of all the batches was also within the limit as per the British Pharmacopoeia i.e. between 0.08 and 0.36 which is below 1%.

4.1.2 Drug Content: The drug content of all the batches is shown in Table No. 1which is between 91.22% and 98.87%. As per the British pharmacopoeia the limit is from 95.0% to 105.0%. So it was found that batch No. B2, B3, B4, B5 & B7 are within the limit.

4.1.3 Dissolution Profile:The result of drug dissolution profile of all the batches are represented in below table. The release of drug in batch 1 & 5 was found to be

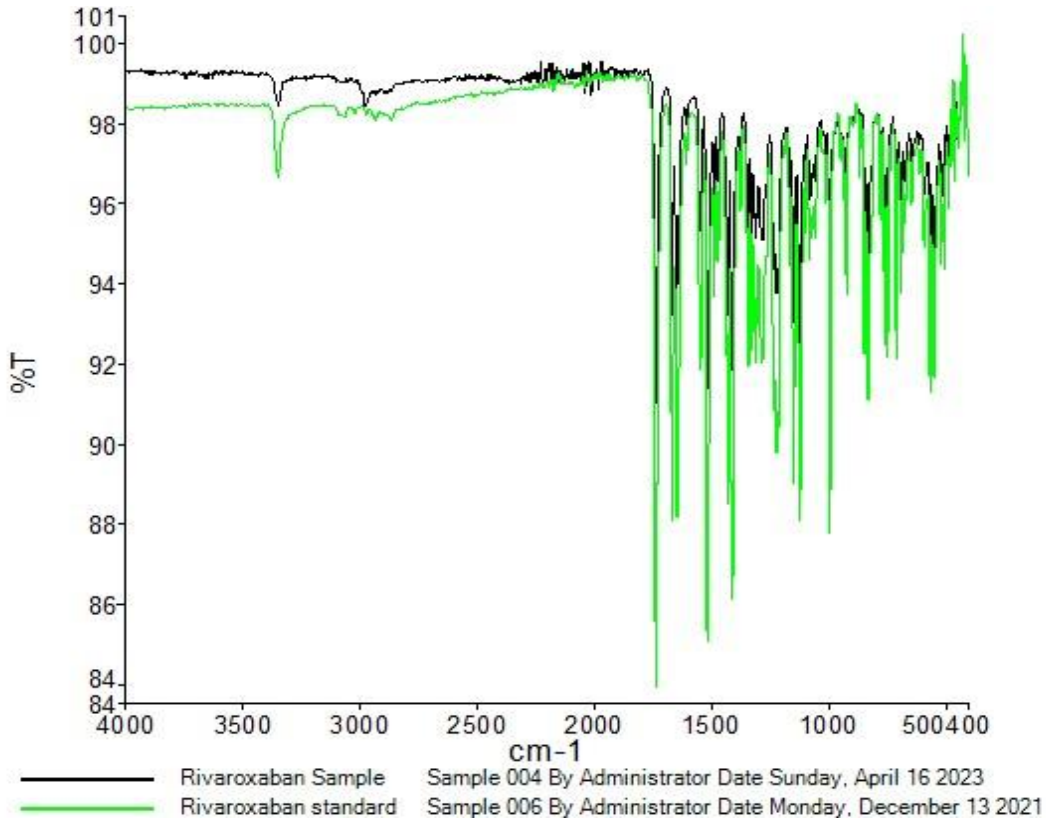
relatively low i.e. 59.64% and 37.98%. As per the limit of dissolution of drug other batches were found to be in the limit as shown in the below table which is from 85.10% to 94.14%. The time period for the dissolution was set as 45 minutes and it was seem to be complete release which is above 85%.

Figure 4.1: Dissolution release profile of Rivaroxaban buccal tablets



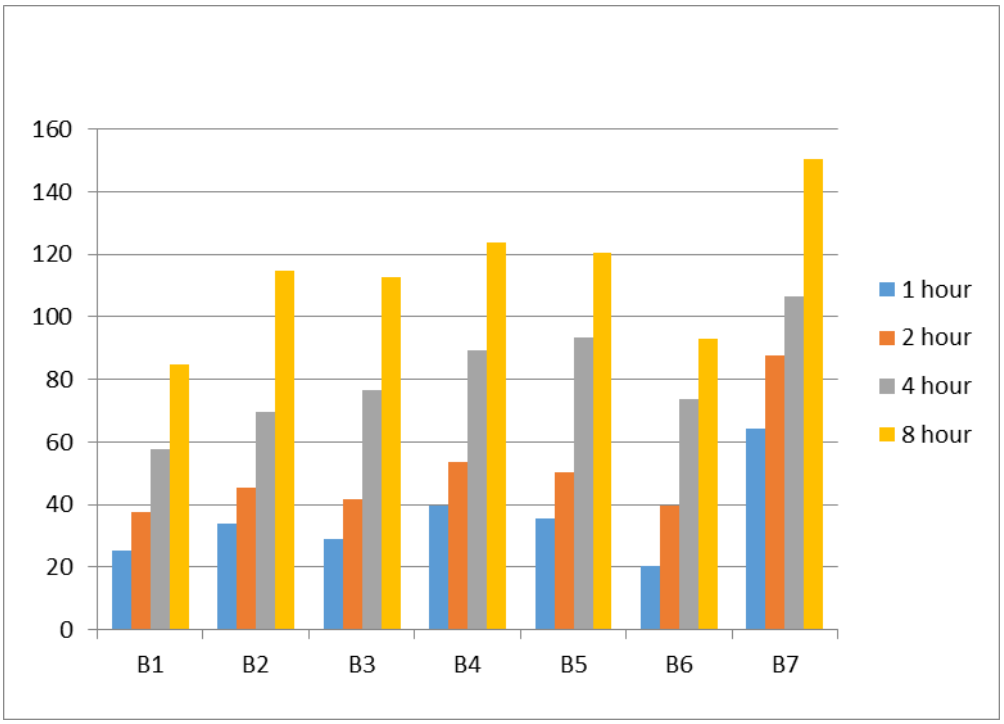
4.1.4 Compatibility study: The compatibility study was done by using Infrared spectrophotometer. The spectra of Reference and Test are shown in the figure 4.2 Form this we can see that interaction between the drug and excipient is not found.

Figure 4.2: Spectrum of Infrared



4.1.5 Swelling Index: The tablet's swelling properties was done on different time intervals i.e. 1, 2, 4 & 8 hours. The results of all the batches are represented in below figure. There was no any change in the shape & size in the tablets. Batch B7 showed the highest swelling capacity and batch B1 showed the lowest swelling capacity as per the result obtained during analysis.

Figure 4.3: Bar diagram of Swelling Index



4.2 Optimization of chromatographic condition and Calibration curve for standard:

The chromatographic condition of the analysis of Rivaroxaban buccal tablet was done as per British Pharmacopoeia 2022 which was used as quantitative analysis. For the system suitability relative standard deviation of replicate injections, average areas were found to be 0.036 and 6714127.

Figure 2 represent the chromatogram of standard. Whereas figure 3 represent the chromatogram of sample, like wise figure 4 and figure 5 represents the chromatogram of blank and placebo.

Figure 4.4:Chromatogram of Rivaroxaban Standard

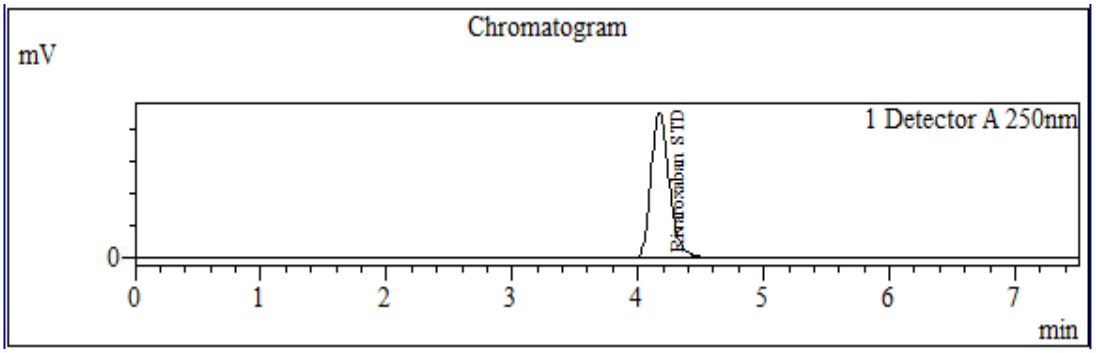


Figure 4.5:Chromatogram of Rivaroxaban Sample

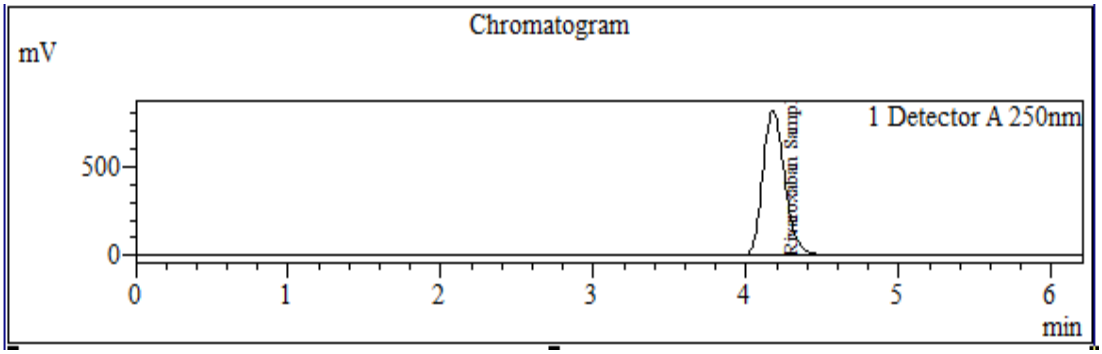


Figure 4.6: Chromatogram of Blank

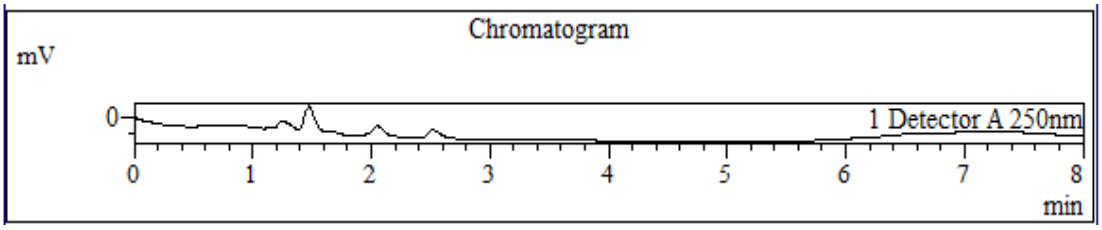
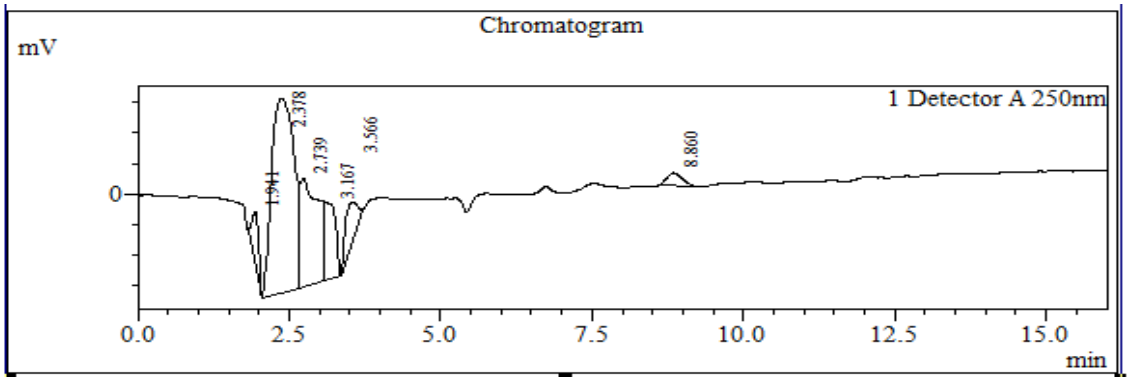


Figure 4.7: Chromatogram of Placebo



5. DISCUSSION

Formulation of Rivaroxaban buccal tablets was prepared and evaluation was done by using different parameters such as assay, dissolution, disintegration time, Swelling index, weight variation, dimension, hardness and friability. To evaluate this parameters HPLC, dissolution test apparatus, disintegration test apparatus, weighing balance, hardness tester, vernier caliper, IR spectrophotometer, Friability tester were used in order to find the better formulation among the above 7 formulations. As shown in the table 4.1 except batch 1 & 6, all have good drug content that is within the limit but batch 3 shows the best result in the formulation due to its swelling property which has a good swelling property and it has complete dissolution as shown in the figure 4.1.

6. CONCLUSION

The study was done to perform the formulation of the Rivaroxaban Buccal tablets. 7 different batches were taken to study the formulation. Among the 7 different batches, B3 shows the better results after the evaluation of the samples. It shows complete dissolution, release content and swelling property than other formulations as mentioned in the results. In the formuation for all the batches same excipients were used but the concentration were different. The amount of excipient used in the batch B3 shows the better result during the analysis and the physical and chemical properties also complies as per the standards. From this study we can conclude that the rivaroxaban buccal tablets can be an alternative route for those patient who have difficult in swallowing the tablets and it can also avoid the first pass effect.

7. ABBREVIATION

API: Active Pharmaceutical Ingredient

HPMC: Hydroxypropyl Methylcellulosse

MCCP:Microcrystalline Cellulose Powder

FTIR: Furier Transform Infrared Spectrometry

RPM: Revolution per Minute

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