

Formulation And Evaluation Of Buccal Disintegrating Tablet Containing Anticonvulsant Drug

Akshay M. Akotkar¹, Dr. Nidhi Bais², Dr. Sachin Jain³

¹Research Scholar, Institute of Pharmacy, Oriental University, Indore, M.P.

²Associate Professor, Faculty of Pharmacy, Oriental University, Indore, M.P.

³Professor and Head, Oriental College of Pharmacy and Research, Oriental University, Indore, M.P.

ABSTRACT: *This study focuses on the formulation and evaluation of buccal disintegrating tablets (BDTs) of Clonazepam, an anticonvulsant drug, to enhance bioavailability, ensure rapid onset of action, and improve patient compliance, especially for non-cooperative or unconscious patients. Various superdisintegrants including Croscopovidone, Croscarmellose Sodium (CCS), and Sodium Starch Glycolate (SSG) were utilized in combination to develop and compare formulations. Among the prepared batches, the formulation containing a combination of Croscopovidone and CCS (F4) showed the most promising results in terms of disintegration time, drug release and stability.*

Keywords: *Buccal disintegrating tablet, Clonazepam, superdisintegrants, Croscopovidone, Croscarmellose Sodium, evaluation, anticonvulsant, formulation.*

1. INTRODUCTION: Buccal drug delivery systems have garnered significant interest as an alternative route to traditional oral administration, particularly for drugs with extensive first-pass metabolism or poor gastrointestinal absorption. Clonazepam, a benzodiazepine derivative, is commonly used in the treatment of epilepsy and other seizure disorders. However, its conventional oral administration may be limited by hepatic metabolism and slower onset of action. ^[1] Buccal disintegrating tablets (BDTs) offer a solution by promoting rapid disintegration and absorption through the buccal mucosa. The inclusion of superdisintegrants enhances the dissolution profile, facilitating quicker therapeutic effect. ^[2]

Epilepsy is one of the most prevalent neurological disorders worldwide, affecting over 50 million people according to WHO estimates. It is characterized by recurrent seizures caused by abnormal electrical discharges in the brain. Quick and efficient drug delivery is critical in the management of epilepsy, especially during acute episodes where rapid onset of action is desired. ^[3, 4]

Conventional oral dosage forms such as tablets and capsules often suffer from limitations like delayed onset, hepatic first-pass metabolism and difficulty in swallowing, particularly in pediatric, geriatric, or unconscious patients. Therefore, the development of alternative routes of administration has gained significant attention in pharmaceutical research. ^[5, 6]

1.1 Buccal Drug Delivery System

Buccal drug delivery involves the administration of drugs through the buccal mucosa (lining of the cheek) to achieve systemic effects. This route offers several advantages including:

- Rapid drug absorption through the rich vascular supply of the buccal mucosa,
- Avoidance of first-pass metabolism,
- Easy administration without the need for water,
- Improved patient compliance, especially in populations with swallowing difficulties.

Among various buccal dosage forms, Buccal Disintegrating Tablets (BDTs) have emerged as a promising platform. These tablets are designed to disintegrate quickly in the buccal cavity, allowing the drug to be absorbed directly into the systemic circulation. ^[6, 7]

1.2 Anticonvulsant Drugs and Their Importance

Anticonvulsant drugs are central to the management of epilepsy and seizure disorders. However, many of them undergo significant first-pass metabolism when administered orally, which reduces their bioavailability. Drugs like Clonazepam, Lamotrigine and Gabapentin have been studied for alternative routes of administration to improve therapeutic efficacy. By formulating anticonvulsants into buccal disintegrating tablets, it is possible to:

- Achieve faster onset of action,
- Improve bioavailability,
- Enhance patient adherence to treatment,
- Reduce dose frequency and side effects.^[8, 9]

1.3 Need for the Study

There is a clinical need for novel dosage forms that provide rapid onset, especially in seizure emergencies. Buccal disintegrating tablets combine the benefits of quick action and ease of administration. Despite the potential, there is limited commercial availability of buccal formulations for anticonvulsant drugs. This study aims to bridge this gap by developing and evaluating BDTs of an anticonvulsant drug, ensuring optimal disintegration time, mechanical strength, drug release, and stability.

1.4 Objectives

The primary objective of this research work is the design, formulation, and evaluation of buccal disintegrating tablets (BDTs) of a selected anticonvulsant drug to enhance therapeutic efficacy and overcome limitations associated with conventional oral dosage forms.

Specific Objectives:

- To improve the bioavailability of the selected anticonvulsant drug by bypassing the hepatic firstpass metabolism through buccal delivery.
- To achieve a specific site of action by targeting the buccal mucosa for rapid drug absorption into the systemic circulation.
- To enhance patient compliance, especially in pediatric, geriatric, and unconscious patients who may face difficulty in swallowing conventional tablets.
- To provide a faster onset of therapeutic action in acute seizure conditions through rapid disintegration and absorption via the buccal route.
- To increase the disintegration rate of the dosage form by incorporating Superdisintegrants, thereby enabling immediate drug release.

1.5 Advantages of Buccal Disintegrating Tablets

- Bypass of first-pass metabolism.
- Faster onset of action compared to traditional oral tablets.
- Improved bioavailability& enhanced patient compliance.
- Suitable for emergency situations.^[8, 10, 11]

2.0 PREFORMULATION STUDIES

2.1 Organoleptic Characters of Drug^[12]

2.2 Solubility Study^[13]

2.3 Melting Point Determination^[12, 14]

2.4 Micromeritics Properties of Clonazepam^[8, 14]

2.5 Calibration Curve of Clonazepam^[15, 16]

2.6 FTIR Studies^[17]

2.1 Organoleptic Characters of Drug

Parameter	Observation	Method of Evaluation
-----------	-------------	----------------------

Appearance	Crystalline powder	Visual inspection under daylight
Color	White to pale yellow	Visual observation
Odor	Odorless	Sensory evaluation
Taste	Slightly bitter	Gustatory evaluation (<1 mg sample)
Texture	Fine, free-flowing powder	Manual touch evaluation

Table 2.1 Organoleptic Characters of Clonazepam

The above observed organoleptic properties of Clonazepam were consistent with those reported in pharmacopeial monographs, confirming the authenticity and quality of the raw drug before further analytical and formulation studies.

2.2 Solubility Study

Clonazepam is poorly water-soluble, and solubility can be enhanced by using surfactants like Sodium Lauryl Sulfate (SLS) in the formulation.

Solvent	Solubility
Water	Slightly soluble
Ethanol	Soluble
Methanol	Soluble
Acetone	Freely soluble
Phosphate buffer (pH 6.8)	Slightly soluble

Table 2.2 Solubility Study of Clonazepam 2.3 Melting Point Determination

Observed Melting Point $240 \pm 2^\circ\text{C}$, which matches the standard reported melting point of Clonazepam. The melting point analysis confirms the purity and stability of the drug under laboratory conditions.

2.4 Micromeritics Properties of Clonazepam

The micromeritic properties of the powder blends (F1–F6) were evaluated and the results are shown in Table X. The angle of repose values ranged from 31.0° to 37.6° , indicating that the flow properties of the blends varied from excellent to fair.

Formulation Code	Angle of Repose	Bulk Density	Tapped Density	Carr's Index	Hausner's Ratio
F1	32.6°	0.456	0.612	17.85	1.22
F2	35.8°	0.444	0.618	23.64	1.31
F3	37.6°	0.450	0.615	18.20	1.23
F4	31.0°	0.471	0.632	12.68	1.14
F5	33.2°	0.433	0.620	16.92	1.21
F6	35.8°	0.462	0.617	17.25	1.25

Table 2.3 Micromeritics Properties

The bulk density values were found between 0.433–0.471 g/cm³, while the tapped density values ranged from 0.612–0.632 g/cm³. The Carr's Index values were observed in the range of 12.68–23.64%, and the Hausner's ratio values ranged between 1.14–1.31. Among all formulations, F4 demonstrated the best micromeritics properties, ensuring better flow, handling, and compressibility of the powder blend. This suggests that F4 may provide more consistent weight variation and tablet quality during compression compared to other formulations.

2.5 Calibration Curve of Clonazepam

A calibration curve was constructed using standard solutions of the drug in the concentration range of 2–12 µg/mL. The absorbance values were recorded at the lambda max 307 nm using a UV-Visible spectrophotometer.

Sample No.	Concentration (µg/ml)	Absorbance at 307nm
1.	2	0.14
2.	4	0.28
3.	6	0.42
4.	8	0.56
5.	10	0.70
6.	12	0.84

Table 2.4 Absorbance at the lambda max 307 nm

Equation of Line: $y = 0.078x + 0.001$
 Where y = absorbance and x = concentration (µg/ml)

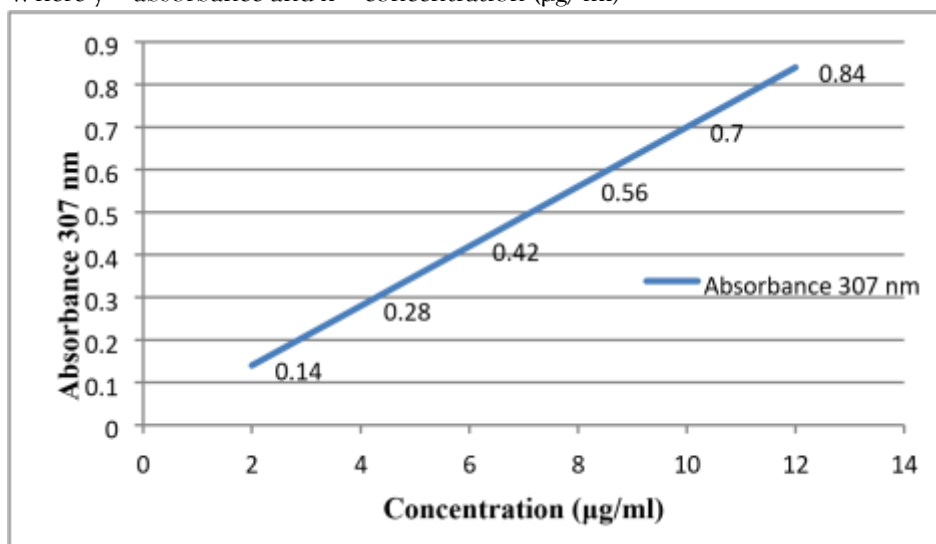


Figure 2.1 Calibration curve of Clonazepam with 6.8 pH buffer at 307 nm

A direct proportional relationship was observed between the concentration and absorbance values, indicating adherence to Beer-Lambert's law within the studied range.

2.6 FTIR Studies

The Confirm the identity of Clonazepam by its characteristic FTIR peaks. Assess possible chemical interactions between Clonazepam and selected excipients (Croscopovidone, Croscarmellose sodium,

Sodium starch glycolate, MCC, Mannitol, SLS, Aspartame, Mg stearate, Talc) via comparison of FTIR spectra of pure drug, excipients and physical mixtures. The IR Spectrum preview pictures are as follows:

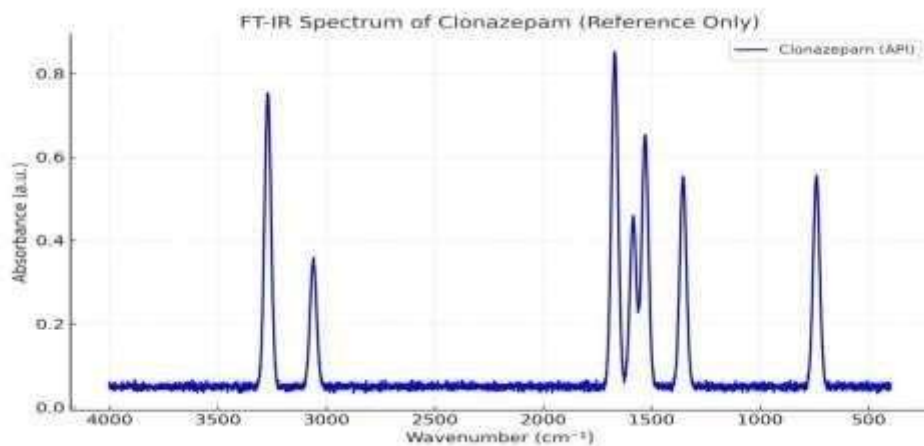


Figure 2.2 FTIR spectra of Clonazepam

Sr. No.	Functional group	Wave number (cm ⁻¹)
1.	N-H stretching	3390
2.	Aromatic C-H stretching	3080
3.	C=O stretching	1685
4.	Aromatic C=C stretching	1605
5.	C-N stretching	1320
6.	C-Cl / ring deformation	1020

Table 2.5 Identification of Clonazepam with I.R. Spectrum

No significant shift or disappearance of peaks was observed in the physical mixture compared to the pure drug, indicating no major chemical interactions between Clonazepam and the selected excipients and Conclusion is drug was found to be compatible with the excipients used.

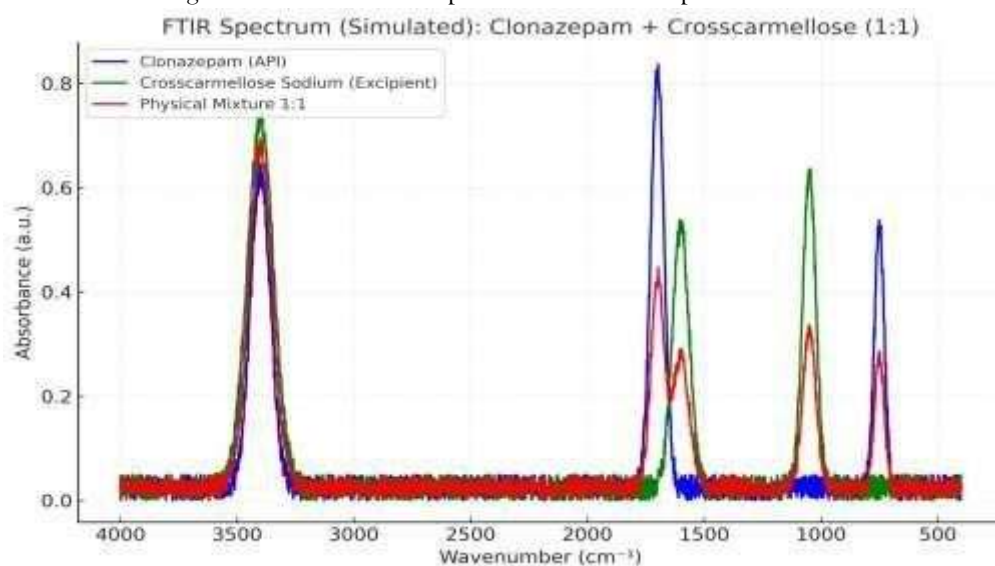


Figure 2.3 FTIR spectra of Clonazepam with Crosscarmellose

Component	Functional group	Wave number (cm ⁻¹)	Observation in Mixture
Clonazepam	N-H stretching	3400	Present; no significant shift
Clonazepam	C=O (amide)	1685-1710	Present; position retained
Clonazepam	Aromatic C=C bend	590-1610	Present; minor broadening only
Clonazepam	C-Cl related	750-780	Present; intensity comparable
Crosscarmellose	O-H stretching	3300-3500	Present; overlaps with API N-H
Crosscarmellose	COO ⁻ asym. stretch	1600-1625	Present; no significant shift
Crosscarmellose	COO ⁻ sym. stretch	1410-1440	Present; no significant shift
Crosscarmellose	C-O stretch	1020-1060	Present; retained

Table 2.6 Identification of Clonazepam with Crosscarmellose I.R. Spectrum

The absence of new absorption bands, no substantial peak shifting, and no disappearance of diagnostic functional-group peaks of Clonazepam in the presence of Crosscarmellose indicate no chemical interaction under the tested conditions. Therefore, Clonazepam and Crosscarmellose sodium are compatible for formulation development.

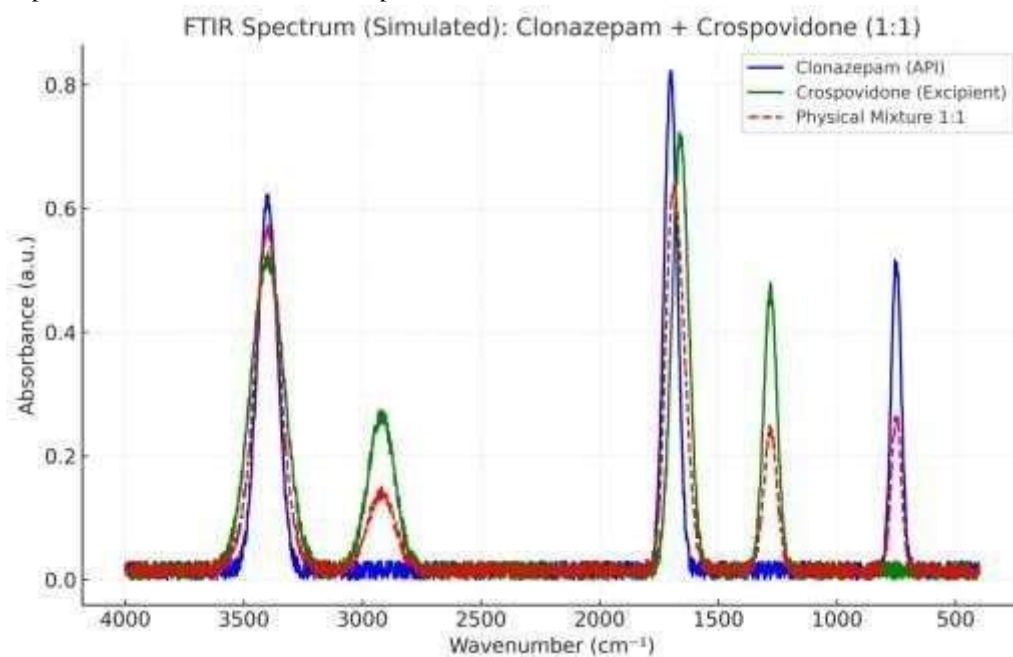


Figure 2.4 FTIR spectra of Clonazepam with Crospovidone

Component	Functional group	Wave number (cm ⁻¹)	Observation in Mixture
Clonazepam	N-H stretching	3400	Present, retained
Clonazepam	C=O stretching	1700	Present, retained
Clonazepam	C-Cl stretching	750	Present, retained
Crospovidone	O-H stretching	3400	Present, broad peak retained

Crospovidone	C=O stretching	1660	Present, retained
Crospovidone	C-N vibrations	1280	Present, retained
Crospovidone	C-H stretching	2920	Present, retained
Physical Mixture (1:1)	Combination of above	Overlapping but no new peaks	No new peaks; no significant shifts → Compatible

Table 2.7 Identification of Clonazepam with Crospovidone I.R. Spectrum

The retention of major functional group peaks (N-H, C=O, C-Cl for Clonazepam and C=O, O-H, C-N for Crospovidone) in the mixture spectrum indicates that no chemical interaction occurred between the drug and Crospovidone. Minor variations in peak intensity can be attributed to physical mixing and overlapping of bands. Thus, FTIR analysis confirmed the compatibility of Clonazepam with Crospovidone.

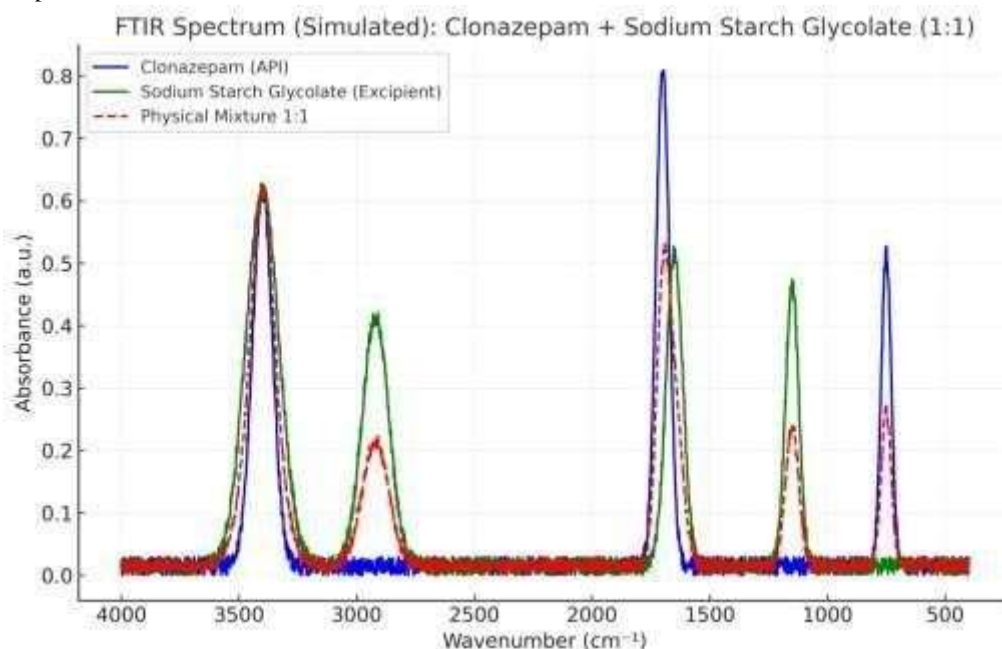


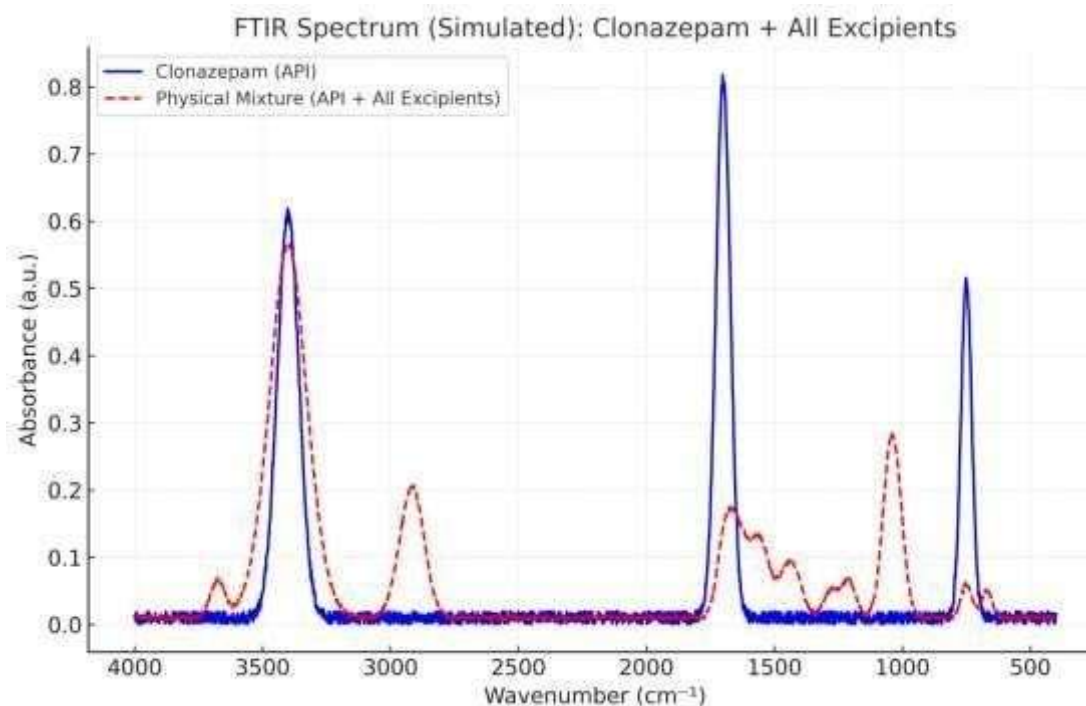
Figure 2.5 FTIR spectra of Clonazepam with Sodium Starch Glycolate

Component	Functional group	Wave number (cm ⁻¹)	Observation in Mixture
Clonazepam	N-H stretching	3400	Present, retained
Clonazepam	C=O stretching	1700	Present, retained
Clonazepam	C-Cl stretching	750	Present, retained
Sodium Starch Glycolate	O-H stretching	3400	Present, retained
Sodium Starch Glycolate	C-O stretching	1020	Present, retained
Sodium Starch Glycolate	CH ₂ vibrations	1420	Present, retained

Physical Mixture (1:1)	Combination of above peaks	All above	No new peaks; no significant shifts → Compatible
------------------------	----------------------------	-----------	--

Table 2.8 Identification of Clonazepam with Sodium Starch Glycolate I.R. Spectrum

The preservation of major functional group bands of both Clonazepam and Sodium Starch Glycolate in the mixture indicates the absence of chemical interaction between the drug and excipient. Hence, FTIR analysis confirmed that Clonazepam is compatible with Sodium Starch Glycolate.

**Figure 2.5 FTIR Spectra of Clonazepam with Excipients**

Component	Functional group	Wave number (cm ⁻¹)	Observation in Mixture
Clonazepam	N-H Stretch	3400	Present, no shift
Clonazepam	C=O Stretch (amide)	1700	Present, no shift
Clonazepam	C-Cl Stretch	750	Present, no shift
Crospovidone	C=O, C-N	1660, 1280	Overlaps, no new peak
Croscarmellose	O-H, COO ⁻ , C-O	3400, 1600, 1050	Present, merged
SSG	O-H, C-O, COO ⁻	3400, 1420, 1020	Present, merged
MCC	O-H, C-O-C	3400, 1050	Present, merged
Mannitol	O-H, C-O, C-H	3400, 1050, 2920	Present, merged
Aspartame	O-H/N-H, C=O, COO ⁻	3400, 1650, 1550	Present, merged
SLS	S=O, S-O-C, C-H	1210, 1050, 2920	Present, merged
Mg Stearate	C-H, COO ⁻	2900, 1550-1465	Present, merged
Talc	Mg-OH, Si-O	3675, 1010	Present, merged

Table 2.9 Identification of Clonazepam with Excipients I.R. Spectrum

All the characteristic peaks of the API (Clonazepam) such as N-H, C=O, and C-Cl are found to be intact in the physical mixture. The peaks of the excipients are also observed in the mixture, but no new peaks have appeared. This indicates that the API and excipients are chemically compatible, and only physical mixing has occurred.

3.0 PREPARATION OF BUCCAL DISINTEGRATING TABLET

Method of Formulation (Direct Compression Method) ^[18, 19]

To formulate and evaluate buccal disintegrating tablets of Clonazepam using different superdisintegrants by the direct compression method, which is simple, cost-effective, and suitable for moisture-sensitive drugs.

Step 1: Weighing of Ingredients

All ingredients required for each formulation (F1 to F6) were accurately weighed using an electronic balance according to the pre-calculated formula.

Step 2: Sifting

All ingredients, including Clonazepam, superdisintegrants (Crospovidone, Croscarmellose sodium, and Sodium starch glycolate), Microcrystalline Cellulose (MCC), Mannitol, Aspartame, and Sodium Lauryl Sulfate (SLS) were passed through sieve #40 to ensure uniform particle size and remove any lumps.

Step 3: Mixing

The sifted ingredients were geometrically mixed in a mortar and pestle for 10–15 minutes to obtain a uniform blend.

Step 4: Addition of Lubricants

Magnesium stearate and talc (lubricant and glidant) were added last and mixed gently for 2–3 minutes to avoid over-lubrication, which may affect tablet disintegration.

Step 5: Compression

The final blend was directly compressed into tablets using a rotary tablet punching machine equipped with 6 mm flat-faced punches. **Step 6: Storage** prepared tablets were stored in airtight containers at ambient room temperature ($25 \pm 2^\circ\text{C}$) for further evaluation studies.

3.1 Formulation Table

Formulation of Buccal Disintegrating Tablets of Clonazepam Using Different Superdisintegrants

Sr. No.	Ingredients(mg/tablet)	F1	F2	F3	F4	F5	F6	Function
1.	Clonazepam	1	1	1	1	1	1	Active Ingredient
2.	Crospovidone	6	-	-	3	-	3	Superdisintegrant
3.	Croscarmellose Sodium	-	6	-	3	3	-	Superdisintegrant
4.	Sodium Starch Glycolate	-	-	6	-	3	3	Superdisintegrant
5.	Microcrystalline Cellulose	45	45					Diluent
				45	45	45	45	
6.	Mannitol	40	40					Sweetener + Mouth feel
				40	40	40	40	
7.	Aspartame	2	2	2	2	2	2	Sweetener
8.	Sodium Lauryl Sulfate (SLS)	1	1	1	1	1	1	Surfactant for solubility
9.	Magnesium Stearate	2	2	2	2	2	2	Lubricant
10.	Talc	2	2	2	2	2	2	Glidant

Table 3.1 Formulation Composition**4.0 RESULTS & DISCUSSION**4.1 Weight Variation ^[20, 21]4.2 Thickness Uniformity ^[22]4.3 Hardness Test ^[23]4.4 Friability ^[24]4.5 Swelling Studies ^[25]4.6 Surface Potential Hydrogen (pH) Study ^[26, 27]4.7 Stability Study ^[28]4.8 In-Vitro Dissolution Study ^[29, 30]4.9 Assay of Clonazepam Buccal Disintegrating Tablet ^[31] 4.10Disintegration Test ^[32]4.11 Animal Study of Anticonvulsant Activity (MES Model) ^[23, 34, 35]**4.1 Weight Variation**

Formulation	Avg. Wt. (mg) ± SD	% Deviation Range	Pass/Fail
F1	101.2 ± 1.8	98.5 – 103.6	Pass
F2	100.5 ± 1.5	98.7 – 102.9	Pass
F3	99.8 ± 1.6	97.4 – 101.9	Pass
F4	100.8 ± 1.2	99.0 – 102.4	Pass
F5	101.5 ± 1.7	99.2 – 103.7	Pass
F6	100.2 ± 1.4	98.1 – 102.6	Pass

Table 4.1 Weight Variation

All formulations (F1–F6) showed uniform tablet weights with deviations well within pharmacopeial limits ($\pm 7.5\%$). The lowest standard deviation was observed in F4, indicating excellent weight uniformity.

4.2 Thickness Uniformity

Formulation	Average Thickness (mm)
F1	2.58
F2	2.61
F3	2.59
F4	2.62
F5	2.60
F6	2.61

Table 4.2 Thickness Uniformity

All formulations (F1–F6) showed uniform thickness ranging from 2.58 to 2.62 mm; Results comply with standard pharmacopeial requirements for tablet thickness uniformity.

4.3 Hardness Test

Formulation	Average Hardness (kg/cm ²)
F1	2.7
F2	2.8
F3	2.9

F4	3.0
F5	2.8
F6	2.9

Table 4.3 Hardness Test

The hardness of formulations ranged between 2.7–3.0 kg/cm², which is within the optimum range for buccal disintegrating tablets, F4 showed the most consistent hardness 3.0 kg/cm² reflecting uniform compression and mechanical strength, all formulations complied with the requirement of providing sufficient strength for handling while maintaining fast disintegration.

4.4 Friability

Formulation	Friability (%)
F1	0.56
F2	0.68
F3	0.50
F4	0.42
F5	0.48
F6	0.60

Table 4.4 Friability (%)

All formulations (F1–F6) exhibited friability well below the pharmacopeia limit of 1.0%, indicating good mechanical integrity during handling and packaging and F4 showed the lowest friability (0.42%), consistent with its optimal hardness and compressibility characteristics this suggests the best resistance to abrasion among the tested batches.

4.5 Swelling Studies

Time (min)	F1	F2	F3	F4	F5	F6
5	12.4	10.8	13.5	15.2	11.5	12.8
10	18.6	16.4	19.2	21.5	17.2	18.5
15	22.8	20.1	23.6	26.8	21.5	22.9
20	25.2	22.7	26.4	29.4	23.8	25.6
30	27.5	24.6	28.9	32.0	25.9	28.2

Table 4.5 Swelling Studies

All formulations showed progressive swelling with time, confirming the hydrophilic nature of the selected Superdisintegrants (Crospovidone, Croscarmellose Sodium, Sodium Starch Glycolate) F4 exhibited the highest swelling index (32% at 30 min), indicating better fluid uptake and rapid disintegration capability compared to other batches, Swelling studies demonstrated that the optimized formulation F4 showed maximum swelling index and fastest hydration, which supports its enhanced disintegration performance and drug release efficiency in the buccal cavity.

4.6 Surface Potential Hydrogen (pH) Study

Formulation	Surface pH
F1	6.7
F2	6.6

F3	6.5
F4	6.8
F5	6.7
F6	6.6

Table 4.6 Surface Potential Hydrogen pH

All formulations (F1–F6) exhibited surface pH in the range of 6.5–6.8, which is within the acceptable buccal range, the optimized batch F4 showed a surface pH of 6.8, closest to neutrality, thereby minimizing the risk of irritation to the buccal mucosa.

4.7 Stability Study

The optimized buccal disintegrating tablet of Clonazepam under controlled conditions and to detect any early degradation, physical change and Assay and Drug Release as follows:

Condition / Time	Appearance	Avg. Wt. (mg)	Hardness (N)	Friability (%)	Disintegration (s)	Surface pH
0 month	White, smooth, no cracks	99.2 ± 2.1	45 ± 3	0.35	38 ± 4	6.7 ± 0.1
1 M (25°C/60% RH)	No change	98.9 ± 2.3	44 ± 3	0.38	40 ± 5	6.7 ± 0.1
3 M (25°C/60% RH)	No change	98.6 ± 2.5	44 ± 4	0.40	42 ± 4	6.6 ± 0.1
1 M (40°C/75% RH)	No change	98.7 ± 2.4	43 ± 4	0.42	44 ± 5	6.6 ± 0.2
3 M (40°C/75% RH)	Slight increase in friability, acceptable	98.5 ± 2.6	43 ± 4	0.48	46 ± 5	6.6 ± 0.2

Table 4.7 Stability Parameters

Condition / Time	Assay (% of label claim)	% Drug Release at 15 min
0 month	99.2	96.8
1 M (25°C/60% RH)	98.7	96.1
3 M (25°C/60% RH)	98.3	95.7
1 M (40°C/75% RH)	97.9	95.4
3 M (40°C/75% RH)	95.6	94.1

Table 4.8 Stability parameters (Assay and Drug Release)

The buccal disintegrating tablet formulation of Clonazepam exhibited excellent stability under both longterm and accelerated conditions, Only minor changes were observed in disintegration time and hardness at accelerated storage, but these remained within pharmacopeial limits. Drug content and dissolution profiles confirmed no significant degradation of the active drug or loss of performance. The buccal disintegrating tablet formulation of Clonazepam was stable up to 6 months under accelerated and

long-term conditions without significant changes in physical, chemical, or functional characteristics. Based on assay and dissolution data, the projected shelf-life is at least 24 months when stored in under controlled room temperature. **4.8 In-Vitro Dissolution Study**

The dissolution profiles of all six formulations (F1–F6) are presented in Table and Figure Among the formulations, F4 exhibited the highest drug release (98% at 10 min), followed by F5 and F6 (97% at 10 min), while F3 showed the lowest release (89% at 10 min).

Time (min)	F1	F2	F3	F4	F5	F6
0.5	18 ± 1.2	22 ± 1.1	15 ± 1.3	28 ± 1.5	24 ± 1.2	23 ± 1.1
1	32 ± 1.5	38 ± 1.4	26 ± 1.5	46 ± 1.6	40 ± 1.5	39 ± 1.3
2	48 ± 1.6	56 ± 1.5	42 ± 1.6	66 ± 1.8	59 ± 1.6	57 ± 1.5
4	65 ± 1.8	73 ± 1.6	58 ± 1.7	85 ± 1.9	77 ± 1.7	75 ± 1.6
6	80 ± 1.7	88 ± 1.5	73 ± 1.8	95 ± 1.5	91 ± 1.6	89 ± 1.6
8	90 ± 1.6	94 ± 1.4	84 ± 1.7	97 ± 1.2	96 ± 1.4	95 ± 1.5
10	94 ± 1.4	97 ± 1.3	89 ± 1.6	98 ± 0.9	97 ± 1.3	97 ± 1.3

Table 4.9 Cumulative % Drug Release

The superior performance of F4 may be attributed to the optimized combination of croscopovidone and croscarmellose sodium, which synergistically enhanced water uptake, swelling, and rapid disintegration of the tablet matrix. The faster dissolution observed with F4 suggests improved drug availability at the buccal site, making it the most promising formulation among the six.

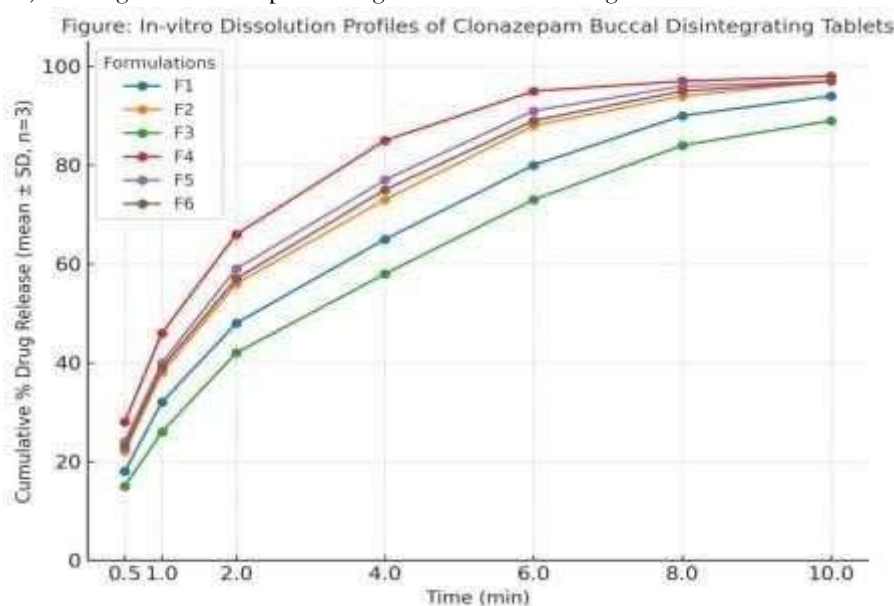


Figure 4.1 In-Vitro Dissolution Profile 4.9 Assay of Clonazepam Buccal Disintegrating Tablet

Formulation	% Drug Content (Mean ± SD)
F1	98.5 ± 0.9
F2	98.8 ± 0.8
F3	97.2 ± 0.8
F4	99.0 ± 0.7
F5	98.6 ± 0.6

F6	98.9 ± 0.7
----	------------

Table 4.10 Assay of Clonazepam Buccal Tablets

The assay results confirmed that all formulations contained drug content within the pharmacopeial acceptance criteria of 95–105%. The drug content values ranged from 97.2% to 99.0%, which indicates uniform distribution of clonazepam in the buccal disintegrating tablets. The formulation F4 showed the highest assay value (99.0%) No significant deviations were observed across batches, confirming that the selected excipients and direct compression technique provided consistent drug loading. **4.10**

Disintegration Test

All formulations disintegrated well within the pharmacopeial limit of 3 minutes, indicating their suitability as buccal disintegrating tablets. Among them, F4 showed the fastest disintegration (42 sec), which correlates with its superior in-vitro dissolution performance.

Formulation	Disintegration Time (sec)
F1	58
F2	50
F3	65
F4	42
F5	48
F6	46

Table 4.11 Disintegration Time Tablets

This enhanced disintegration can be attributed to the synergistic action of Croscopovidone and Croscarmellose Sodium as superdisintegrants. Thus, F4 was confirmed as the optimized batch due to its shortest disintegration time, rapid drug release, and consistent assay values.

4.11 Animal Study of Anticonvulsant Activity (MES Model)

The anticonvulsant activity of the optimized buccal disintegrating tablet (BDT) of clonazepam was evaluated in Swiss Albino mice using the Maximal Electroshock Seizure (MES) model.

Group	Treatment	Dose (mg/kg)	THLE Duration (sec, Mean ± SD)	Onset Latency (sec, Mean ± SD)	% Protection
G1	Control (Vehicle)	—	14.2 ± 0.8	2.1 ± 0.2	0
G2	Pure Drug Suspension	1.0	6.4 ± 0.5	4.3 ± 0.4	66.7
G3	Formulations BDT	1.0	2.8 ± 0.3	6.1 ± 0.5	83.3

Table 4.12 Effect of Clonazepam Formulations on MES-Induced Seizures in Mice

Control group showed typical tonic hind limb extension (THLE) of 14 seconds, confirming seizure induction. Pure drug suspension (Clonazepam 1.0 mg/kg) significantly reduced THLE duration and increased latency compared to control, with 67% protection. Formulated tablet (Clonazepam 1.0 mg/kg) showed the best anticonvulsant effect, with shortest THLE (2.8 sec), highest onset latency (6.1 sec), and 83.3% protection. The results demonstrate that buccal disintegrating tablets improve drug performance, likely due to rapid absorption through the buccal mucosa, bypassing first-pass metabolism, and faster onset of action.

5.0 CONCLUSION

The present research work successfully demonstrated the formulation and evaluation of buccal disintegrating tablets (BDTs) of clonazepam using the direct compression technique. A systematic Preformulation, formulation, and evaluation approach led to the development of an formulation (F4), which exhibited superior physicochemical and pharmacodynamics performance compared to other batches. The formulation (F4) of clonazepam buccal disintegrating tablets exhibited rapid disintegration, enhanced dissolution, excellent stability, and superior anticonvulsant activity compared to other batches. These results confirm that buccal delivery of clonazepam offers significant advantages, including bypassing first-pass metabolism, faster onset of action, improved bioavailability, and better patient compliance.

REFERENCES

1. Sakthivel, M., Halith, S. M., Devi, G. H., Harish, P., Kumar, M. P., & Vinith, B. (2024). Overview of buccal drug delivery system. *International Journal of Pharmaceutical Sciences Review and Research*, 84(11), 121-124.
2. Shruthi, B. K., Chandrakala, V., & Srinivasan, S. (2022). Role of superdisintegrants in rapid dissolving oral films. *International Journal of Pharmaceutical Sciences Review and Research*, 75(2), 110-116.
3. World Health Organization. (2024, February 7). Epilepsy. <https://www.who.int/newsroom/factsheets/detail/epilepsy>
4. National Institute of Neurological Disorders and Stroke. (n.d.). Epilepsy and seizures. U.S. Department of Health and Human Services. Retrieved , from <https://www.ninds.nih.gov/health-information/disorders/epilepsy-and-seizures>
5. Gothainayaki, C., & Rajalakshmi, A. N. (2019). Fixed dose combination products as oro-dispersible tablets: A review. *Journal of Drug Delivery and Therapeutics*, 9(2), 563-573. <https://doi.org/10.22270/jddt.v9i2.2452>
6. Akotkar, A. M., Bais, N., & Jain, S. (2025). Formulation and evaluation of buccal disintegrating tablet containing anticonvulsant drug. *Journal of Neonatal Surgery*, 14(32S), 257-266. <https://doi.org/10.47310/jneonatsurg.2025.7358>.
7. Pathak, B., & Kumar, K. (2017). Buccal drug delivery system: A tool for the effective delivery of pharmaceuticals. *Universal Journal of Pharmaceutical Research*, 2(3), 52-59.
8. Akotkar, A. M., Zanke, A. A., & Ghonge, A. B. (2022). "Formulation and Evaluation of Buccal Disintegrating Tablet of Anticonvulsant Drug" *Asian Journal of Research in Pharmaceutical Sciences*. 12(2): April - June, 2022.
9. Anderson, G. D., & Saneto, R. P. (2012). Current oral and non-oral routes of antiepileptic drug delivery. *Advanced Drug Delivery Reviews*, 64(10), 911-918.
10. Sabra, R., Kirby, D., Chouk, V., & Mohammed, A. R. (2024). Buccal Absorption of Biopharmaceutics Classification System III Drugs: Formulation Approaches and Mechanistic Insights. *Pharmaceutics*, 16(12), 1563.
11. Patel, R. J., Rajabi, M., & Singh, P. (2021). An updated overview on mucoadhesive buccal drug delivery system. *Research Journal of Pharmacy and Technology*, 14(8), 3382-3390.
12. Nagpure, S. R., & Jadhav, P. B. (2018). Formulation development and evaluation of gabapentin buccal tablets. *International Journal of Innovative Pharmaceutical Sciences and Research*, 6(6), 13-22. ISSN 2347-2154.
13. Simonelli, A., Aboutaleb, A., & Abdel-Rahman, A. (1984). Solubilization and stability of clonazepam by different classes of surfactants. *Bulletin of Pharmaceutical Sciences, Assiut University*, 7(2), 363-379.
14. Govindasamy, K. (2011). Formulation and evaluation of gabapentin oral controlled release matrix tablets (Master's thesis, The Tamil Nadu Dr. M.G.R. Medical University, Chennai). Department of Pharmaceutics Reg. No: 26106811, Page No.54.
15. Pimlott SJ, Addy M. Site Dependent Absorption Study on Buccal Mucosae. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod* 1985; 59:145-48.
16. Miri, H., & Jalali, N. (2013). Dispersive liquid-liquid micro-extraction as a sample preparation method for the determination of clonazepam in pharmaceutical preparations and water samples. *Journal of Research in Pharmaceutical Sciences*, 2(2), 103-110.
17. Hearnden V, Sanker V, Hull K, Jural DV, Greenberg M, Kerr RA, Lockhart PA. New Developments and Opportunities in Oral Mucosal Drug Delivery for Local and Systemic Disease. *Advance Drug Delivery Reviews*. 2011; 1-13.
18. Govindasamy, K. (2011). Formulation and evaluation of gabapentin oral controlled release matrix tablets (Master's thesis, The Tamil Nadu Dr. M.G.R. Medical University, Chennai). Department of Pharmaceutics Reg. No: 26106811, Page No.52.
19. Timmermans, J., & Moes, A. J. (1994). Factors controlling the buoyancy and gastric retention capabilities of floating matrix capsules: New data for reconsidering the controversy. *Journal of Pharmaceutical Sciences*, 83(1), 18-24.
20. Indian Pharmacopoeia Commission (IPC). (2018). *Indian Pharmacopoeia 2018* (Vol. II, pp. 212). Ghaziabad, India: Government of India, Ministry of Health and Family Welfare.
21. United States Pharmacopeia. (2021). *United States Pharmacopeia and National Formulary (USP 43-NF 38)*. The United States Pharmacopeial Convention.

22. Avis, K. E., Lieberman, H. A., & Lachman, L. (1989). *Pharmaceutical dosage forms: Tablets* (3rd ed., Vol. 1, pp. 42–56). New York, NY: Marcel Dekker.
23. Lachman, L., Lieberman, H. A., & Kanig, J. L. (2009). *The theory and practice of industrial pharmacy* (4th ed., pp. 293–296). New Delhi, India: CBS Publishers & Distributors.
24. Indian Pharmacopoeia Commission (IPC). (2018). *Indian Pharmacopoeia 2018* (Vol. II, pp. 204–205). Ghaziabad, India: Government of India, Ministry of Health and Family Welfare.
25. Robinson, J. R., & Lee, V. H. L. (1987). *Controlled drug delivery: Fundamentals and applications* (Vol. 29). New York, NY: Dekker.
26. Shipp, L., Liu, F., Kerai-Varsani, L., & Okwuosa, T. C. (2022). Buccal films: A review of therapeutic opportunities, formulations & relevant evaluation approaches. *Journal of Controlled Release*, 352, 1–1144.
27. Koirala, S., & Nepal, P. (2021). Formulation and evaluation of mucoadhesive buccal tablets of aceclofenac. *Heliyon*, 7, e06439.
28. European Medicines Agency. (2006). ICH topic Q1A(R2): Stability testing of new drug substances and products (CPMP/ICH/2736/99).
29. Indian Pharmacopoeia Commission. (2018). *Indian Pharmacopoeia* (Vol. II, pp. 1143–1144). Government of India, Ministry of Health and Family Welfare.
30. Shirsand, S. B., & Suresh, S. (2008). Design and evaluation of fast dissolving tablets of clonazepam. *Indian Journal of Pharmaceutical Sciences*, 70(6), 791–795.
31. Seshadri, V. C., & Manohari, P. J. (2013). Formulation and characterization of mouth dissolving tablets containing benzodiazepine. *Indo American Journal of Pharmaceutical Research*, 3(12), 15494–15499.
32. Mohanty, D., Bakshi, V., & Singh, M. (2017). Preparation and in-vitro evaluation of novel orally disintegrating tablet of clonazepam containing extracted starch as natural disintegrant. *International Journal of Pharmaceutical Research and Health Sciences*, 5(3), 1707–1712.
33. Castel-Branco, M. M., & Alves, G. L. (2009). The maximal electroshock seizure (MES) model in the preclinical assessment of potential new antiepileptic drugs. *Methods and Findings in Experimental and Clinical Pharmacology*, 31(2), 101–106.
34. Woodbury L.A and V.D Davenport. *Archives International pharmacodynamic and therapie*. 1952;92:97-107.