Chinese Journal of Health Management
Volume 19 Issue 12, Year of Publication 2025, Page 1105-1113 | DoI-10.564220/1674-0815.2025.152

ISSN: 1674-0815

cjhmonline.com

DoI-10.564220/1674-0815

Chinese Journal of Health Management

Chinese Medical Association

Formulation and Evaluation of Sublingual Tablets of Mirtazapine

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Article Information
Received: 05-10-2025
Revised: 18-10-2025
Accepted: 17-11-2025
Published: 22-12-2025

Keywords
Mirtazapine, Sublingual tablets, SSG, Crospovidone, In Vitro Disintegration time, In vitro dissolution.

ABSTRACT:
The objective of the present investigation is to develop a formulation of Sublingual tablets of Mirtazapine by Direct compression method. For the preparation of Sublingual tablets various Super disintegrants were used like sodium starch glycolate (SSG) and Crospovidone. Precompression parameters like Carr's Index, Hausner's Ratio and Angle of Repose meets the standard values of powder flow properties. The average weight variation, friability and hardness were within compendial limits which showed that all formulations possessed good mechanical strength. The optimized formulation M3 showed minimum disintegration time of 24.52 ± 1.08 secs, and drug release of 97.12 % in 10 mins among all other batches of tablets. The result of stability study of the batch M3 showed that there were no significant changes in Hardness, In-vitro Disintegration time, Friability, Drug content and In Vitro dissolution profile when stored at room temperature for period of one month. From the study it was concluded that Sublingual tablets of Mirtazapine is an acceptable dosage form which suggests that it is likely to become one of the choices of Mirtazapine preparations for the treatment of Depression.

INTRODUCTION:
Mirtazapine is a tetra-cyclic antidepressant that was FDA approved in 1997 as treatment for moderate and severe depression. The drug has sedative, antiemetic, anxiolytic, and appetite stimulatory effects, which explains its off-label use for conditions such as insomnia, panic disorder, posttraumatic stress disorder, obsessive-compulsive disorder, generalized anxiety disorder, social anxiety disorder, headaches, and migraines.[1] Clinicians usually prescribe mirtazapine for major depressive disorder after a trial of selective serotonin reuptake inhibitors (SSRIs). Mirtazapine is primarily prescribed to patients with depression and insomnia or a low body mass index (BMI). It displays antagonist effects on alpha-adrenergic, muscarinic, and histaminic receptors. It acts as a serotonin–norepinephrine reuptake inhibitor (SNRI) (a reuptake inhibitor of serotonin and norepinephrine), with additional antiadrenergic, antihistamine, anti-serotonergic, and anticholinergic activities.[2-5]

Mirtazapine's low bioavailability due to favorable pharmacokinetics can be fixed by producing the drug as a sublingual tablet. Also, ageing is an important risk factor for the development of depression. However, as patients age, they often stop taking their medications for a variety of reasons, the most common of which being swallowing difficulties and changes in the bioavailability profile brought on by biological profile changes. Therefore, a sublingual tablet containing an anti-depressant medication can help in overcoming those issues. Therefore, an effort is being made to create a Mirtazapine sublingual tablet as the perfect substitute to improve oral bioavailability, patient compliance, and drug delivery.[6-7]

Sublingual tablets bypass the gastrointestinal tract and liver, allowing the active ingredient to enter the bloodstream directly through the mucous membranes under the tongue. This results in faster absorption and enhanced bioavailability, as the drug avoids the first-pass metabolism that typically occurs when taken orally. This mechanism can lead to quicker onset of action and more reliable drug levels in the body.[8-10]

Sublingual tablets show higher bioavailability in comparison to other conventional dosage forms. This phenomenon can be explained by the drug's direct absorption into the sublingual blood vessels and lymphatic system, which promotes systemic circulation without passing through the liver. Therefore, it is expected that medications will be absorbed under the tongue quickly, producing a therapeutic impact more quickly. So the objective of the study was to formulate and evaluate Mirtazapine Sublingual Tablets.

However, because it is in BCS class II, its permeability is high, but it offers a very low oral bioavailability of only 50%. It has a half-life of 20-40 hours and is recommended as a once-daily dose of 15-45 mg.[11-12]

MATERIALS AND METHOD:

Materials:

Mirtazapine an API was procured from Cadia Pharmaceuticals Ltd, Ahmedabad, Gujarat, India. Microcrystalline cellulose (MCC) talc, mannitol, magnesium stearate, Sodium starch glycolate (SSG), sodium lauryl sulphate (SLS), and crospovidone were procured from Chemdyes Corporation, Rajkot, Gujarat, India.

Method:[13-14]

Mirtazapine sublingual tablets were prepared by the direct compression method. All ingredients were accurately weighed and passed through a mesh sieve to ensure uniform particle size. The required quantity of Mirtazapine 15 mg was mixed uniformly with excipients such as mannitol, microcrystalline cellulose (MCC), crospovidone, sodium starch glycolate (SSG), and sodium lauryl sulphate (SLS) as per the formulation table 1. The mixture was blended thoroughly to obtain a uniform powder. Finally, magnesium stearate and talc were added and mixed gently for a few minutes. The prepared blend was compressed into tablets using rotary tablet compression machine.

Table 1: Formulation of batches M1 to M6 by direct compression technique

INGREDIENTS (mg)	M1	M2	M3	M4	M5	M6
Mirtazapine	15	15	15	15	15	15
Crospovidone	2.5	3.5	4.5	-	-	-
Sodium starch glycolate	-	-	-	2.5	3.5	4.5
Microcrystalline cellulose	65.66	64.66	63.66	65.66	64.66	63.66
Mannitol	33	33	33	33	33	33
Sodium lauryl sulphate	0.24	0.24	0.24	0.24	0.24	0.24
Talc	1.2	1.2	1.2	1.2	1.2	1.2
Magnesium stearate	2.4	2.4	2.4	2.4	2.4	2.4
Total weight	120	120	120	120	120	120

Determination of Melting point of Mirtazapine: [15]

Melting point of Mirtazapine was measured by capillary apparatus. Minimum amount of drug was placed in a thin-walled capillary tube closed at one end. This capillary was then mounted in a melting point apparatus with thermometer and then their temperature range over which Mirtazapine melts is measured. The readings were taken in triplicate.

Estimation of drug by UV Spectroscopy: [16]

Preparation of Phosphate buffer at pH 6.8: Amount of 28.80 gm of Disodium Hydrogen Phosphate, 11.45 gm of potassium Dihydrogen Phosphate and were diluted up to 1000 ml with distilled water to prepare 6.8 PH

phosphate buffer solution.

Preparation of standard stock solution in phosphate buffer at pH 6.8: Standard stock solution of Mirtazapine was prepared by dissolving 10 mg of Mirtazapine in 100 ml phosphate buffer (pH 6.8), which make the stock solution of concentration of 100 µg/ml.

Determination of λ_{max} of Mirtazapine in phosphate buffer at pH 6.8: For determination of λ_{max}, stock solution was scanned between 200-400 nm against phosphate buffer (pH 6.8) as a blank in the UV-Visible spectrophotometer.

Preparation of working solutions: Working solution of concentration 5, 10, 15, 20 and 25 ppm were prepared by pipette outing 0.5, 1, 1.5, 2 and 2.5 ml respectively from the stock solution of 100 ppm and diluted up to 10 ml volumetric flask. Absorbance of working solutions was measured in triplicate at λmax at 293 nm against phosphate buffer (pH 6.8) as a blank.

Fourier Transform Infrared Spectroscopy (FTIR): FTIR was performed for identification of pure Mirtazapine. FTIR spectroscopy was also used for drug and excipients identification and to evaluate their compatibility. FTIR spectroscopy of pure drug and physical mixture of drug and excipients was carried out to check the compatibility of drug and excipients.

Precompression parameter [17]

Flow parameter of powder: Flow properties were determined by various parameters such as bulk density, tapped density, angle of repose. Carr's index, and Hausner's ratio.

Bulk density: Accurately weighed the powder mixture and transferred to measuring cylinder carefully measures the volume of powder without compacting. It is expressed as gm/ml.

$$\textbf{Bulk Density} = \frac{\textbf{Mass of powder (gm)}}{\textbf{Bulk Volume of powder (ml)}}$$

Tapped density: Tapped density was measured by placing graduated cylinder containing formulation blend on mechanical tapping apparatus. Tapped volume was measured until constant tapped volume is not achieved. It is expressed as gm/ml.

$$\textbf{Tapped Density} = \frac{\textbf{Mass of powder (gm)}}{\textbf{Tapped Volume of powder (ml)}}$$

Hausner's ratio: Hausner's ratio is a ratio of tapped density to bulk density. Value of 1.25 Hausner's ratio indicates good powder flow and more than 1.25 indicated poor powder flow. Generally, glidant were added to improve the powder flow of the material.

$$\textbf{Hausner's ratio} = \frac{\textbf{Tapped density}}{\textbf{Bulk density}}$$

Compressibility index: Compressibility index is a ratio of difference of tapped density and bulk density to tapped density. It is expressed in percentage (%).

$$\textbf{Compressibility Index} = \frac{\textbf{Tapped density} - \textbf{Bulk density}}{\textbf{Tapped density}} \times 100$$

Angle of repose: Angle of repose was determined by funnel method. Powder blend was poured from funnel that can be raised vertically until it reaches maximum cone height (h) was obtained. Radius (r) of the pile was measured. Angle of repose was measured by following formula.

$$\textbf{Tan}\ \theta = \frac{h}{r} \qquad \theta = \tan^{-1}\frac{h}{r}$$

Post-compression parameter [18]

Thickness and diameter: Tablet thickness and diameter were measured by Digimatic Vernier calipers. Five tablets were randomly collected and their thickness and diameter were measured by placing between two arms of Vernier calipers.

Hardness: Tablet hardness is described as the amount of force necessary to cause tablet breakage when pressure is applied across its diameter. It reflects the crushing strength of the tablet and was evaluated using a Monsanto-type hardness tester.

Weight variation: Twenty tablets were randomly collected and average weight was determined by using an electronic balance.

Friability test: The friability of tablets was measured by Roche type friabilator. Twenty tablets were initially weighed and then tablets were placed in friabilator at 25 rpm for 4 min then tablets were deducted and weighed again. Loss in weight should not be more than 1%. % friability determined by using following equation.

$$\% \textbf{ Friability} = \frac{\textbf{Initial weight} - \textbf{Final weight}}{\textbf{Initial weight}} \times \textbf{100}$$

***In Vitro* Disintegration test [19]:** This test performed on six tablets using digital tablet disintegration test apparatus. Phosphate buffer (pH 6.8) at 37°±0.5 °C was used as a disintegration media and time in second was recorded for complete disintegration of tablet with no residue remaining in apparatus.

Wetting time: Five circular tissue papers of 10-cm diameter were placed in a Petri dish. Ten ml of water at 37± 0.5°C containing eosin, a water-soluble dye, was added to the petri dish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time.

Drug content: Ten tablets were powdered and equivalent to 15 mg of Mirtazapine was weighed and dissolved in 100 ml of phosphate buffer pH 6.8. The solution was filtered and 0.5 ml from filtrate was diluted to 10 ml and absorbance of this solution was analyzed by UV spectrophotometer at 293 nm.

***In Vitro* Drug release study:** % drug release of sublingual tablets was determined by USP type II (paddle type) dissolution apparatus. This test performed using 900ml of phosphate buffer (pH 6.8) at 37° ± 0.5 °C at 50 rpm. 5 ml sample solution was withdrawn from dissolution apparatus at regular time interval and the same quantity of sample was replaced with fresh dissolution media. The sample was filtered through 0.45 µm membrane filter. Absorbance of these samples was analyzed by using UV spectrophotometer at 293 nm.

Stability study of optimized batch: In the present study, stability study of optimized batch was carried out at 40° ± 2°C / 75 ± 5% RH for time period of 1 month by wrapping the formulation in aluminum foil to prevent the formulation from exposure to light under the 40° ± 2 °C / 75 ± 5% RH for 1 month as prescribed by ICH guidelines for accelerated stability study. After completion of 30 days tablets were evaluated for Hardness, Friability, Drug content, *In Vitro* Disintegration time and *In Vitro* Drug Release study.

RESULTS:

Determination of melting point of Mirtazapine:

Melting point determination is one of the popular techniques used to identify drug using melting point apparatus and melting point of Mirtazapine was found in the range of 115-117°C. Reported melting point of Mirtazapine is 114-116°C and is thus similar to the melting point of Mirtazapine.

Estimation of drug by UV Spectroscopy:

The absorbance of Mirtazapine in a phosphate buffer at pH 6.8 was scanned between 200–400 nm by UV-Visible spectrophotometer. The spectrum of Mirtazapine showed 293 nm at λmax. Calibration curve of Mirtazapine is constructed in phosphate buffer of pH 6.8. From stock solution of Mirtazapine, working solution of concentration range i.e., 5, 10, 15, 20 and 25 ppm were prepared in phosphate buffer of pH 6.8. Absorbance of prepared working solutions were measured at λ_{max} 293 nm against phosphate buffer of pH 6.8 as a blank in UV–Visible Spectrophotometer. Calibration curve of prepared working solutions of Mirtazapine was constructed by plotting a graph between concentration and absorbance (Figure 1) Absorbance of different concentration is mentioned in Table 2.

Table 2: Absorbance of different concentration of Mirtazapine in phosphate buffer at pH 6.8

Sr. No.	Concentration (ppm)	Absorbance			Mean Absorbance± SD
		I	II	III	
1	5	0.153	0.152	0.154	0.153±0.0011
2	10	0.309	0.307	0.311	0.309±0.002
3	15	0.458	0.456	0.46	0.458±0.002
4	20	0.598	0.6	0.597	0.598±0.0015
5	25	0.731	0.733	0.73	0.731±0.0015

*** All values are expressed as mean ± SD; (n=3)**

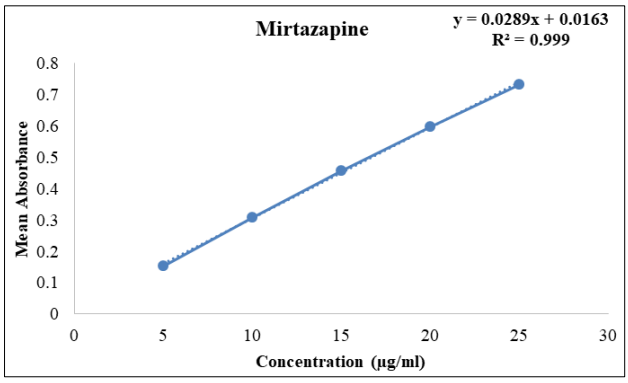

Figure 1: Calibration curve of Mirtazapine in phosphate buffer at pH 6.8

Fourier Transform Infrared Spectroscopy (FTIR) study:

To identify drug, IR was performed on a pure drug sample. A drug pellet was created by compressing drug with IR grade potassium bromide under 5.5 metric tons of pressure in a KBr press. Pellet was placed in IR compartment and scanned with an FTIR spectrophotometer (Model-8400 S, Shimadzu, Japan) between wave numbers 4000-600 cm^{-1}.

When Mirtazapine was mixed with polymers, no changes in IR peaks were observed. These findings suggest that polymers are compatible with Mirtazapine. (Figure 2 and figure 3)

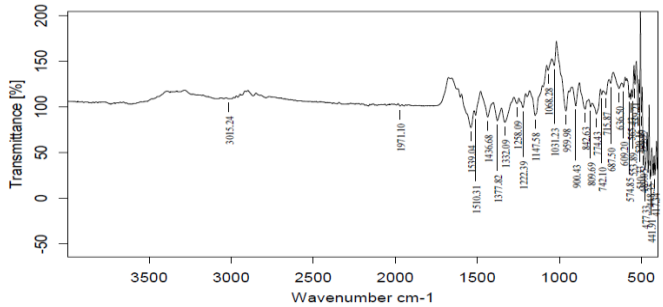

Figure 2: FTIR Spectra of pure Mirtazapine

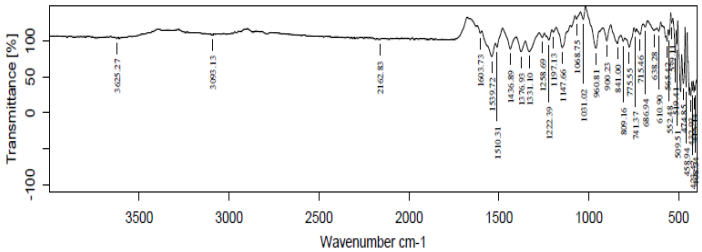

Figure 3: FTIR Spectra of Pure Mirtazapine with excipients

Precompression parameter

All formulation blends were evaluated for bulk density and tapped density. Bulk density was found to be 0.49±0.022 gm/ml to 0.55±0.026 gm/ml and tapped density was found to be 0.62±0.026 gm/ml to 0.69±0.029 gm/ml. Percentage Compressibility Index was determined by using bulk density and tapped density. Carr's

index of all formulation blend lies within the range of 15.38±1.669 to 28.98±1.543 %. Hausner's ratio of all formulation was evaluated from bulk and tapped density and it was found in the range of 1.18±0.205 to 1.81±0.211. Angle of repose of all formulation was in the range of 28.5±1.203°θ to 32.1±1.623°θ. From observed Angle of repose, flow of powder was found to be good flow. All precompression parameters data are mentioned in table 3.

Table 3: Bulk density, Tapped density, Carr's index, Hausner's ratio and Angle of Repose data

Batch code	Bulk density (gm/ml)	Tapped density (gm/ml)	Hausner's ratio	Carr's index (%)	Angle of repose (°θ)
M1	0.55±0.026	0.69±0.029	1.81±0.211	20.28±1.225	32.1±1.623
M2	0.50±0.023	0.65±0.025	1.30±0.228	23.07±1.873	30.6±1.374
M3	0.51±0.029	0.62±0.026	1.21±0.207	17.74±1.764	28.5±1.203
M4	0.49±0.022	0.69±0.023	1.40±0.270	28.98±1.543	31.1±1.04
M5	0.53±0.021	0.66±0.020	1.24±0.221	19.69±1.390	30.4±1.408
M6	0.55±0.026	0.65±0.024	1.18±0.205	15.38±1.669	29.2±1.265

*** All values are expressed as mean ± SD; (n=6)**

Post-Compression Parameter:

Thickness of the formulated batches was found to be in the range of 2.96 ± 0.021 to 3.95 ± 0.044 mm. Diameter of the formulated batches was in the range of 5.93 ± 0.060 mm to 6.10 ± 0.060 mm. Weight variation limits for tablet weight 120 mg is ± 7.5 mg according to Indian Pharmacopoeia. Weight variation range was found to be from 121.1 ± 2.93 mg to 125.75 ± 5.14 mg. Thus, all the formulated batches prepared comply with the weight variation limits of the pharmacopeia. It is well known that tablets with more hardness shows longer disintegration time. Since mechanical integrity is of paramount importance in successful formulation of sublingual tablet, hence hardness of tablets was determined. Hardness of sublingual tablet prepared by direct compression method was found in the range of 2.63± 0.12 kg/cm^2 to 3.07 ± 0.12 kg/cm^2. Friability of the tablets was found in the range of 0.38 to 0.74 %. According to IP, Limits of Friability is less than 1%. Observed values of friability indicated that tablets were having a good mechanical stability (Table 4).

Table 4: Weight variation, Thickness, Diameter, Hardness and Friability data

Batch code	Thickness (mm ± S.D.)	Diametermm ± S.D.)	Weight variation (mg ± S.D.)	Hardness (kg/cm^2 ± S.D.)	Friability (%)
M1	3.07 ± 0.058	6.03 ± 0.012	125.75±5.14	2.97 ± 0.15	0.51
M2	2.96 ± 0.021	6.00 ± 0.010	121.85±4.25	2.87 ±0.21	0.62
M3	3.13 ± 0.058	6.10 ± 0.060	121.5± 3.72	3.07 ± 0.12	0.38
M4	3.95 ± 0.044	5.93± 0.060	122.7 ± 5.60	2.87± 0.6	0.57
M5	3.13 ± 0.061	5.97± 0.060	121.1 ± 2.93	3.03± 0.15	0.42
M6	3.09 ± 0.012	6.00 ± 0.010	122.3 ± 3.32	2.63± 0.12	0.74

*** All values are expressed as mean ± SD; (n=6)**

Wetting time of all the batches was found to be in the range of 17.33 ± 0.58 to 31.00 ± 2.82 seconds. In Vitro Disintegration time of the formulated batches was found in the range of 24.52 ± 1.08 to 35.64 ± 1.63. Drug content of the tablets prepared by direct compression method was found to be 96.38 % to 98.32 %. These results of drug content indicated that sublingual tablet had uniform distribution and proper dose of active ingredient (Table 5).

Table 5: Wetting time, In-Vitro disintegration time and Drug Content

Batch code	Wetting time(sec. ± S.D.)	*In Vitro* disintegration time(sec. ± S.D.)	Drug content (%)
M1	21.00 ± 0.73	29.28± 2.18	97.18
M2	19.00 ± 1.32	26.81 ± 1.93	97.45
M3	17.33 ± 0.58	24.52 ± 1.08	98.32
M4	31.00 ± 2.82	35.64 ± 1.63	96.53
M5	28.00 ± 1.73	33.44± 1.53	97.42
M6	26.23 ± 2.52	30.12 ± 1.43	96.38

*** All values are expressed as mean ± SD; (n=6)**

Based on all above parameter, it was concluded that the batch M3 was an optimized batch, as it had good surface appearance, Mechanical strength, and Drug Content. Moreover, it showed 97.12±1.65% of drug release in just 10 mins and In-vitro disintegration time was just 24.52± 1.08sec which was least as compared to all other batches. Thus, batch M3 containing crospovidone (3.75%) was selected as an optimized batch. From the data we can conclude that as the concentration of Crospovidone increases drug release is also increases (Table 6, figure

4 and figure 5).

Table 6: Percentage drug release of batches M1 to M6

TIME (min)	% CDR					
	M1	M2	M3	M4	M5	M6
0	0	0	0	0	0	0
2	13.8 ± 1.12	27.6 ± 1.23	34.14 ± 1.36	14.61 ± 1.35	16.52 ± 1.28	20.42 ± 1.51
4	21.5 ± 1.36	38.45 ± 1.45	48.24 ± 1.54	31.45 ± 1.36	26.71 ± 1.23	30.25 ± 1.56
6	32.68 ± 1.69	47.36 ± 2.04	66.94 ± 2.27	48.67 ± 1.89	38.92 ± 1.54	40.16 ± 1.48
8	49.83 ± 2.01	61.98 ± 2.47	82.98 ± 2.35	62.15 ± 2.16	53.27 ± 2.34	50.47 ± 2.54
10	74.95 ± 2.36	87.59 ± 2.84	97.12 ± 1.65	79.48 ± 2.67	71.83 ± 2.36	80.62 ± 2.85
12	89.6 ± 2.15	94.34 ± 2.47	-	82.92 ± 2.98	89.47 ± 2.78	95.26 ± 2.84

*** All values are expressed as mean ± SD; (n=6)**

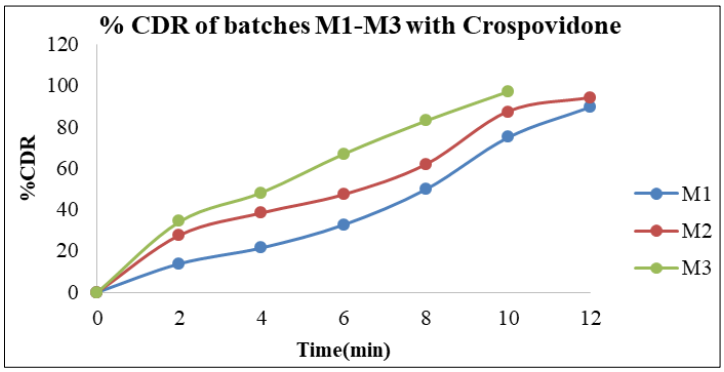

Figure 4: In-vitro drug release of Batches M1 to M3

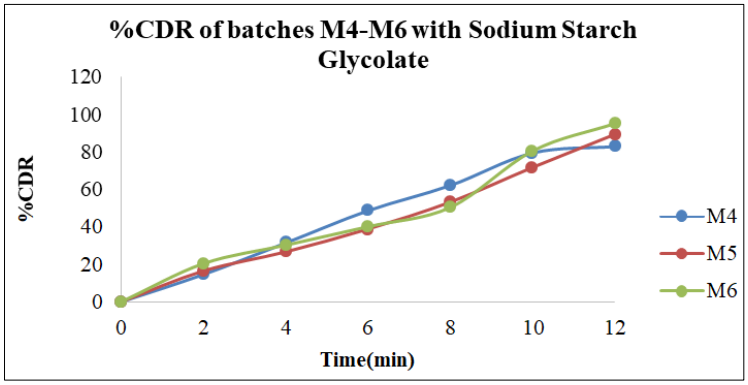

Figure 5: In-vitro drug release of Batches M4 to M6

Stability studies:

As indicated in Table 7 and Table 8, the optimized batch underwent a month of stability testing and was determined to be stable in terms of hardness, In Vitro Disintegration Time, drug content, Friability, Weight variation and in vitro drug release research.

Comparison study between the result of optimized batch and after time period of stability is graphically illustrated in Figure 6.

Table 7: Results of stability study

Sr. No.	Evaluation parameter	Results	
		optimized batch M3	after 1 month at 40° ± 2 °C and 75 ± 5 % RH
1	Hardness	3.07 ± 0.12	2.93 ± 0.12
2	In Vitro Disintegration Time	24.52 ± 1.08	26.12 ± 1.52
3	Drug Content	98.32	97.22
4	Friability	0.38	0.40
5	Weight variation	121.5 ± 3.72	120.7 ± 2.59

Table 8: In Vitro Drug Release study of Stability batch

Time (Min.)	% CDR of Optimized Batch M3 (%)	% CDR of batch M3 After Time Period of 1 Month (%)
0	0	0
2	34.14 ± 1.36	33.68 ± 1.25
4	48.24 ± 1.54	47.24 ± 2.21
6	66.94 ± 2.27	65.93 ± 1.54
8	82.98 ± 2.35	81.55 ± 1.03
10	97.12 ± 1.65	96.89 ± 1.05

*** All values are expressed as mean ± SD; (n=6)**

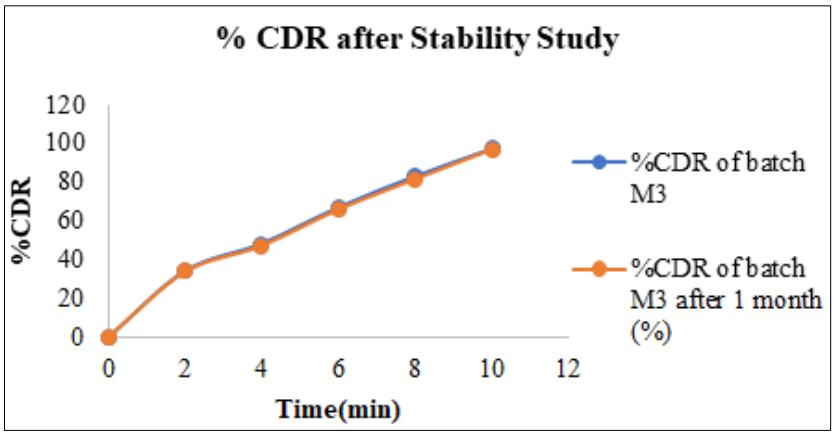

Figure 6: Comparison of In Vitro Drug Release study of Optimized batch and Stability batch

CONCLUSION:

The present study demonstrated that sublingual tablets of Mirtazapine can be effectively prepared by the direct compression method for the management of depression, anxiety, and insomnia. All precompression and post compression parameters were found within acceptable limits, indicating good flow properties and satisfactory mechanical strength of the tablets. There were not any significant changes in FTIR study. Among all formulations, batch M3 containing 4.5 mg of Crospovidone as a super disintegrant showed the least disintegration time (24.52 ± 1.08 sec) and maximum drug release (97.12 ± 1.65 % in 10 min). Stability studies of batch M3 revealed no significant changes in hardness, disintegration time, drug content and dissolution profile after one month at accelerated conditions (40 ± 2 °C and 75 ± 5% RH). Thus, the optimized formulation ensures rapid onset of action and enhanced patient compliance, offering a promising approach for effective treatment of depression across different age groups.

REFERENCES:

1. K.prasanna kumari, R. Sarvanan, D. Dhchinamoorthi "Formulation and evaluate oral disintegrating tablets of mirtazapine." *World journal of pharmaceutical and medical research,* **2019**.5(9),263-27.
2. Afshan Maqbool, Muhammad Naeem Aamir, Muhammad Naeem. "Formulation and evaluation of fast dissolving films embedded with nanoparticles of mirtazapine hydrochloride. *Journal of contemporary pharmacy* **2022**,6(1),6-18.
3. Sanjay Kumar, Darsh Gautama, Poonam Talwan "Formulation and evaluation of Mirtazapine Oral Thin film.*" International journal of research in pharmacy and chemistry* **2020,**10(1),35-41.
4. Sara nageeb El-Helay, Amira Arshad,*"* Mirtazapine loaded polymeric micelles for rapid release tablet: A novel formulation- in vivo and in vitro studies." *Drug Delivery and Translational Research*,**2024**,14,2488–2498
5. Ramarao CT, Laxmi SB. "Floating Drug Delivery of Sustained Release Antidepressant Mirtazapine Tablets by Box-Behnken Design: Formulation and Optimization." *Indian J of Pharmaceutical Education and Research,* **2024,** 58(1s), s113-s125.
6. Reem Abd Elhameed Aldeeb, Mahmoud Abd El Ghani Mahdy, Hanan Mohamed El Nahas, Abeer Abdelaziz Musallam. "Design of mirtazapine solid dispersion with different carriers' systems: optimization, in vitro evaluation, and bioavaibility assessment" *Drug Delivery and Translational Research,* **2023,** 13,2340–2352
7. Denisa ciecioban, Adriana ledeti, "Compatibility study of mirtazapine with several excipients used in pharmaceutical dosage forms employing thermal and non-thermal methods." *Journal of Thermal Analysis and Calorimetry* **2024.**
8. Kanade TS, Gupta A and Mahajan S, "Review on Sublingual Tablets-A Promising Formulation for Instant Action." *Int J Pharm Sci*. **2023,** *3(1),* 1–6.
9. Gupta A, Kanade T.S, Mahajan S, and Darwhekar G.N," Review on sublingual Tablet-a promising formulation for Instant Action" *international journal of pharmaceutical science.***2023**,3(1),1-6.
10. Darwhekar G., Gupta A., "formulation and evaluation of sublingual tablet: Meclizine Hydrochloride. *"International journal of new gen research in pharmacy & healthcare.* **2023.**
11. Pol A., Sarawade R. "Development And Evaluation Of Sublingual Tablets Of Levodopa", *Int. J. of Pharm. Sci.,* **2024**, 2(5),125-140.
12. Patel J. K. ,Patel D. ,Patel Y. K. , Patel V.K. ,Patel R. K. ,Shah T." Formulation and evaluation of sublingual tablet of clopidogrel bisulphate." **2022**.

13. Nishijo J., Raymond CR., Paul JS. Marian EQ. In Handbook of excipients; 6th Edn; RPS publication, Unites states of America, 2009.
14. Suzuki Y, Sugiyama H, Kano M, Shimono R, Shimada G, Furukawa R, Mano E, Motoyama K, Koide T, Matsui Y, Kurasaki K, Takayama I, Hikage S, Katori N, Kikuchi M, Sakai H and Matsuda Y. "Control strategy and methods for continuous direct compression processes." *Asian J Pharm Sci.* **2021,** 16(2), 253-262.
15. Reddy C, Khan A K.K. and Nagaraja C, "A Review on the Determination of Melting Point Measurement System." *International Journal of Advanced Research in Electrical, Electronics and Instrumentation Engineering.* **2016,** 5(2), 975-979.
16. SK. Benajeer, K.Venkata ramana, V.koti reddy, A.Anil kumar *"*New simple UV spectrophotometric Methods for determination of Mirtazapine in bulk and pharmaceutical dosage forms" *international journal of pharma science and research* .**2012**
17. Kumar P. "An Overview on Preformulation Studies." *Indo Am. J. Pharm. Sci.* **2015,** *2(10),* 1399-1407.
18. Yadav D.B, Rana H.A, DR. Maheshwari A M and DR. Patani P. "Post Compression Evaluation Parameters of Paracetamol Tablets: a Review." *Journal of Emerging Technologies and Innovative Research (JETIR).* **2020,** *7(2),* 1243-1247.
19. Solanki H. J. , Raval B. A., Taretiya K. D. , Bhangale J. O. "Formulation and Evaluation of Sublingual tablets Of Doxepin HCL" *Journal of applied Bioanalysis, December,* **2025,** 11(4),427-434.