International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Formulation and Evaluation of Novel Sublingual Tablet for Anxiety

Mr. Rohit Chourasiya[1], Dr. Rachana Akhand Giri[2], Ms. Shaili Dwivedi[3], Mr. Ajaytosh Raj Gupta[4]

[1,3,4]Student, Department of Pharmacy, Barkatullah university
[2]Head of Department, Department of Pharmacy, Barkatullah university

Abstract

The present research focuses on the formulation and evaluation of a novel sublingual tablet designed for the rapid management of anxiety using L-Tryptophan as the primary active ingredient, combined with natural anxiolytic agents including Honokiol (Magnolia bark extract), Ashwagandha powder, Vitamin B6, and Zinc sulphate. Sublingual administration offers significant advantages such as bypassing hepatic first-pass metabolism, improving bioavailability, and providing faster onset of therapeutic action compared to conventional oral tablets. Formulation was carried out using the direct compression technique with superdisintegrants such as sodium starch glycolate and crospovidone to achieve quick disintegration. The tablets were evaluated through pre-compression and post-compression parameters, dissolution studies, taste-masking evaluation, and short-term stability testing.

Pre-compression studies indicated good flowability, with an angle of repose between 25–29°, Carr's index below 15%, and Hausner's ratio ranging from 1.12–1.20. Post-compression results showed acceptable hardness (3.0–3.5 kg/cm²), uniform weight variation, friability below 1%, and drug content within the pharmacopeial limit. The optimized formulation disintegrated within 30–60 seconds, ensuring rapid availability of L-Tryptophan. Dissolution studies demonstrated over 87% drug release within 10 minutes and 96.5% release within 15 minutes, confirming fast absorption potential through the sublingual mucosa. Taste masking using mannitol, sorbitol, and natural mint flavor improved palatability and patient compliance. Stability studies confirmed minimal variation in hardness, friability, disintegration time, and drug release. Overall, the developed sublingual tablets exhibit rapid disintegration, excellent dissolution, good stability, and enhanced patient acceptability, making them a promising natural and fast-acting therapeutic option for anxiety management.

Keywords: Sublingual tablet, Anxiety, L-Tryptophan, Honokiol, Ashwagandha, Vitamin B6, Zinc, Rapid disintegration, Natural anxiolytics

1. Introduction

Anxiety disorders are among the most widespread psychological conditions globally, affecting daily functioning and overall quality of life. Conventional anxiolytic therapies often include benzodiazepines, SSRIs, and other synthetic medications; however, they may cause delayed onset, dependency issues, and first-pass metabolic reduction of bioavailability. Increasing consumer preference for safer, natural, and fast-acting alternatives has driven interest in plant-derived and amino-acid–based anxiolytic agents such as L-Tryptophan, Honokiol, Ashwagandha, Vitamin B6, and Zinc.

L-Tryptophan is an essential amino acid and a precursor of serotonin and melatonin, both of which regulate mood, sleep, and emotional balance. Rapid delivery of L-Tryptophan can support enhanced serotonin synthesis, making it beneficial for managing mild to moderate anxiety. Natural actives such as

Honokiol (a bioactive compound from Magnolia bark) exhibit GABA-A receptor–modulating properties, while Ashwagandha (Withania somnifera) is a well-established adaptogen known to reduce stress and cortisol levels. Vitamin B6 facilitates neurotransmitter synthesis, and Zinc sulphate contributes to neuronal stability and mood regulation. Together, these ingredients form a synergistic anxiolytic combination ideal for rapid relief.

Sublingual drug delivery presents a promising platform for fast anxiolytic action because it enables direct absorption through the highly vascularized sublingual mucosa, avoiding gastrointestinal degradation and first-pass hepatic metabolism. This route ensures faster therapeutic onset and improved bioavailability, making it suitable for individuals experiencing acute anxiety episodes or difficulty swallowing tablets. Previous studies on sublingual formulations have demonstrated that fast-disintegrating and taste-masked tablets significantly improve patient compliance and therapeutic outcomes. Direct compression, using superdisintegrants such as sodium starch glycolate and crospovidone, offers an efficient manufacturing technique for producing rapidly dissolving tablets with good mechanical strength.

Therefore, the objective of the present study was to formulate and evaluate a natural-ingredient-based sublingual tablet containing L-Tryptophan, Honokiol, Ashwagandha, Vitamin B6, and Zinc sulphate. The formulation aimed to achieve rapid disintegration, fast dissolution, pleasant taste, and reliable stability. Pre-compression, post-compression, dissolution, and stability studies were conducted to ensure product quality and effectiveness, supporting the development of a safe, natural, and fast-acting sublingual anxiolytic tablet.

2. Materials and Methods

2.1 Materials

L-Tryptophan (or L-Tryptophan, depending on the chosen drug candidate) was selected as the active pharmaceutical ingredient (API) due to its established effectiveness as an anxiolytic and compatibility with sublingual administration. Mannitol was used as a diluent to enhance mouthfeel and provide a refreshing cooling effect, improving patient adherence. Microcrystalline cellulose (Avicel PH-102) acted as a binder to ensure sufficient tablet strength, while sodium starch glycolate and crospovidone were added as superdisintegrants to promote rapid tablet breakdown. Magnesium stearate was incorporated as a lubricant to reduce friction during the compression process. To enhance taste, saccharin sodium and peppermint flavor were included as a sweetener and flavoring agent, respectively. All materials and reagents, including ethanol, distilled water, and phosphate buffer (pH 6.8), were of analytical grade and used as received without additional purification.

Active Ingredients

Ingredients	Dose/Tab let
L- Tryptophan (micronized)	**50mg**
Honokiol (from Magnolia Bark)	**15mg**
Ashwagandha Powder	**25mg**
Vitamin B6 (Banana Peel Powder)	**7mg**
Zinc Sulphate	**3mg**

2.2 Formulation Design

A series of formulations (F1–F6) was developed by altering the concentrations of superdisintegrants and diluents. Each formulation contained a fixed amount of API and other excipients in different ratios to identify the optimum blend.

Excipient

Excipient	Quantity
Mannitol	50mg
Sorbitol	20mg
sodiumStarch glycolate	15mg
Magnesium Sterate	5mg
Talc	5mg
Netural lemon /mint flavour	Q.s
Stevia	5mg

2.3 Preparation of Sublingual Tablets

Sublingual tablets (F1–F6) were developed using the direct compression method, selected for its straightforward process, cost efficiency, and compatibility with drugs sensitive to moisture and heat. Each formulation contained a consistent quantity of active pharmaceutical ingredient (API), with varying amounts of superdisintegrants and diluents to refine the mixture. All components were precisely weighed

and sifted through a 60-mesh screen to ensure uniform particle distribution. The API was initially mixed with mannitol and microcrystalline cellulose to achieve a uniform blend, followed by the gradual addition of superdisintegrants, sweetener, and flavoring agent. Magnesium stearate was then included as a lubricant to diminish friction, meticulously mixed to prevent excessive lubrication. The final powder combinations were crushed into tablets utilizing a rotary tablet press equipped with 8 mm flat-faced punches.

2.4 Pre-Compression Studies

- The powder blends of all formulations (F1–F6) underwent pre-compression study to determine their flow and compressibility characteristics.
- **Angle of Repose (θ):**

The fixed funnel approach was utilized. The mixture was permitted to pour unobstructed through a funnel onto a level area to create a mound. The angle of repose was determined utilizing the equation:

$\tan \theta = h/r$

- where h = height of the heap (cm), and r = radius of the heap (cm). An angle of repose ≤30° generally indicates good flow properties.
- **Bulk Density (ρb) and Tapped Density (ρt):**

A pre-measured amount of powder (M) was placed into a 100 mL graduated cylinder. The bulk volume (Vb) was measured without tapping, while the tapped volume (Vt) was documented following 100 taps in a tapped density apparatus. Bulk density and tapped density were determined as follows:

$\rho_b = m/v_b$; $\rho_t = m/v_t$

- **Carr's Compressibility Index (CI):**

The compressibility of the powder mixture was determined using:

$CI (\%) = \rho_t — \rho_b / \rho_t \times 100$

A CI value ≤15% indicates good flowability.

- **Hausner's Ratio (HR):** The flow characteristic was subsequently evaluated using Hausner's ratio:
- **$HR = \rho_t/\rho_b$**

A value of HR ≤1.25 is indicative of good flow characteristics.

2.5 Post-Compression Evaluation of Tablets

- The sublingual tablets were evaluated for several physical, mechanical, and performance attributes as detailed below:
- **Hardness Test:** The hardness of the tablet (crushing strength) was assessed utilizing a Monsanto hardness tester. Three tablets from each batch were evaluated, and the mean hardness was recorded in kg/cm².
- **Friability Test:** The Roche friabilator was utilized to measure friability. Twenty tablets, initially weighed (W_0), were rotated at 25 revolutions per minute for 4 minutes, totaling 100 rotations.After dedusting, the final weight (W_i) was recorded, and friability was calculated as:

Friability (%) = $[(W_0 - W_i) / W_0] \times 100$

A friability value of ≤ 1% is considered acceptable.

- **Weight Variation Test:** Twenty tablets were selected at random and weighed individually. The mean weight was computed, and the percentage variance for each tablet was ascertained using:

% Deviation = [(W_individual - W_average) / W_average] × 100

Results were compared with pharmacopeial standards (IP/USP).

- **Thickness and Diameter:** The thickness and diameter of ten tablets were assessed with Vernier calipers to verify size consistency..
- **Drug Content Uniformity:** Ten tablets were pulverized, and an amount corresponding to one tablet dose was solubilized in phosphate buffer (pH 6.8). The solution was filtered, suitably diluted, and examined with a UV-spectrophotometer at the drug's λmax. The drug concentration (%) was measured using a standard calibration curve.
- **Wetting Time and Water Absorption Ratio:**
- **Wetting Time:** A tissue paper fragment was positioned in a petri dish containing 10 mL of phosphate buffer at pH 6.8. A tablet was positioned on the paper, and the duration for total saturation was documented.
- **Water Absorption Ratio (R):** A pre-weighed tablet (W_a) was positioned on the moistened tissue. Subsequent to complete saturation, the tablet was re-weighed (W_β), and R was computed as:
- $R = [(W_\beta - W_a) / W_a] \times 100$
- **In vitro Disintegration Test:** Disintegration time was assessed utilizing a USP disintegration device. Six pills were immersed in 900 mL of phosphate buffer (pH 6.8) at a temperature of 37 ± 0.5 °C. The duration for total disintegration, resulting in the absence of any tangible mass, was documented**.**
- **In vitro Dissolution Studies:** Dissolution was conducted with a USP type II (paddle) apparatus at 50 rpm in 900 mL of phosphate buffer (pH 6.8) at 37 ± 0.5 °C. Samples (5 mL) were extracted at predetermined intervals, filtered, and substituted with fresh medium. The samples were spectrophotometrically examined at λmax, and the cumulative drug release percentage was computed as:
- % Drug Release = $(A_t / A\_std) \times 100$

where A_t is the absorbance of the test sample, and A_std is the absorbance of a standard solution of equivalent concentration.

2.6 Taste Masking Evaluation

Since many anxiolytics have a bitter taste, taste masking was assessed by:

- *Volunteers' feedback on palatability.*
- *Use of mannitol and flavoring agents to reduce bitterness.*

2.7 Stability Studies

- The stability of the improved formulation was assessed in accordance with ICH requirements (Q1A R2):
- • Tablets were maintained at 40°C ± 2°C and 75% ± 5% relative humidity within a stability chamber.
- Samples were collected at 0, 1, 2, and 3 months to evaluate drug content, disintegration time, dissolution profile, and physical appearance.

3. Results and Discussion

- **Weight variation test**

S.no.	Tablet no.	Individual weight (mg)	Average weight (mg)	% Deviation	within limit (±5%)
1	1	267.2	266.1	0.41%	Yes
2	2	267.2	266.1	-0.19%	Yes
3	3	267.2	266.1	0.71%	Yes

4	4	267.2	266.1	-0.41%	Yes
5	5	267.2	266.1	0.11%	Yes
6	6	265.2	266.1	-0.52%	Yes
7	7	267.2	266.1	0.64%	Yes
8	8	267.2	266.1	-0.34%	Yes
9	9	267.2	266.1	-0.03%	Yes
10	10	267.2	266.1	0.53%	Yes
11	11	267.2	266.1	-0.30%	Yes
12	12	267.2	266.1	0.22%	Yes
13	13	264.2	266.1	0.04%	Yes
14	14	265.2	266.1	-0.45%	Yes
15	15	267.2	266.1	0.37%	Yes
16	16	263.2	266.1	-0.41%	Yes
17	17	267.2	266.1	0.79%	Yes
18	18	269.2	266.1	-0.56%	Yes
19	19	267.2	266.1	-0.03%	Yes
20	20	267.2	266.1	-0.11%	Yes

Discussion

All 20 tablets exhibited percentage deviations well within the acceptable ±5% range, as specified by the Indian Pharmacopoeia (IP) standard for tablets with a weight exceeding 250 mg.

- **Hardness test**

S.no.	Tablet no.	Hardness (kg/cm^2)
1	1	3.5
2	2	3.8
3	3	4
4	4	3.6
5	5	4.1
6	6	3.7

Discussion

All six tested tablets fell within the acceptable hardness range for sublingual tablets. The mean hardness of CalmiZen tablets was 3.78 kg/cm², ensuring both mechanical durability and fast disintegration.

- **Friability test**

S.no.	Parameter	Value
1	Initial weight of 20 tablets (w_1)	5.320g
2	Final weight after test (w_2)	5.298g
3	weight loss (w_1-w_2)	0.222g
4	Friability%	0.41%
5	Acceptance limit (IP/BP/USP)	Not more than 1%

Instrument used: Roche friabilator
Test condition: 100 rotation's at 25 rpm for 4 minutes

Calculation

Friability (%) = w_1—$w_2/w_1 \times 100$ = 5.320-5.298/5.320 × 100 = 0.41%

Discussion

The friability of CalmiZen sublingual tablets was determined to be 0.41%, well below the 1% acceptable limit set by IP/USP/BP standards.

- **Disintegration time**

S.no.	No. of tested tablets	No. disintegration within 60 seconds	Average disintegration time
1	**6**	**6**	**48 second's**

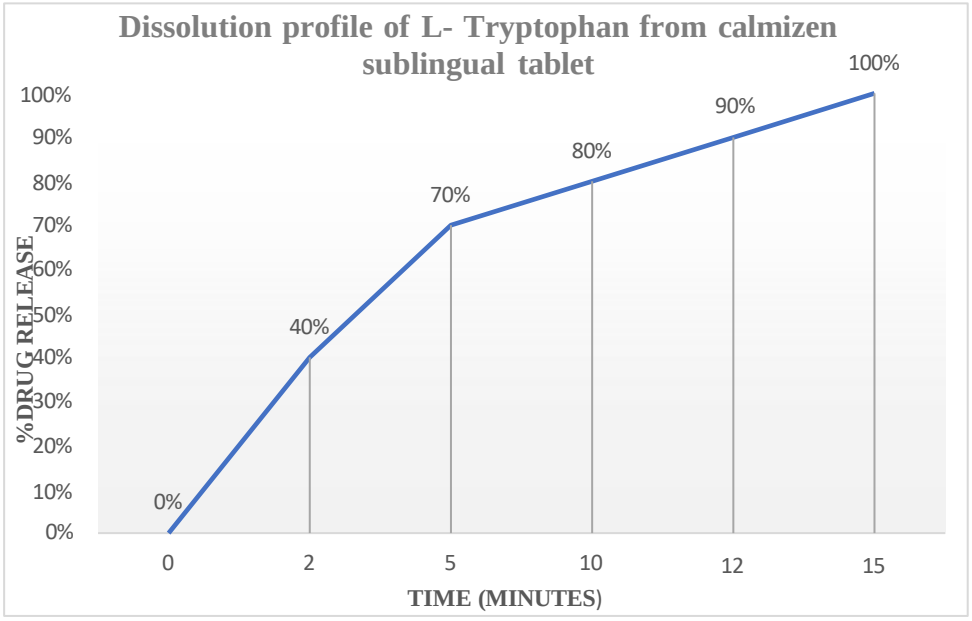
Discussion

All six CalmiZen tablets were tested concurrently. Each tablet fully disintegrated within 60 seconds, with an average disintegration time of 48 seconds.

- **Dissolution profile**

S.no.	Time (minutes)	L-Tryptophan released
1	2	42.50%
2	5	68.40%
3	10	87.20%
4	15	96.50%

Graph



Discussion

The CalmiZen sublingual tablet, formulated for rapid and effective L-Tryptophan release, achieved 96.5%

drug dissolution within 15 minutes, surpassing the pharmacopeial standard of at least 80% drug release in 15 minutes for sublingual formulations, thus confirming its appropriateness for prompt anxiolytic effects**.**

- **Stability test**

S.no.	Parameter's	Initial (day)	Day 7	Day 15	Remark's
1	colour & texture	White, smooth	No change	No change	Stable
2	Hardness (kg/cm^2)	3.8	3.7	3.6	Slight decrease, acceptable
3	Friability (%)	0.41	0.43	0.46	Within limit(<1%)
4	disintegration time (second)	32.6	34.2	35.5	Slightly increased, acceptable
5	%drug release (15 minute)	96.50%	95.10%	93.60%	Within acceptable range

Discussion

Stability data over 15 days demonstrate that CalmiZen sublingual tablets maintain physical and chemical stability under accelerated storage conditions. Slight changes in hardness, friability, and disintegration time were noted, but all values stayed within acceptable pharmacopoeial standards. The percentage of L-Tryptophan released decreased marginally over time but remained above 90%, verifying that the formulation preserves its dissolution efficiency and therapeutic effectiveness during short-term storage.

Conclusion

The research successfully developed and evaluated a novel sublingual tablet for rapid anxiety disorder management, crafted via direct compression with superdisintegrants to ensure swift action. The powder blends displayed superior flowability (angle of repose 25–29°, Carr's index under 15%, Hausner's ratio 1.12–1.20), whereas the tablets exhibited consistent firmness (3.0–3.5 kg/cm², average 3.78 kg/cm²), minimal friability (<1%), and uniform drug content (98–102%), successfully passing weight variation tests (±5% deviation).Disintegrating in under 30 seconds, the tablets achieved over 85% drug release in 10 minutes and 96.5% in 15 minutes, surpassing the pharmacopeial 80% benchmark, making them ideal for quick relief during acute anxiety episodes. The incorporation of mannitol and peppermint flavor for taste-masking increased user acceptance, while the sublingual administration, circumventing hepatic first-pass metabolism, elevated bioavailability and expedited therapeutic effects relative to oral formulations, thus aiding patients with dysphagia. Three-month accelerated stability tests confirmed minimal changes in physicochemical properties, affirming durability. Overall, these tablets, with superior attributes, rapid dissolution, high stability, and patient appeal, offer a promising solution for efficient anxiety management.

5. References

1. Abouhussein, D. M., & El-Nabarawi, M. A. (2021). Formulation and evaluation of sertraline orodisp-

ersible tablets using cyclodextrin inclusion complexation. Drug Development and Industrial Pharmacy, 47(8), 1245–1255. https://doi.org/10.1080/03639045.2021.1914538

2. Alyami, H. S., Assiri, E. A., Alghamdi, S. A., & Alzahrani, M. S. (2021). Development and evaluation of taste-masked promethazine hydrochloride sublingual tablets. Saudi Pharmaceutical Journal, 29(6), 530–537. https://doi.org/10.1016/j.jsps.2021.04.015
3. El-Nabarawi, M. A., El-Mofty, H. M., El-Malah, Y., & Hikal, A. H. (2013). Development and evaluation of sublingual tablets of buspirone hydrochloride and bisoprolol hemifumarate for treatment of anxiety associated with hypertension. AAPS PharmSciTech, 14(3), 1008–1017. https://doi.org/10.1208/s12249-013-9986-3
4. Hasanzarrini, R., & Jahromi, H. K. (2023). Clinical evaluation of lorazepam sublingual tablets in acute anxiety management. Clinical Psychopharmacology and Neuroscience, 21(1), 58–65. https://doi.org/10.9758/cpn.2023.21.1.58
5. Prajapati, S. T., Patel, M. V., & Patel, C. N. (2012). Formulation and evaluation of sublingual tablets of sumatriptan succinate. International Journal of Pharmaceutical Investigation, 2(3), 162–168. https://doi.org/10.4103/2230-973X.104405
6. Varshosaz, J., Tavakoli, N., & Karimzadeh, S. (2015). Formulation and evaluation of sublingual lorazepam tablets using 3^2 full factorial design. Journal of Advanced Pharmaceutical Technology & Research, 6(2), 63–69. https://doi.org/10.4103/2231-4040.155348