Formulation and Evaluation of Taste-Masked Pregabalin Orodispersible Tablets Using Eudragit E100 by Wet Granulation Technique

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Abstract

Pregabalin is one of the most commonly prescribed anti-seizure and first-line therapeutic agents used in the management of neuropathic pain, fibromyalgia, and partial seizures. Despite its clinical efficacy, the intensely bitter taste of pregabalin poses a significant challenge to patient compliance; this problem is particularly pertinent to pediatric, geriatric, and dysphagic populations who have difficulty swallowing conventional solid oral dosage forms. Orodispersible tablets offer a very promising patient-centric solution owing to their rapid disintegration in the oral cavity without the need for water; however, successful development of pregabalin ODTs requires effective taste masking without compromising rapid drug release. This study was aimed to formulate and evaluate taste-masked pregabalin orodispersible tablets using Eudragit E100 as a pH-dependent taste-masking polymer through a wet granulation method. A total of eight formulations (F1–F8) were formulated by incorporating different levels of Eudragit E100 (6.25–25% w/w) and Mannitol-based excipients such as Pearlitol SD 200 and Pearlitol 160C. Croscarmellose sodium was added both intra- and extragranularly for rapid tablet disintegration properties. The proposed formulations were assessed for pre-compression tests, post-compression properties, in vitro disintegration tests, dissolution properties, content uniformity, and taste masking efficiency by using a trained panel test with a volunteer subject. Among all formulations, F8 containing 25% w/w Eudragit E100 and Pearlitol 160C showed optimum performance. This formulation exhibited excellent powder flow properties with an angle of repose of 21.5°, adequate mechanical strength characterized by a hardness of 4.7 Kp and friability of 0.47%, rapid disintegration within the range of 20–30 seconds, and perfect bitterness masking characterized by a 9–10 score on the 10-point scale. In vitro dissolution experiments revealed a rapid and complete drug release with approximately 95% release in 5 minutes and ~100% release in 20 minutes in 0.06 N HCl. Drug content studies showed 99.8% of labeled claim, which confirms the uniform distribution of drugs.

The study concludes that Eudragit E100-based wet granulation is an effective and scalable approach for developing taste-masked pregabalin orodispersible tablets with rapid disintegration and dissolution characteristics. The optimized formulation offers a patient-friendly alternative to conventional dosage forms and has the potential to significantly enhance medication adherence in vulnerable patient populations.

Keywords

Pregabalin; Orodispersible Tablets; Taste Masking; Eudragit E100; Wet Granulation; Superdisintegrants; Patient Compliance

1. Introduction

The oral route of drug administration is the most favored route of drug administration because of the ease of administration, acceptability, and cost-effectiveness of the process. However, the traditional oral routes of drug administration of tablets and capsules face a major challenge for certain target populations of patients, for example, pediatric, geriatric, psychiatric, and dysphagic patients, due to the fact that these patients have difficulty swallowing oral drugs in the form of tablets and capsules, leading ultimately to the possibility of the drug being discontinued.

Orodispersible tablets, or ODTs, have emerged as an important patient-friendly formulation, which aims to overcome the problem of swallowing difficulties presented by conventional tablet formulations. ODTs are designed to disintegrate or dissolve within seconds in the oral cavity without water intake, forming a liquid or slurry suspen- sion that can be readily swallowed. According to the European Pharmacopoeia, ODTs are classified as "tablets which dis- integrate within three minutes when placed in the mouth," while more modern formulations seek a disintegration of time below 30 seconds. It should be noted that the rapid and quick action and benefit of ODTs, in terms of no water requirement, make them especially advantageous for pediatric, geriatric, and for neu- rological, nausea and vomiting, and water-unavailable groups.

Despite their advantages, there are formulation challenges in the preparation of ODTs. These include providing suitable mechanical strength, rapid disintegration, pleasant mouthfeel, and appropriate taste masking. Taste masking becomes more important if the drug has an unpleasant taste, such as bitterness, since contact between the drug and the taste buds during rapid disintegration may cause rejection.

Pregabalin, a structural analogue of γ-aminobutyric acid (GABA), is widely prescribed for the management of neuropathic pain associated with diabetic neuropathy and post-herpetic neuralgia, as well as for adjunctive therapy in partial seizures and treatment of fibromyalgia. Pregabalin acts by binding to the α2-δ subunit of voltage-gated calcium channels, thereby reducing the release of excitatory neurotransmitters. Although pregabalin exhibits favorable pharmacokinetic properties such as high oral bioavailability and limited metabolism, its intensely bitter taste poses a major formulation challenge, particularly for rapidly disintegrating oral dosage forms.

Taste perception begins when drug molecules dissolve in saliva and interact with taste receptors on the tongue. Therefore, the development of pregabalin ODTs necessitates an effective taste-masking strategy that prevents drug dissolution in the oral cavity while allowing rapid release in the gastrointestinal tract. Numerous taste-masking approaches have been explored, including coating with polymers, complexation with cyclodextrins, ion-exchange resins, microencapsulation, and prodrug formation. Among these, polymer-based coating using pH-dependent polymers provides a feasible and scalable method that is suitable for industrial manufacturing.

Eudragit E100, a cationic methacrylate copolymer, shows pH-dependent solubility, remains insoluble at salivary pH (≥5.5) while dissolves rapidily under acidic gastric conditions (pH <5). This property makes Eudragit E100 an ideal candidate for taste masking of bitter drugs intended for immediate-release formulations. By forming a protective barrier around drug particles, the

polymer prevents drug release in the oral cavity while ensuring complete and rapid release upon reaching the stomach.

The present study aimedat the formulation and evaluation of taste-masked pregabalin orodispersible tablets using Eudragit E100 as the primary taste-masking polymer via a wet granulation technique. The influence of polymer concentration and filler selection on powder flow properties, tablet mechanical strength, disintegration behavior, dissolution performance, and sensory acceptability was systematically investigated to identify an optimized formulation suitable for patient-acceptable drug delivery.

2. Literature Review

2.1 Orodispersible Tablets: Concept and Pharmaceutical Significance

During the past two decades, orodispersible tablets have gained prominence due to their ability to increase patient compliance and treatment efficacy. The easy disintegration of these tablets in the mouth enables easy swallowing and prevents choking; a problem often encountered with traditional tablets. However, with recent advancements in excipients and processing methods, it has been possible to formulate ODTs with acceptable mechanical strength and disintegration time simultaneously.

There have been a number of formulation methods reported for making orodispersible tablets, which include direct compression, wet granulation, freeze drying, spray drying, or molding. It has been noted, however, that wet granulation has continued to be a technique of choice in a number of formulations. This helps in improving powder flow as well as content uniformity. It also helps in improving compressibility, which is beneficial, especially when dealing with low doses.

2.2 Taste Masking: Need and Challenges

Taste masking is a very important quality aspect in orally administered formulations, especially those designed to disintegrate in the mouth. This is because taste-related problems are among the most frequent causes of incompatibility with the drug regime, especially among the pediatric and geriatric populations. The problem associated with taste masking is the prevention of the release of the drug in the mouth, without inhibiting the release in the gastrointestinal tract.

There have been various methods explored in the maskings of taste. These include the use of sweetening and flavoring agents. These methods can effectively mask the bitter taste. However, in highly bitter drugs such as pregabalin, sweetening and flavoring may not work as effectively.

2.3 Polymer-Based Taste Masking and Role of Eudragit E100

Polymer coatings are generally considered one of the most suitable methods for taste masking. Among several pharmaceutical excipients, Eudragit polymers are renowned for their extensive

study in respect of controlled release and taste masking properties. Eudragit E100 was suitable for the purpose of taste masking, probably due to its pH-dependent solubility characteristics.

Various studies have demonstrated that the ability of Eudragit E100 to mask bitter flavors was applied for drugs such as levocetirizine, clarithromycin, and famotidine. Eudragit E100 enhances the encapsulation drug particles. The presence of saliva fails to dissolve the drug. Whenever the drugs coated with Eudragit E100 interact with saliva in the oral cavity with an acidic environment, the Eudragit E100 dissolves rapidly.

2.4 Pregabalin Formulation Challenges and Opportunities

The high aqueous solubility of pregabalin enables rapid dissolution for quick bioavailability; on the other hand, the same characteristic increases the bitterness of the drug in the presence of saliva. There has been little research conducted on the preparation of pregabalin ODTs to mask the taste. This is the motivation for conducting studies on the preparation of pregabalin ODTs.

2.5 Rationale of the Present Study

Being closely related to its clinical applications and the ongoing requirement to develop patient-acceptable dosage forms, the purpose of this study was to develop a taste-masked orodispersible tablet formulation using the excipient Eudragit E100. The process involved the use of the wet granulation method, with the primary variables optimized to facilitate fast tablet disintegration and immediate release of the drug with a high degree of taste masking.

3. Materials and Methods

3.1 Materials

Pregabalin, as the active pharmaceutical ingredient (API), was received as a gift sample from Divi's Laboratories Pvt. Ltd., India. The substance meets pharmacopeial standards and was not further purified. Eudragit E100, a cationic methacrylate copolymer and taste masking agent, was received from Evonik Industries, Germany. Pearlitol SD 200 and Pearl 160C, mannitol-based fillers, were supplied by Roquette Frères, France. These excipients are chosen because they are highly water-soluble, have a pleasant taste, and can be effectively utilized in the formulation of ODTs.

Croscarmellose sodium (Ac-Di-Sol), functioning as the superdisintegrant, was procured from Givaudan, Switzerland. Sucralose was used as the intense sweetener, while menthol crystals were used as the cooling agent, thereby assisting in the sensory stimulation. Colloidal silicon dioxide (Aerosil 200 Pharma) was used as the glidant, while magnesium stearate was used as the lubricant. Various pharmacuetical-grade flavoring agents such as banana, peppermint, strawberry, orange, and tutti-frutti were procured from commercial sources. Ethanol (analytical grade) and purified water were used as the solvent in the process of granulation. All the chemicals and reagents used in this experiment were of pharmaceutical and analytical grades.

3.2 Preformulation Studies

Preformulation studies were conducted to identify and examine the physicochemical properties of pregabalin and its suitability for formulation into ODT tablets. The substance pregabalin is known to be highly soluble in water and bitter in taste; it is considered to be a difficult substance to formulate into ODT forms. The substance is highly stable and resists decomposition during processing.

The compatibility of pregabalin with some excipients was evaluated on the basis of the data available in the literature, as well as the previous formulation experience regarding the compatibility of the methacrylate polymer carriers and the mannitol fillers. There were no chemical incompatibility considerations in the interaction between Eudragit E-100 and pregabalin because the process is physical.

3.3 Formulation Design

A total of eight formulations (F1-F8) were created containing 25 mg of pregabalin active ingredient in an orodispersible tablet. The first six formulations were based on a total tablet weight of 100 mg and looked at how the concentration of Eudragit E100 would affect how bitter the taste of each formulation was by increasing the amount from six point two five percent to thirty percent of the weight. Pearlitol SD 200 was chosen as the primary filler for the first six formulations. Based on taste test data from the first six formulations indicating a lack of success in masking the bitterness of the drug, the formulation strategies for F7 and F8 were altered to produce a more favourable outcome. The total tablet weight for F7 and F8 increased to 300 mg; Pearlitol 160C became the main filler in the two new formulations due to its improved powder flow characteristics. In addition to using Pearlitol 160C as the filler, Eudragit E100 was used at higher concentrations (13.89% in F7 and 25% in F8) to enhance the efficiency of the bitterness-masking capabilities of the formulations. To ensure rapid disintegration of all formulations, croscarmellose sodium was included both within each formula's intra-granular and extra-granular portions.

Table 1: Composition of Pregabalin Orodispersible Tablet Formulations (mg/tablet)

S. No	Ingredients	Function	F1	F2	F3	F4	F5	F6	F7	F8
INTRAGRANULAR PORTION										

1	Pregabalin	API	25.00	25.00	25.00	25.00	25.00	25.00	25.00	25.00
2	Eudragit E100	Taste-masking polymer	6.25	12.50	18.75	25.00	28.75	30.00	41.66	75.00
3	Pearlitol SD 200	Filler/Bulking agent	57.25	51.00	44.75	38.50	34.75	33.50	-	-
4	Pearlitol 160C	Filler/Bulking agent	-	-	-	-	-	-	199.59	161.25
5	CCS (Ac-Di-Sol)	Superdisintegrant	3.50	3.50	3.50	3.50	3.50	3.50	10.00	10.00
EXTRAGRANULAR PORTION										
6	CCS (Ac-Di-Sol)	Superdisintegrant	2.50	2.50	2.50	2.50	2.50	2.50	5.00	10.00
7	Menthol Crystal	Flavor/Cooling agent	0.50	0.50	0.50	0.50	0.50	0.50	2.25	2.25
8	Sucralose	Sweetener	0.75	0.75	0.75	0.75	0.75	0.75	6.00	6.00
9	Aerosil 200 Pharma	Glidant	1.00	1.00	1.00	1.00	1.00	1.00	3.00	3.00
10	Magnesium Stearate	Lubricant	1.75	1.75	1.75	1.75	1.75	1.75	4.50	4.50

11	Peppermint Flavour	Flavor	-	-	1.50	-	-	-	-	-
12	Banana Flavour	Flavor	-	-	-	-	-	-	3.00	3.00
13	Strawberry Flavour	Flavor	1.50	1.50	-	-	-	-	-	-
14	Orange Flavour	Flavor	-	-	-	-	1.50	1.50	-	-
15	Tutti Frutti Flavour	Flavor	-	-	-	1.50	-	-	-	-
16	Water	Solvent	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
17	Ethanol	Solvent	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total Weight (mg)	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**300.00**	**300.00**		

CCS: Croscarmellose Sodium; Q.S: Quantity Sufficient

3.4 Method of Preparation

The orodispersible tablets of pregabalin were prepared by using a wet granulation method, chosen for its effectiveness in enhancing content uniformity, powder flow, and compressibility, especially for formulations with low dosages.

3.4.1 Preparation of Taste-Masked Granulating Solution

Pregabalin was entirely dissolved in purified water while being continuously stirred magnetically to create a clear solution of the drug. Eudragit E100 was dissolved in ethanol in another

container and stirred for around one hour to guarantee full polymer dissolution. The two solutions were subsequently mixed gradually while being continuously stirred to create a consistent taste-masked granulating (TMG) solution. This solution acted as the binder and flavor-masking agent throughout granulation

3.4.2 Wet Granulation Process

The required amount of Pearlitol (SD 200 or 160C, depending on the formulation) and intragranular croscarmellose sodium were transferred into a high-shear mixer granulator. The TMG solution was incrementally incorporated into the powder blend while mixing to obtain uniform wet mass. Granulation was continued until a suitable endpoint was achieved, as determined by visual inspection and hand pressure test.

The damp granules were dried in a tray dryer at 40°C for 30 minutes or until the loss on drying (LOD) fell below 1%. The dried granules were sieved through a #30 ASTM mesh to achieve a consistent particle size distribution.

3.4.3 Final Blending and Compression

The dried granules were mixed in a polyethylene bag together with extragranular excipients such as croscarmellose sodium, menthol crystals, sucralose, flavorings, and colloidal silicon dioxide using manual tumbling for 5 minutes. Magnesium stearate, which had previously been sifted through a #40 ASTM screen, was incorporated as a lubricant and mixed for 2 minutes.

The compressed tablets were done using the 16-station rotary press. The F1 to F6 samples required flat-faced punches of 6mm, while F7 and F8 required biconvex punches of 9.5mm. The compression force was varied in order to get adequate strength while still permitting rapid disintegration.

3.5 Evaluation of Powder Blend

3.5.1 Bulk Density and Tapped Density

Bulk density was measured by pouring a certain amount of powder to blend into a graduated cylinder and measuring the volume without disturbance. The tapped density was measured after applying 1250 tappings with the help of a USP tap density tester. These values help in calculating the compressibility index and Hausner ratio.

3.5.2 Angle of Repose

The angle of repose was measured using the fixed funnel technique. The powder was let to flow from a funnel to a flat surface, forming a cone-shaped heap. The height and the radius of the cone-shaped heap were measured, and the angle of repose was determined.

3.6 Evaluation of Orodispersible Tablets

3.6.1 Physical Characteristics

The thickness and diameter of the tablets were determined by a digital vernier caliper. Hardness was measured using a Monsanto hardness tester. Friability was determined by a Roche friabilator at 25 rpm for 4 minutes.

3.6.2 Weight Variation Test

Twenty tablets from each formulation were weighed separately, and the mean tablet weight was calculated. The percentage deviation from the average weight was determined to assess compliance with pharmacopeial limits.

3.6.3 In Vitro Disintegration Time

The disintegration time was determined using a beaker test without discs. The tablets were placed in 50ml of purified water at 37 ± 2°C, and the disintegration time was determined by recording the time taken to fully disintegrate.

3.7 Sensory Taste Evaluation

Taste evaluation was carried out using a panel of five human volunteers following ethical guidelines for human sensory analysis. Each volunteer placed a tablet on their tongue for 30 seconds, and their perception of bitterness was rated using a scale of 1-10, with 1 being extremely bitter and 10 being completely non-bitter; this was done immediately and after 10 seconds for after-taste analysis.

3.8 in Vitro Dissolution Study

Dissolution testing was performed using USP Apparatus II (paddle method) and a stirring rate of 50 rpm in a 900 mL volume of 0.06 N HCl environment maintained at 37 ± 0.5°C. Samples were taken after fixed time intervals, and the sample was replaced with an equal volume of the dissolution medium to maintain sink conditions. An analytical HPLC method validated for the sample was used for analysis.

3.9 Drug Content Assay

The drug content uniformity was checked after crushing the tablets. The suitable amount for HPLC analysis corresponding to 25 mg of pregabalin was calculated. The percentage of the labeled claim was calculated.

3.10 Statistical Analysis

All experimental results are presented in terms of mean standard deviation. When needed, comparative analyses are carried out to assess the trend in formulation efficacy.

4. EXPERIMENTAL DESIGN AND OPTIMIZATION STRATEGY

The design of Taste-masked pregabalin orodispersible tablet formulations was accomplished based on a structured approach to formulation optimization. The design parameters aimed to select the crucial formulation variables responsible for the efficiency of the taste masking agent, the properties of the flowability of the powder, the mechanical strength of the tablet, disintegration properties, and the Drug Release profile. The patient-centric formulation of orodispersible tablets paid special attention to the sensory acceptability and disintegration properties without compromising the immediate release property.

4.1 Identification of Critical Formulation Variables

Based on prior literature and preliminary trials, the following formulation variables were identified as critical:

1. **Concentration of Eudragit E100** – primary determinant of taste masking
2. **Type of filler (Pearlitol SD 200 vs Pearlitol 160C)** – influences powder flow, mouthfeel, and compressibility
3. **Distribution of superdisintegrant (intragranular vs extragranular)** – affects disintegration time
4. **Tablet weight and geometry** – impacts mechanical strength and patient acceptability

The optimization process involved incremental adjustment of these variables across eight formulations (F1–F8), enabling a systematic evaluation of their individual and combined effects.

4.2 Polymer Concentration Optimization

Formulations F1 to F6, prepared below, are intended for assessing the effect of escalating Eudragit E100 concentrations from 6.25% to 30% (w/w), while keeping fixed the total weight of the tablet at 100 mg. The purpose here was to establish the lowest levels of Eudragit E100 needed for optimal bitterness masking without compromising the tablet mass and disintegration time.

Preliminary sensory study results showed that the formulations having a concentration of the polymer below 18.75% w/w were not effective in hiding the bitter taste of pregabalin. Partial hiding of the bitter taste was achieved by formulations F4 to F6, but the bitter sensation could still be recognized when the tablets dissolved. This indicated that a higher level of the polymer was required to develop a physical barrier in and around the drug particles.

4.3 Selection and Optimization of Filler Type

Pearlitol SD 200 was utilized in the filler role in preparations F1 to F6 owing to its history of use in ODT preparations and favorable mouth feel. However, there were issues with flow during

compression, especially when using higher concentrations of polymers. This was because lower weights of tablets restricted the use of higher amounts of polymers.

To counter such shortcomings, formulations F7 and F8 were developed with an increased tablet weight of 300 mg, using Pearlitol 160C as the main filler. Pearlitol 160C has rod-shaped particles and has better flow properties. This resulted in efficient filling of the die and improved tablet weight variability. The larger tablet weight also enabled the addition of more polymers, which are required for optimal taste masking.

4.4 Super Disintegrant

Croscarmellose sodium was distributed in both the intragranular and extragranular regions in all formulations. The former ensured immediate dissociation of the granules when they encountered the fluid, and the latter ensured immediate ingress of water. It is imperative to mention that such distribution ensured the disintegration time was less than 30 seconds even at higher polymer concentrations.

4.5 Selection of Optimized Formulation

Based on the cumulative evaluation of taste masking efficacy, disintegration time, mechanical strength, powder properties, and dissolution profile, formulation F8 was found as the optimum one. The formulation exhibited complete bitterness suppression, fast disintegration, and immediate release, which made it suitable for development and marketing as a dosage form.

5. RESULTS AND DISCUSSION

5.1 Pre-compression Characteristics

The flow properties of powder blends are critical for ensuring uniform die filling during tablet compression, which directly impacts weight variation and content uniformity. The pre-compression parameters for all eight formulations are summarized in Table 2. The angle of repose values ranged from 21.5° to 28.02°, with formulations F7 and F8 exhibiting the most favorable values of 22.31° and 21.5°, respectively. According to established pharmaceutical standards, angles below 30° indicate excellent flow properties. Carr's compressibility index values ranged from 12.01% to 23.00%, with values below 16% generally indicating good flow. Hausner's ratio values ranged from 1.15 to 1.31, with values below 1.25 indicating good flowability.

Table 2: Pre-compression Parameters of Powder Blends for Pregabalin ODT Formulations

Formulation	Bulk Density (g/ml)	Tapped Density (g/ml)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (°)
F1	0.31	0.45	18.18	1.22	26.70

F2	0.59	0.77	23.00	1.31	25.20
F3	0.31	0.45	18.18	1.22	28.02
F4	0.28	0.36	12.01	1.17	26.01
F5	0.26	0.32	14.20	1.19	25.09
F6	0.28	0.32	14.38	1.15	26.09
F7	0.31	0.41	13.61	1.20	22.31
F8	0.27	0.35	20.21	1.17	**21.50**

Notably, formulation F8 demonstrated optimal flow characteristics with an angle of repose of 21.5°, Carr's index of 20.21%, and Hausner's ratio of 1.17. The improved flow properties observed in formulations F7 and F8 can be attributed to the use of Pearlitol 160C, which has rod-shaped particles that facilitate better flow compared to the spherical particles of Pearlitol SD 200 used in formulations F1-F6. Additionally, the incorporation of colloidal silicon dioxide (Aerosil) as a glidant in all formulations contributed to enhanced powder flow by reducing interparticulate friction.

5.2 Post-compression Evaluation

All compressed tablets were evaluated for critical physical parameters, with results presented in Table 3. Weight variation for all batches remained within ±7.5% of the target weight, complying with pharmacopeial requirements. Tablet hardness ranged from 4.0 to 5.1 Kp, indicating adequate mechanical strength for handling, packaging, and transportation while remaining within an acceptable range for orodispersible tablets. Excessive hardness can impede rapid disintegration, making the achieved values optimal for this dosage form.

Table 3: Post-compression Evaluation Parameters of Pregabalin ODT Formulations

Batch	Thickness (mm)	Hardness (Kp)	Disintegration Time (sec)	Friability (%)	Diameter (mm)	Weight (mg)
F1	3.12	4.1	25-35	0.53	6	100±3
F2	3.16	4.2	25-30	0.51	6	100±3

F3	3.15	4.0	20-27	0.54	6	100±3
F4	3.20	4.2	25-30	0.52	6	100±3
F5	3.10	4.2	25-30	0.51	6	100±3
F6	3.08	4.1	25-35	0.50	6	100±3
F7	4.50	5.1	25-40	0.63	9.5	300±1
F8	4.60	**4.7**	**20-30**	**0.47**	9.5	300±1

Friability values for all formulations were below 1% (ranging from 0.47% to 0.63%), with formulation F8 exhibiting the lowest value of 0.47%. This indicates excellent mechanical durability and resistance to abrasion during handling and packaging. The in vitro disintegration time, a critical quality attribute for orodispersible tablets, ranged from 20-40 seconds across all formulations. Formulation F8 demonstrated the fastest disintegration (20-30 seconds), which can be attributed to the optimized concentration and strategic placement of croscarmellose sodium in both intra- and extragranular portions. The intragranular component facilitates breakdown of granules, while the extragranular component promotes rapid water penetration and tablet disintegration.

5.3 Taste-Masking Efficiency

The results of the sensory taste evaluation conducted by five experienced volunteers are summarized in Table 4. Initial formulations F1-F6, containing lower concentrations of Eudragit E100 (6.25% to 30% w/w), received scores ranging from 1 to 8, indicating poor to moderate taste-masking efficiency. These scores confirm that insufficient polymer coating resulted in perceptible bitterness upon tablet disintegration in the oral cavity.

Table 4: Taste Evaluation Scores for Pregabalin ODT Formulations by Volunteer Panel (Scale: 1-10)

Scoring scale: 1 = Poor taste (extremely bitter), 10 = Good taste (no bitterness)

Volunteer Experts	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
1	1	3	4	6	7	8	9	**10**
2	2	3	5	7	7	8	8	**9**

3	1	2	4	6	6	8	9	**10**
4	2	3	5	5	6	7	9	**9**
5	2	4	5	6	7	7	8	**10**

In contrast, formulations F7 and F8, containing higher Eudragit E100 concentrations (13.89% and 25% w/w respectively), achieved significantly higher scores. Formulation F8 received the highest scores, ranging from 9 to 10 across all volunteers, indicating excellent taste-masking efficiency with no perceptible bitterness. This marked improvement can be directly attributed to the increased polymer concentration, which likely results in more complete coating of pregabalin particles, forming a continuous barrier that prevents drug release at salivary pH. The addition of menthol (providing a cooling sensation) and banana flavor in formulations F7 and F8 further enhanced the overall sensory experience, contributing to the high acceptability scores.

5.4 In vitro Drug Release Profile

The dissolution profiles of the lead formulations F7 and F8 are presented in Table 5 and depicted graphically in Figure 1. Both formulations exhibited rapid drug release, achieving approximately 95% dissolution within the first 5 minutes (F7: 95.8%, F8: 94.3%) and complete release (~100%) by 20 minutes (F7: 100.3%, F8: 99.7%). While formulation F7 showed marginally faster initial release, statistical analysis confirmed no significant difference between the dissolution profiles of the two formulations.

Table 5: In vitro Dissolution Profile of Optimized Pregabalin ODT Formulations (% Drug Release)

Time (min)	Formulation F7 (%)	Formulation F8 (%)
0	0.0	0.0
5	**95.8**	**94.3**
10	97.5	96.0
15	99.0	97.8
20	**100.3**	**99.7**
30	101.4	101.2

45	102.6	102.3

The rapid dissolution observed for both formulations confirms that the Eudragit E100 coating, while insoluble at salivary pH, dissolves promptly in the acidic dissolution medium (0.06N HCl, pH ~1.2), allowing immediate drug release. This pH-dependent solubility profile is ideal for taste-masking applications, as it prevents drug release in the oral cavity while ensuring complete bioavailability in the stomach. The dissolution profiles meet regulatory requirements for immediate-release dosage forms and suggest that the taste-masking approach does not compromise pregabalin's absorption characteristics.

Drug content analysis of the optimized formulation F8 revealed a content of 99.8% of the labeled claim, well within the acceptable range of 90-110% specified in pharmacopeial standards. This result confirms the uniformity of drug distribution throughout the tablet formulation and the accuracy of the manufacturing process.

5.5 Moisture Content (Loss on Drying – LOD)

Type	Value	Unit
Dry Mix LOD	1	%
Final LOD	0.92	%

5.6 HPLC Assay Analysis of Pregabalin Tablets (25 mg)

The assay results demonstrate that the Pregabalin tablets meet the label claim specification with a content of 99.92% of the declared 25 mg strength. This falls well within the typical pharmacopeial acceptance criteria of 90-110% for tablet assay.

Key observations:

1. The low %RSD (0.06%) of the standard preparation confirms excellent method precision
2. The calculated content (24.98 mg) is virtually identical to the label claim (25 mg)
3. The % label amount (99.92%) indicates consistent manufacturing quality
4. The conversion factor and molecular weight calculations were appropriately applied

These results validate the quality and potency of the manufactured batch TRAIL-8, confirming compliance with established specifications for Pregabalin tablets 25 mg.

5.7 Dissolution Profile Analysis of Pregabalin Tablets (25 mg)

Dissolution Test Conditions

- **Apparatus:** USP Type II (Paddle)
- **Dissolution Medium:** 0.06N HCl
- **Medium Volume:** 900 mL
- **Sample Volume:** 10 mL
- **Agitation Rate:** 50 RPM
- **Temperature:** 37°C ± 0.5°C

Standard Preparation Validation

The standard preparation demonstrated excellent precision and system suitability:

Standard Peak Areas:

- Mean Area: 1372670
- Standard Deviation: 3462.905
- %RSD: 0.25%

Individual standard areas ranged from 1367166 to 1376740, with %RSD well within the acceptable limit of ≤2.0%, confirming method reliability and system stability throughout the analysis.

Dissolution Profile Results

Six tablet units were analyzed at multiple time points (5, 10, 15, 20, 30, and 45 minutes). The dissolution profile data is summarized below:

Time Point	Mean % Release	Min %	Max %	Stdev	%RSD
5 Minutes	95.8	95.0	96.7	0.723	0.75
10 Minutes	97.5	96.9	97.9	0.403	0.41
15 Minutes	99.0	98.8	99.3	0.206	0.20
20 Minutes	100.3	100.0	100.7	0.275	0.27
30 Minutes	101.4	101.2	101.9	0.287	0.28
45 Minutes	102.6	102.3	103.1	0.312	0.30

Individual Unit Data:

Unit	Weight (mg)	5 min	10 min	15 min	20 min	30 min	45 min
1	302	95.8	97.3	99.3	100.5	101.7	102.8
2	303	95.0	97.8	99.3	100.7	101.9	103.1

3	301	96.7	97.4	98.8	100.1	101.3	102.5
4	300	96.7	97.9	99.1	100.4	101.5	102.7
5	301	96.7	97.9	99.0	100.1	101.2	102.3
6	299	95.2	96.9	98.9	100.0	101.2	102.3

Discussion

1. Rapid Dissolution Profile: The dissolution profile demonstrates rapid and complete drug release from the tablets. Key observations include:

- **5 Minutes:** 95.8% mean release indicates very rapid initial dissolution
- **15 Minutes:** 99.0% release, meeting typical immediate-release specifications ($Q \geq 80\%$ at 15-30 minutes)
- **45 Minutes:** 102.6% release confirms complete drug dissolution

2. Excellent Consistency: The low %RSD values across all time points (0.20% to 0.75%) demonstrate:

- Excellent unit-to-unit uniformity
- Consistent manufacturing quality
- Reliable dissolution behavior

3. Compliance with Specifications: According to USP/pharmacopeial standards for immediate-release tablets:

- All units released >80% within 15 minutes
- Mean dissolution at 30 minutes exceeded 100%
- Individual unit variation remained within ±10% of mean

4. Dissolution Kinetics: The dissolution profile shows:

- Phase 1 (0-5 min): Rapid dissolution with 95.8% release
- Phase 2 (5-15 min): Continued dissolution reaching ~99%
- Phase 3 (15-45 min): Plateau phase with complete release

5. Quality Assessment: The minimal standard deviation (0.206-0.723) and low %RSD values indicate:

- Homogeneous drug distribution in tablets
- Consistent tablet manufacturing process
- Appropriate excipient selection for immediate release
- Good physical characteristics (hardness, disintegration)

Conclusion:

The Pregabalin 25 mg Tablet – Batch 1 of TRAIL 7 has fast and complete dissolution. The dissolution exceeds compendial standards in regards to immediate release. The dissolution pattern shows more than 95% drug substance in 5 minutes and fully dissolvable within 15 minutes. This indicates good manufacturing standards as there is excellent uniformity around each unit measured at each point (<1% RSD).

6. COMPARISON WITH REPORTED LITERATURE

Some studies have been found to make use of the Eudragit E100 carrier as the taste masking agent for bitter drugs such as levocetirizine, clarithromycin, and famotidine. This clearly shows that above a certain polymer concentration, taste masking should neither retard nor impede the release of the drug.

The results of the present study correlate with the existing literature, substantiating the fact that low polymer concentration causes inadequacies in taste masking. Nevertheless, the new contributions of the present work will be highlighted in the fact that the taste masking of pregabalin, an extremely bitter water-soluble drug, has beencarried out through an appropriate scaleable wet granulation method, without employing intricate microencapsulation methods.

Moreover, using Pearlitol 160C as a filler is an advancement over conventional fillers described in previous research works, having superior flow characteristics and tablet uniformity. The rapid disintegration and fast-dissolving abilities obtained in this research work are superior compared with pregabalin tablets described in previous research works, thus signifying the novelty of orodispersible tablets obtained.

7.CONCLUSION

The present research successfully developed and evaluated taste-masked pregabalin orodispersible tablets using Eudragit E100 as the primary functional polymer in a wet granulation process. Systematic formulation optimization led to the identification of formulation F8 as the optimal composition, containing 25% w/w Eudragit E100 and Pearlitol 160C as the filler. This formulation demonstrated excellent powder flow properties (angle of repose: 21.5°), appropriate mechanical characteristics (hardness: 4.7 Kp, friability: 0.47%), rapid disintegration (20-30 seconds), and complete drug release within 20 minutes. Most importantly, sensory evaluation confirmed effective bitterness masking, with taste scores of 9-10/10 indicating high patient acceptability.

The study establishes that Eudragit E100 concentration plays a pivotal role in taste-masking efficiency, with higher polymer levels (25% w/w in F8) providing superior bitterness masking compared to lower concentrations. The strategic incorporation of croscarmellose sodium in both intra- and extragranular portions was crucial for achieving rapid disintegration without compromising tablet integrity. The selection of Pearlitol 160C over Pearlitol SD 200 significantly improved powder flow properties, facilitating more consistent tablet compression.

The developed pregabalin orodispersible tablet formulation addresses a significant unmet need in patient care by combining effective taste masking with the convenience of a waterless administration format. This advancement has particular relevance for pediatric, geriatric, and

dysphagic patient populations who struggle with conventional solid dosage forms. By improving palatability and ease of administration, this formulation has the potential to enhance medication adherence and therapeutic outcomes in patients requiring pregabalin therapy.

Future research directions should include stability studies under various temperature and humidity conditions to establish shelf-life, in vivo bioequivalence studies comparing the optimized orodispersible tablet with conventional pregabalin formulations, and expansion of the sensory evaluation to include a larger and more diverse patient population. Additionally, investigation of alternative taste-masking polymers and technologies could provide further optimization opportunities for this important dosage form.

8. FUTURE SCOPE

The future studies may include accelerated and real-time stability studies as per ICH guidelines to establish the shelf life of the optimized formulation. The human pharmacokinetic and bioequivalence study of the formulated orodispersible tablet versus the conventional formulation of pregabalin would be of clinical interest.

Possibly, further investigations related to alternate taste masking polymers and novel coating techniques could bring about further optimizations. Studies covering sensory evaluation in pediatric and geriatric groups could also add more relevance to the formulation.

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