Palestinian Medical and Pharmaceutical Journal

Formulation and Evaluation of Orodispersible Tablets Containing Paracetamol and Ibuprofen

Zubaida AlQashi[1], Suhad Alahmad[2], Sajida Salah[3] & Hatem A Hejaz[4,*]

(Type: Full Article). Received: 23rd Jul. 2025, Accepted: 7th Oct. 2025, Published: ××××, DOI: https://doi.org/10.xxxx

Accepted Manuscript, In Press

Abstract: Background: Orodispersible tablets (ODTs) are an effective alternative to traditional oral medications, especially for individuals who have difficulty swallowing, such as children, the elderly, and patients with certain medical conditions. These tablets dissolve quickly in the mouth without the need for water, enhancing both convenience and treatment compliance. However, developing ODTs presents several challenges, including poor tablet strength, fragility, and an often-unpleasant taste. **Aims:** This study set out to formulate and assess an optimized ODT that combines paracetamol and ibuprofen for fast and effective relief from pain and inflammation. The objective was to achieve quick disintegration, adequate mechanical strength, and improved taste, while ensuring the final product meets pharmacopeial quality standards. **Methods:** A total of seventeen formulations (F1–F17) were developed using both direct compression and wet granulation techniques. Various concentrations of croscarmellose sodium (as a superdisintegrant), polyvinylpyrrolidone (as a binder), and different flavoring agents were tested. Each formulation was evaluated based on pre-compression flow properties, particle size, and post-compression quality parameters such as disintegration time, drug release profile (using UV spectrophotometry), hardness, friability, and taste. **Results:** Tablets prepared using direct compression showed rapid disintegration but lacked structural integrity and had an unpleasant taste. Switching to wet granulation significantly improved tablet strength, consistency, and flavor. The final optimized formulation (F17), which included 41.7% paracetamol, 33.3% ibuprofen, 2% croscarmellose sodium, and raspberry flavoring, passed all key quality tests. Tablets disintegrated within 3 minutes, complying with the European Pharmacopoeia criterion for ODTs, had a friability of ~1%, and released more than 90% of the drug content within 10 minutes. Raspberry flavoring effectively masked the bitterness of the active ingredients. **Conclusion:** The study demonstrates that wet granulation, when combined with carefully selected excipients and effective flavoring, can produce a high-quality, fast-acting orodispersible tablet. The optimized F17 formulation shows strong potential for improving medication adherence and therapeutic outcomes, especially in patients who struggle with swallowing conventional tablets.

Keywords: Orodispersible Tablets (ODTs); Paracetamol; Ibuprofen; Wet Granulation; Croscarmellose Sodium; Disintegration Time; Taste Masking.

Introduction

Oral dosage forms are the most commonly used methods of drug administration, largely due to their simplicity, accurate dosing, affordability, and non-invasive nature [1]. These include tablets, capsules, suspensions, and solutions, all designed for absorption through the gastrointestinal tract. However, conventional oral forms often pose difficulties for patients with dysphagia—a condition that makes swallowing difficult. This issue is particularly prevalent among children, the elderly, patients with neurological impairments, and individuals undergoing chemotherapy, often leading to reduced adherence and compromised treatment outcomes [2].

To overcome these challenges, orodispersible tablets (ODTs) have been developed as an attractive alternative. These tablets are designed to break down quickly in the mouth, without the need for water or chewing. The European Pharmacopoeia sets an upper limit of three minutes for their disintegration, while the U.S. FDA recommends a much shorter, ideal time of under 30 seconds [3]. Also referred to as fast-dissolving, rapid-melt, or quick-dispersible tablets, ODTs are known for their rapid onset of action, pleasant taste, and ease of administration. These features are especially beneficial for individuals who have trouble swallowing [4, 5]. Their rapid disintegration and absorption make them particularly useful in managing acute conditions like fever and pain. Despite their advantages, ODTs come with formulation challenges such as moisture sensitivity, mechanical fragility, limited drug loading capacity, and the need for precise uniformity, highlighting the importance of proper excipient selection and manufacturing techniques.

A significant amount of research has gone into optimizing ODT formulations by experimenting with different active pharmaceutical ingredients (APIs) and superdisintegrants. For example, Khora *et al*. (2021) studied nine paracetamol-based ODT formulations using crospovidone, sodium starch glycolate (SSG), and carboxymethyl cellulose (CMC). They found that a 12% concentration of crospovidone yielded the best results, achieving a disintegration time of 1.19 seconds, a wetting time of 43 seconds, and a drug content of 99.46% [2]. In another study, Malang *et al*. (2020) developed six ODT formulations combining paracetamol and chlorpheniramine, using different concentrations of croscarmellose sodium (CCS), SSG, and

1 Department of Pharmacy, Faculty of Pharmacy, Arab American University, Jenin, Palestine zubaida.alqashi@aaup.edu
2 Department of Pharmacy, Faculty of Pharmacy, Arab American University, Jenin, Palestine suhad.alahmad@aaup.edu.
3 Department of Pharmacy, Faculty of Pharmacy, Arab American University, Jenin, Palestine sajida.salah@aaup.edu
4 Department of Pharmacy, Faculty of Pharmacy, Arab American University, Jenin, Palestine
* Corresponding author email: hatem.hijaz@aaup.edu

microcrystalline cellulose (MCC). The formulation with 27% CCS exhibited a 20-second disintegration time and an 81% water absorption ratio [6]. Similarly, Sivadasan *et al*. (2020) evaluated ODTs containing fexofenadine hydrochloride and found that a 12% concentration of CCS offered optimal performance [7]. Muneera *et al*. (2019) explored the effects of different sweeteners and superdisintegrants on paracetamol ODTs, concluding that the combination of crospovidone and mannitol achieved the fastest disintegration time of 25 seconds [3].

Additional evidence supports these findings. Gupta (2020) emphasized the increasing popularity of ODTs due to their improved solubility, patient adherence, and fast therapeutic action [1]. Kanathe *et al*. (2020) demonstrated that fluvastatin sodium ODTs showed significantly enhanced disintegration with 5.3% CCS [5]. Karina *et al*. (2018) found that incorporating 10–20% CCS into atenolol ODTs reduced disintegration times without compromising mechanical strength [4]. Further validation came from Khora *et al*. (2021), who noted that formulations with 8% crospovidone delivered a favorable balance between rapid dispersion and high drug content [2]. Several manufacturing techniques are used to produce ODTs, each with its own pros and cons. Direct compression is the simplest and most cost-effective method, involving the blending of APIs and excipients followed by tablet compression. This approach requires excipients with good flowability and compressibility to ensure consistent product quality [8-10]. Lyophilization, which involves freezing a drug solution and removing the solvent through sublimation, creates highly porous and fast-dissolving tablets, but is expensive and time-intensive [11]. Molding uses soluble ingredients to enhance mouthfeel, though the resulting tablets often lack mechanical strength [4]. Wet granulation is a multi-step process that involves blending, wet massing, drying, and compression. While it enhances uniformity and durability, it is more complex than direct compression [12].

The choice of API and excipients is crucial to the success of an ODT. Paracetamol is a widely used analgesic and antipyretic that acts both centrally and peripherally. Although it offers a relatively fast onset of action—within about 60 minutes—it has poor water solubility [13-15]. Ibuprofen, a non-steroidal anti-inflammatory drug (NSAID), inhibits cyclooxygenase (COX) enzymes to reduce inflammation and pain. It has an onset of 30–60 minutes and is nearly 100% bioavailable, but its aqueous solubility is very low (0.021 mg/mL) [16-18]. Excipients play a key role in ODT formulation. CCS, a superdisintegrant, is commonly used in concentrations ranging from 0.5% to 5% and swells rapidly upon contact with saliva to promote quick disintegration [19]. MCC is often added to improves tablet compressibility and also aids in disintegration [20]. Polyvinyl pyrrolidone (PVP), or povidone, acts as a binder to ensure cohesion during granulation [21]. Water is frequently used as the granulating agent in wet granulation methods. To enhance taste and patient acceptability, flavoring agents such as vanillin, saccharin, and raspberry are incorporated [22]. Magnesium stearate is used as a lubricant to reduce friction during tablet compression, helping maintain structural integrity [23].

A thorough evaluation of ODTs is essential to ensure their effectiveness, stability, and overall quality. Granule size analysis is performed to confirm uniformity in particle distribution, which helps prevent segregation and ensures dose consistency. Hardness testing assesses the mechanical strength of the tablets, ensuring they can withstand handling and packaging. Friability tests further evaluate the tablets' resistance to abrasion and chipping during transport and use. Disintegration time is especially critical in ODTs and must typically be under three minutes to ensure fast therapeutic action. Finally, dissolution testing measures how quickly and completely the drug is released from the dosage form—key to ensuring optimal bioavailability [24-28].

Our work stands apart from earlier efforts to develop orodispersible tablets of paracetamol and ibuprofen in a few clear ways. Most previous studies concentrated on formulating just one of the two drugs, while this study combines them into a single tablet, offering both pain relief and fever reduction in a single tablet and reducing the number of pills a patient needs to take. Earlier formulations often relied on direct compression, which led to problems like poor flow, weak tablets that broke easily, or longer disintegration times, especially when higher drug loads were used. In contrast, our study used wet granulation with carefully balanced amounts of microcrystalline cellulose, croscarmellose sodium, polyvinylpyrrolidone, and magnesium stearate, which helped produce tablets with good strength and consistent quality. Another important difference is taste masking. While many past formulations struggled to hide ibuprofen's bitterness with common sweeteners or flavors, our study tested several options and found that raspberry flavoring in the granulating fluid provided effective masking, making the tablets more acceptable to patients. The final tablets disintegrated in less than three minutes, released more than 90% of the drug within ten minutes, and were pleasant enough in taste to encourage better patient use. By addressing both mechanical and palatability issues while combining two widely prescribed drugs in one fast-dissolving dosage form, this work meets a real therapeutic need that earlier single-drug ODTs did not. Thus, this study focuses on the formulation and comprehensive evaluation of orodispersible tablets containing paracetamol and ibuprofen. The aim is to develop a fast-acting, user-friendly dosage form that improves therapeutic efficacy and patient compliance. By combining paracetamol and ibuprofen, the formulation is designed to address both pain and inflammation, offering a synergistic therapeutic benefit. This is particularly valuable for patients with swallowing difficulties and for those in need of rapid symptom relief. The main objectives of this research are to select and assess excipients that facilitate rapid disintegration, to use suitable formulation techniques that ensure product stability and effectiveness, and to evaluate granule characteristics such as particle size to support consistent flow and compression. Quality control measures—including tests for weight variation, hardness, friability, and disintegration—will be applied to the finished tablets. Additionally, calibration curves for paracetamol and ibuprofen will be created using UV spectrophotometry to ensure precise quantification. Finally, drug release will be evaluated using the USP Dissolution Apparatus II to confirm that the formulations meet required standards for bioavailability and therapeutic performance.

Materials and Methods

Materials

This study focused on the formulation and evaluation of orodispersible tablets (ODTs) containing paracetamol and ibuprofen, prepared using both direct compression and wet granulation techniques. All ingredients used were of pharmaceutical grade, sourced primarily from Jerusalem Pharmaceuticals Co. Ltd., unless stated otherwise. Paracetamol and ibuprofen were chosen as the active pharmaceutical ingredients (APIs) because of their widely recognized analgesic, antipyretic, and anti-inflammatory effects. Croscarmellose Sodium (CCS) was used as the superdisintegrant to promote rapid breakdown of the tablet in the oral cavity. Microcrystalline Cellulose (MCC) served as a diluent and dry binder, valued for its excellent compressibility and support in tablet disintegration. Polyvinylpyrrolidone (PVP) was included as a binder, especially

useful in wet granulation formulations. To enhance the tablets' taste and encourage patient compliance, several flavoring agents—vanillin, stevia, and raspberry—were evaluated. Magnesium stearate acted as a lubricant, helping to prevent sticking during tablet compression and aiding in powder flow. The granulating solution consisted of distilled water alone or blended with raspberry flavor. For dissolution testing and UV calibration, phosphate buffer was prepared using potassium phosphate monobasic and potassium hydroxide (KOH). The active ingredients, paracetamol and ibuprofen, were obtained as pharmaceutical-grade powders through Jerusalem Pharmaceuticals Co. Ltd. (Jerusalem, Palestine), which acts as the local distributor. Both APIs are imported from international manufacturers; paracetamol is commonly sourced from Mallinckrodt (Ireland) or BASF (Germany), while ibuprofen is supplied by BASF (Germany) or IOL Chemicals (India). The excipients used in the formulations included croscarmellose sodium (FMC BioPolymer, USA), microcrystalline cellulose (JRS Pharma, Germany), polyvinylpyrrolidone (BASF, Germany), and magnesium stearate (Peter Greven, Germany), all supplied locally by Jerusalem Pharmaceuticals. Flavoring agents were vanillin (Sigma-Aldrich, St. Louis, MO, USA), stevia (Zero Enthalpy Lab, Mumbai, India), and raspberry flavor (Frutarom, Haifa). Buffer components were potassium phosphate monobasic and potassium hydroxide, both purchased from Sigma-Aldrich (St. Louis, MO, USA). Purified water used in the granulation process was provided by the water treatment system at the industrial pharmacy laboratory of the Arab American University (AAUP, Jenin, Palestine).

Equipment and Tools

A range of equipment was employed during formulation and analysis. A UV-Visible double-beam spectrophotometer was used for drug quantification, and a pH meter was used for adjusting buffer solutions. Analytical balances and calipers ensured precision in weight and tablet dimensions. Physical testing equipment included a tablet hardness tester, friability tester, disintegration apparatus, and a USP Type II dissolution tester. Granules were dried using a tray oven, and moisture content was assessed using a moisture analyzer. Particle size was evaluated using a USB digital microscope with image analysis software. All devices were calibrated before use to guarantee reliable results. The formulation and evaluation of the ODTs were carried out using a UV–Visible double-beam spectrophotometer (Shimadzu, Kyoto, Japan), a pH meter (Jenway, Staffordshire, UK), and a digital caliper (Whitworth, UK). An analytical balance (Optika, Ponteranica, Italy) was used for weighing, and a bath sonicator (Labtron, UK) was employed for solubilization. Moisture content was measured using a moisture analyzer (Shimadzu, Kyoto, Japan). Tablet testing was performed with a USP disintegration apparatus (Pharma Test, Hainburg, Germany), a dissolution apparatus type II (Copley Scientific, Nottingham, UK), a friability tester (Copley Scientific, Nottingham, UK), and a tablet hardness tester (Copley Scientific, Nottingham, UK). Drying after granulation was carried out using a tray oven dryer (Thermo Fisher Scientific, Waltham, MA, USA). For microscopic evaluation, a USB digital microscope (RoHS-compliant, Shenzhen, China) was used. In addition, standard laboratory tools such as thermometers, mortars and pestles, pipettes, volumetric flasks, droppers, foil plates, and computers for data collection were available from the industrial pharmacy laboratory at AAUP (Jenin, Palestine).

Methods

A. Preparation of Calibration Curve

To assess drug release, calibration curves were established for both APIs. Stock solutions were prepared by dissolving 10 mg of either paracetamol or ibuprofen in 100 mL of phosphate buffer (pH 7.2). From this solution, 10 mL was diluted to 100 mL to create a working stock, which was then used to prepare final concentrations of 1, 1.5, 2, 2.5, and 3 µg/mL. Absorbance readings were taken at 242 nm for paracetamol and 221 nm for ibuprofen using a UV spectrophotometer, and the calibration curves were generated by plotting absorbance against concentration. The buffer solution used in this process was prepared by dissolving 68 grams of potassium phosphate monobasic in 6 liters of distilled water. Potassium hydroxide was gradually added to adjust the pH to 7.2, confirmed using a calibrated pH meter.

B. Pre-Compression Parameters

Angle of Repose (θ): The flowability of the powder blends was evaluated using the fixed funnel method. The angle of repose was calculated using the height and base radius of the powder cone, following the equation:

Tan θ = height/radius

This parameter provided insight into the blend's flow behavior, essential for ensuring consistent tablet weight during compression. Table 1 presents the angle of repose limits.

Table (1): Angle of Repose Limits.

Sr. No.	Angle of Repose	Flow of Powder
1.	< 25	Excellent
2.	25–30	Good
3.	30–40	Passable
4.	> 40	Very Poor

Bulk and Tapped Density: To assess powder compressibility, bulk and tapped densities were measured. Bulk density was calculated by dividing the mass of the powder by its untapped volume in a graduated cylinder. Tapped density was obtained after mechanically tapping the cylinder until the volume remained constant.

***Hausner's Ratio and Carr's Index*:** These flowability indicators were derived using the bulk and tapped densities:

Hausner's ratio = Tapped Density/Bulk Density

Carr's Index = [(Tapped Density − Bulk Density)/ Tapped Density] × 100

Particle Size Analysis: Granule particle size was determined by capturing microscope images, which were then analyzed. Calibration was set at 1 pixel = 0.086 µm. The projected area of each particle was calculated, from which radius and diameter were derived. Particles were categorized into specific size ranges and plotted in histograms to assess uniformity.

C. Formulation Development

Seventeen different formulations (F1–F17) were developed as shown in **Tables 2 and 3**, using both direct compression and wet granulation methods. Formulations F1–F14 followed the direct compression method, while F15–F17 were prepared using wet granulation. Both single-drug (paracetamol or ibuprofen) and combination-drug (paracetamol + ibuprofen) formulations were explored.

Direct Compression (F1–F14): In this method, the APIs, CCS, MCC, PVP (in selected batches), and flavoring agents were weighed, blended thoroughly, and passed through a #60 mesh sieve. Tablets were compressed using a 5 mm single-punch press under a pressure of 20–40 kN (equivalent to ~100–200 MPa). While formulations with higher CCS concentrations demonstrated favorable disintegration times, they encountered challenges such as poor compressibility, increased friability, and surface roughness. Efforts to improve tablet quality included reducing CCS and increasing PVP content. However, even with

these adjustments, the taste remained subpar—particularly with vanillin and stevia.

Wet Granulation (F15–F17): To resolve the mechanical issues observed in the direct compression method, wet granulation was employed. A mixture of paracetamol, ibuprofen, MCC, and half the required CCS was granulated using a solution of 80% distilled water and 20% raspberry flavoring. The wet mass was dried at 100°C for 15 minutes, with stirring every few minutes to ensure uniform drying. Once cooled, the dried mass was gently milled and passed through a #40 mesh sieve. The resulting granules were then mixed with the remaining CCS and magnesium stearate before being compressed into tablets. This method significantly improved tablet strength, reduced friability, and enhanced taste. Both F16 and F17 demonstrated acceptable disintegration times, pleasant flavor, and consistent weight, with F17 being selected as the optimized formulation.

To resolve the mechanical issues observed in the direct compression method, wet granulation was employed. A mixture of paracetamol, ibuprofen, MCC, and half the required CCS was granulated using a solution of 80% distilled water and 20% raspberry flavoring. The wet mass was dried at 100°C for 15 minutes, with stirring every few minutes to ensure uniform drying. Once cooled, the granules were mixed with the remaining CCS and magnesium stearate before being compressed into tablets. This method significantly improved tablet strength, reduced friability, and enhanced taste. Both F16 and F17 demonstrated acceptable disintegration times, pleasant flavor, and consistent weight, with F17 being selected as the optimized formulation.

Preparation of the Successful Formula (F17): F17 was prepared as a 50-tablet batch, contained paracetamol 41.7% (12.5 g), ibuprofen 33.3% (10 g), croscarmellose sodium (CCS) 2% (0.6 g), magnesium stearate 1% (0.3 g), microcrystalline cellulose (MCC) 22% (6.6 g), and a granulation solution consisting of 80% distilled water (D.W.) and 20% raspberry flavoring agent. Initially, APIs, MCC, and half the CCS were mixed. The angle of repose was measured to assess powder flow. Granulation followed by drying in a tray oven at 100°C for 15 minutes was performed, with mixing every 3–4 minutes. The loss on drying (LOD) was calculated at 3.68%. Granules were then analyzed microscopically for particle size and finally compressed into tablets using a manual single-punch press. Each tablet was formulated to contain 250 mg of paracetamol and 200 mg of ibuprofen as the active ingredients. This dosage regimen is designed so that children and older adults take one ODT per dose (paracetamol 250 mg + ibuprofen 200 mg). Adults who require a higher dose may take two ODTs per dose (500 mg paracetamol + 400 mg ibuprofen) instead of doubling the strength—and size—of a single tablet to reach the recommended therapeutic range.

D. Evaluation of Orodispersible Tablets

Stage 1: Disintegration and Compressibility: Different concentrations of CCS and PVP were tested to optimize both tablet disintegration and mechanical strength. The switch to wet granulation effectively addressed the compressibility issues seen in the direct compression batches. In F17, a 2% concentration of CCS was found adequate for achieving rapid disintegration.

Table (2): Paracetamol, Ibuprofen, and Combination Orodispersible Tablets (Direct Compression Method).

Ingredient (%)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14
Paracetamol	54.17	54.17	54.17	–	54.17	54.17	54.17	54.17	54.17	54.17	54.17	54.17	54.17	54.17
Ibuprofen	–	–	–	33.33	33.33	33.33	33.33	33.33	33.33	33.33	33.33	33.33	33.33	33.33
CCS	10	7.5	5	2.5	2.5	2.5	2.5	2	2	2	2	1.5	1.5	1.5
MCC	34.83	37.33	39.83	61.17	8	7	7	7.5	7	6.5	6	7	6.8	6.8
Vanillin	1	1	1	1	1	1	1	1	1	1	1	0.5	0.3	…
PVP	–	–	–	2	1	1	1.5	1.5	2	2.5	3	3	3	3
Mg-St	–	–	–	–	–	1	0.5	0.5	0.5	0.5	0.5	0.7	0.7	0.7
Stevia	–	–	–	–	–	–	–	–	–	–	–	–	…	0.5
Disintegration	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Compressibility	F	F	F	F	F	F	F	F						

P= Pass, F= Fail.

Table (3): Paracetamol, Ibuprofen, and Combination Orodispersible Tablets (Wet Granulation Method).

Ingredient (%)	F15	F16	F17
Paracetamol	54.17	41.7	41.7
Ibuprofen	33.33	33.33	33.33
CCS	2	2	2
MCC	22	22	22
Vanillin	-	-	-
PVP	-	-	-
Mg-St	1	1	1
Stevia	1%	-	-
Granulation Sol.	Granulation sol. 100%	D.W. 80% + Flavor 20%	D.W. 80% + Flavor 20%
Disintegration	P	P	P
Compressibility	P	P	P
Taste	F	F	P

P= Pass, F= Fail. F16 & F17 (10 and 50 Tablets batch sizes respectively).

Stage 2: Taste Evaluation: Taste was a major focus for patient acceptability. Vanillin and stevia, even at increased levels, failed to eliminate bitterness. Raspberry flavoring, on the other hand, produced a much more pleasant taste and was therefore used in the final formulations, F16 and F17. The taste of the tablets was checked informally by the researcher through personal assessment. Small pieces of each tablet were placed on the tongue, without swallowing, to judge whether any bitterness was present and to get an impression of how well the flavoring agents worked. A formal sensory panel or scoring scale was not used, so the results should be considered a preliminary and subjective evaluation rather than a standardized taste study.

Stage 3: Quality Control Tests: Several quality control parameters were assessed for F16 and F17, which include:

- ***Weight Variation:*** Ten tablets were individually weighed, and their average weight and standard deviation were compared against USP standards.
- ***Hardness:*** Measured using a Copley tester to ensure adequate mechanical resistance.
- ***Thickness and Diameter:*** Measured using a digital caliper to confirm uniform size.

- ***Friability:*** Ten tablets were rotated at 25 rpm for four minutes; weight loss was calculated. Acceptable friability was defined as <1%.
- ***Disintegration Time:*** Using a USP disintegration apparatus, complete disintegration was confirmed to occur within three minutes.
- ***Wetting Time:*** The time taken for the tablet to become completely wet was recorded using a Petri dish setup and phenol red-stained water.
- ***Water Absorption Ratio:*** Calculated by comparing pre- and post-wet weights using the formula:

  R = 100 × (Wa − Wb) / Wa

  where Wa = weight after absorption and Wb = weight before.
- ***Dissolution Testing:*** Conducted in 900 mL of distilled water at 37°C and 50 rpm using USP Apparatus II. Samples were withdrawn at 5, 10, and 15 minutes and analyzed *via* UV spectrophotometry at 221 nm for ibuprofen and 242 nm for paracetamol.

Statistical Analysis: Data are expressed as mean ± SD, and differences between formulations were analyzed by one-way ANOVA followed by Tukey's post hoc test ($p < 0.05$) using GraphPad Prism (GraphPad Software, San Diego, CA, USA).

Results

A. UV Spectrophotometric Analysis

The UV spectrophotometric method confirmed a direct, linear relationship between the concentration of ibuprofen and its absorbance, consistent with Beer-Lambert's Law. As ibuprofen concentrations increased from 0.00172 µg to 0.0178 µg, corresponding absorbance values rose from 0.086 to 0.775. The resulting calibration curve (**Figure 1**) followed the regression equation y = 43.329x – 0.0002, with an R^2 value of 0.9986, indicating high accuracy and linearity for ibuprofen quantification. Drug concentrations were monitored using UV spectrophotometry at two wavelengths: 221 nm for ibuprofen and 242 nm for paracetamol. These wavelengths were selected based on the maximum absorbance (λmax) of each drug, ensuring accurate and specific quantification during the test.

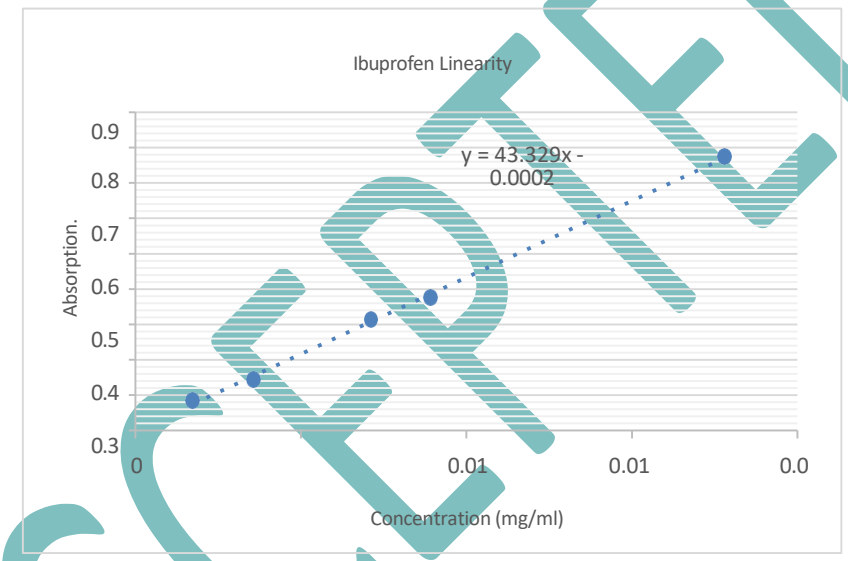

Figure (1): Calibration curve for Ibuprofen.

Paracetamol exhibited similar behavior. Its absorbance increased from 0.214 at a concentration of 0.00324 µg to 0.841 at 0.0133 µg. The regression equation for the calibration curve (**Figure 2**) was y = 63.832x + 0.0133, with an R^2 value of 0.996, confirming the method's reliability for analyzing paracetamol

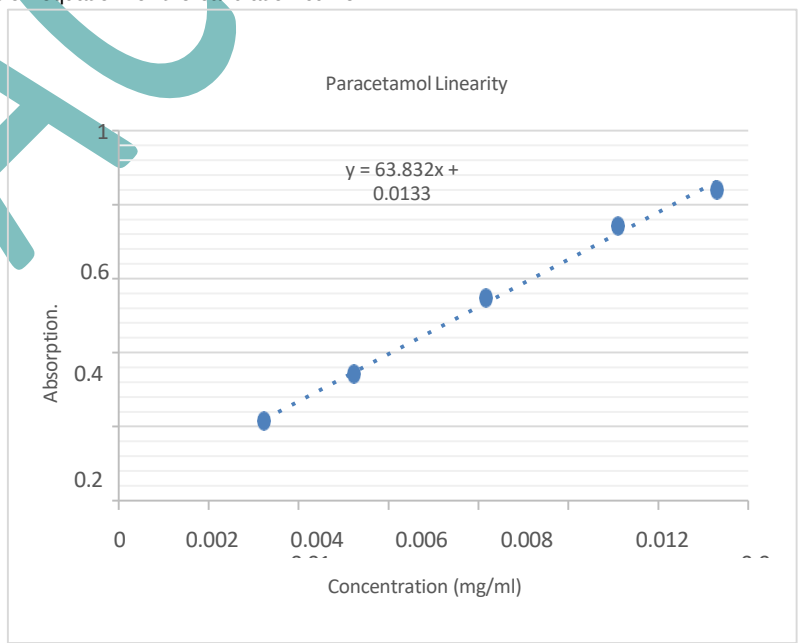

Figure (2): Calibration curve of Paracetamol.

B. Pre-formulation Studies

Angle of Repose: Before granulation, the powder blend exhibited poor flow, with an angle of repose measuring 57.8°. After granulation, flow properties improved significantly, and the angle was reduced to 35.7°, which is classified as passable flow.

Bulk and Tapped Density: The powders of both paracetamol and ibuprofen initially showed poor flow characteristics. Paracetamol had a Carr's Index of 38.7% and a Hausner Ratio of 1.63, while ibuprofen measured 40.75% and 1.7, respectively—values indicative of very poor flow. Granulation improved both compressibility and flow behavior. Lower values for both metrics (Carr's Index and Hausner Ratio) indicate better powder flow, which is important for uniform die filling and tablet integrity. Table 4 shows the Hausner's Ratio and Carr's Index Limits.

Table (4): Hausner's Ratio and Carr's Index Limits.

Compressibility index (%) (Carr's index)	Hausner's Ratio	Carr's Index
1–10	Excellent	1-1.11
11–15	Good	1.12-1.18
16–20	Fair	1.19-1.25
21–25	Passable	1.26–1.34
26–31	Poor	1.35–1.45
32–37	Very poor	1.46–1.59
>37	Very, very poor	>1.59

Particle Size Analysis: Particle size evaluation analysis of granules (**Figure 3**) showed that approximately 75% of the granules fell within the 7.0 to 9.9 µm range. The most common size intervals were 7–7.9 µm (30 particles), 8–8.9 µm (25 particles), and 9–9.9 µm (20 particles). Only a few granules exceeded 10 µm, suggesting a uniform particle distribution suitable for tablet compression. Visual inspection (**Figure 4**) revealed uniform, well-formed granules with smooth surfaces and minimal fines, indicating good packing potential and flow properties.

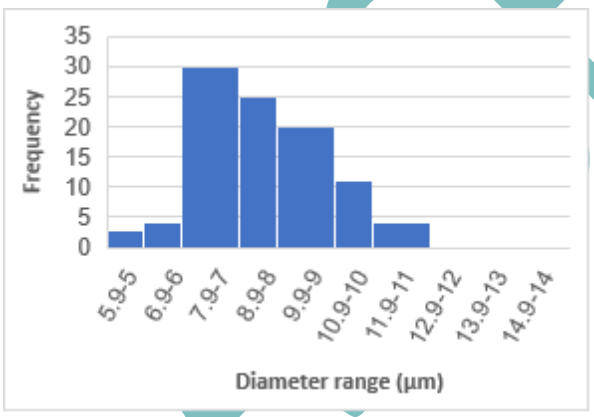

Figure (3): Granule size distribution.

Figure (4): Granules under microscope.

C. Granule Characterization

Angle of Repose: Pre-granulation: Height = 5.5 cm, Radius = 4.31 cm → Angle = 57.8°. Post-granulation: Height = 2.5 cm, Radius = 3.98 cm → Angle = 35.7°. This reduction confirmed that granulation effectively improved powder flow.

Paracetamol Densities: Bulk density: 0.325 g/mL**.** Tapped density: 0.529 g/mL**.** Carr's Index: 38.7%**.** Hausner Ratio: 1.63**.** **Ibuprofen Densities:** Bulk density: 0.33 g/mL**.** Tapped density: 0.557 g/mL**.** Carr's Index: 40.75%**.** Hausner Ratio: 1.7**.** Both sets of values confirmed poor initial flow, reinforcing the need for granulation to enhance manufacturability.

D. Formulation Development

Seventeen formulations (F1–F17) were developed. Formulations F1–F14 were made **via** direct compression, while F15–F17 utilized wet granulation. F1–F3: Incorporated 5%, 7.5%, and 10% CCS, respectively. Although disintegration times were favorable, compressibility and tablet texture were poor. F4: Included 1% PVP to improve cohesiveness, which helped texture slightly but didn't resolve weight variation or friability. F5–F6: Combined both APIs with and without magnesium stearate. Disintegration remained quick but compressibility issues persisted. F7–F11: Increased PVP to 3% and reduced CCS to 2%. Tablet texture improved, but friability and taste remained problematic. F12–F14: Focused on taste masking using vanillin (0.3–0.5%) and stevia (up to 1%). Neither was effective in masking the bitterness. F15: Introduced wet granulation, which significantly improved compressibility and tablet integrity, although taste was still unsatisfactory. F16: Substituted raspberry flavoring, leading to a noticeable improvement in taste. F17: A 50-tablet batch developed using wet granulation and raspberry flavor showed optimal properties and was selected for full evaluation (**Table 5**).

Disintegration and Compressibility: Throughout F1–F14, CCS concentration was gradually reduced from 10% to 1.5%, while PVP was increased up to 3% to strike a balance between rapid disintegration and mechanical strength. Wet granulation, adopted in F15–F17, maintained CCS at 2%, ensuring effective disintegration and improved compressibility.

Taste Evaluation: F11–F13: Used vanillin at 0.3–1% concentrations, but all samples had a residual unpleasant taste. F14–F15: Replaced vanillin with stevia (0.5–1%), which also failed to adequately mask bitterness. F16–F17: Used raspberry flavor, which successfully masked the drug taste and was well accepted in sensory evaluation.

Formulation Evaluation (F17): A Successful Formulation (SF) was selected based on favorable pre-formulation and granulation results. This formulation (F17) was subjected to a comprehensive evaluation.

Weight Variation: Ten tablets were evaluated individually. The average tablet weight was 595.9 mg, with individual values ranging between 588 mg and 608 mg—well within USP's ±5% tolerance range, indicating good content uniformity.

Table (5): Tablet Weight and API Content.

Tablet No.	Tablet Weight (mg)	Paracetamol (mg)	Ibuprofen (mg)	Excipients (mg)	Standard Deviation
1	591	250	200	141	0.82
2	589	250	200	139	1.16
3	595	250	200	155	0.15
4	588	250	200	138	1.3
5	597	250	200	147	0.18
6	593	250	200	143	0.49
7	599	250	200	149	0.58
8	608	250	200	158	2.00
9	596	250	200	146	0.017
10	603	250	200	153	1.19
Average	595.9				

Thickness and Diameter: Tablet thickness ranged from 4.24 to 4.89 mm, averaging 4.454 mm, while diameter was between 12.21 and 12.32 mm, with a mean of 12.29 mm. These values showed minimal variation and reflected consistent compression.

Tablet Hardness: Measured hardness ranged from 4.54 to 6.58 kgf, with an average of 5.541 kgf. Most values fell within acceptable limits for ODTs, although minor variability was noted.

Friability: The friability test results indicate that the tablets are very close to the acceptable limit, which is < 1%. Friability= [(Initial Weight-Final Weight)/ Initial Weight] X 100%= [(6.95−6.88)/6.95]X 100%= 1.007%. Despite this marginal increase, the tablets were considered sufficiently robust.

Disintegration Time: All tablets disintegrated within 1–3 minutes, in compliance with ODT requirements.

Wetting Time and Water Absorption: The F17 tablets demonstrated quick wetting. The wetting test showed that it takes one minute for the fluid to reach the surface of the Tablet-Wetting Time: 62 seconds**.** Water absorption ratio: R = 100 $\times Wa-Wb/Wa$=44.55%**.** These results confirm the tablet's rapid water uptake and fast disintegration in the oral cavity. The fragmentation time, wetting time, and water absorption ratio were approximately 1 min, 20 sec, 62 sec, and 44.55 % respectively.

Dissolution Study: Each tablet contained 200 mg ibuprofen and 250 mg paracetamol. Drug concentrations were determined by applying calibration curve equations and adjusted for dilution and chamber volume. Ibuprofen Release Profile: After 5 minutes: 70.4–85.4% (140.86–170.87 mg)**.** After 10 minutes: 90.5–98.5% (180.91–196.98 mg)**.** After 15 minutes: up to 107.7% (203.03–215.45 mg). Although some values slightly exceeded 100%, likely due to experimental variation, the overall release profile was rapid and consistent, supporting the intended quick onset of action.

Organoleptic Properties: The formula tablets of F17 showed an off-white color**.** A pleasant raspberry flavor**,** a mild, characteristic odor, and a smooth, palatable texture**.** These sensory characteristics are crucial for improving patient acceptability, particularly among children and the elderly.

Formulation F17 disintegrated significantly faster than F15 and F16 ($p < 0.05$), highlighting the effectiveness of the optimized excipient ratio in improving tablet performance. Although all wet-granulated formulations showed friability values within the acceptable limit (<1%), F17 demonstrated significantly lower friability compared to F15 ($p < 0.05$). In terms of mechanical strength, both F16 and F17 showed higher hardness values than the direct compression formulations (F1–F14), with the difference being statistically significant ($p < 0.01$). Furthermore, the dissolution profile of F17 revealed more than 90% drug release within 10 minutes, which was significantly higher than that of F15 ($p < 0.05$), confirming its suitability as the optimized formulation. Formulations F16 and F17 performed almost the same with respect to hardness, friability, disintegration, and dissolution. The only real difference between them was the batch size: F16 was a small trial batch of 10 tablets, whereas F17 was prepared on a larger scale with 50 tablets. Increasing the batch size did not cause any noticeable changes in tablet quality.

The development of ODTs combining paracetamol and ibuprofen achieved several key goals: Improved flow and compressibility through wet granulation. Uniform tablet weight, thickness, and hardness. Rapid disintegration and efficient drug release. Effective taste masking with raspberry flavor. Full compliance with USP standards. These results demonstrate that the optimized formulation (F17) is well-suited for fast-acting, patient-friendly analgesic and antipyretic therapy, particularly in populations with swallowing difficulties.

Discussion

This study provides a thorough evaluation of orodispersible tablets formulated with paracetamol and ibuprofen, aimed at delivering rapid therapeutic relief for patients with swallowing difficulties—particularly pediatric and geriatric populations. The findings are interpreted in light of pharmaceutical performance indicators such as disintegration, dissolution, compressibility, flowability, and palatability, and are further supported by literature comparisons to validate the formulation strategy. Seventeen formulations (F1–F17) were developed and assessed. Early formulations (F1–F14), prepared by direct compression, exhibited challenges including poor compressibility, friability, and notable weight loss (~100 mg). Although rapid disintegration was achieved using superdisintegrants like croscarmellose sodium, these tablets lacked mechanical strength and had poor palatability. In contrast, the switch to wet granulation in F15–F17 significantly improved tablet integrity and surface texture, resolving the issues encountered with direct compression.

Flow properties showed substantial improvement post-granulation. The angle of repose dropped from 57.8° (very poor flow) to 35.7° (passable flow), which is consistent with findings from Shah *et al.* (2018), who reported enhanced flow properties after wet granulation in poorly compressible drugs [29]. This improvement was supported by Carr's Index and Hausner ratio values: both paracetamol (38.7%, 1.63) and ibuprofen (40.75%, 1.7) exhibited poor initial flow, which improved following granulation. Particle size analysis revealed a narrow and consistent granule size distribution, with 75% of particles falling between 7 and 9.9 µm. This uniformity contributed to consistent die filling and minimized variability in weight and tablet thickness. Tiwari *et al*. (2020) similarly noted that a narrow particle size distribution enhances both tablet uniformity and mechanical strength [30]. Taste-masking posed a significant challenge. Attempts using pure vanillin and stevia failed to improve flavor, both producing an unpleasant taste. However, raspberry flavoring introduced in formulations F16 and F17 was notably successful, significantly enhancing palatability. This aligns with findings by Nair *et al*. (2017), who emphasized that effective

flavoring is critical for patient compliance, particularly in pediatric formulations [31].

Analytical validation through UV spectrophotometry confirmed the accuracy and linearity of the method. Ibuprofen and paracetamol showed R^2 values of 0.9986 and 0.996, respectively, in compliance with Beer-Lambert's Law. These results are comparable to those reported by Reddy *et al*. (2016), who demonstrated strong linear relationships ($R^2 > 0.995$) for the same drug combination in spectrophotometric analysis [32].

Among all formulations, F17 emerged as the most successful. Composed of 75% active ingredients, 22% microcrystalline cellulose (MCC), 2% CCS, 1% magnesium stearate, and raspberry-flavored granulating fluid, F17 delivered the best balance of physical, functional, and sensory attributes. It demonstrated excellent weight uniformity (588–608 mg; average 595.9 mg), adequate mechanical strength (average hardness 5.541 kgf), acceptable friability (1.007%), and a disintegration time under three minutes—fulfilling the European Pharmacopoeia's criteria for ODTs. These outcomes are consistent with the work of Ali *et al*. (2018) and Kumar *et al*. (2019), who reported similar performance metrics using MCC and CCS in ODT formulations [33,34]. The dissolution profile of F17 indicated rapid drug release, with over 90% of paracetamol and 93.4% of ibuprofen released within 10 minutes. This is comparable to the findings of Patil *et al*. (2020), who documented efficient dissolution (>85%) in similarly optimized ODTs [35]. The rapid onset of drug release in F17 makes it particularly suitable for the fast management of acute pain and fever. Organoleptic evaluation confirmed that F17 had a pleasant raspberry flavor, characteristic odor, off-white appearance, and smooth texture. Such sensory attributes are vital for ensuring patient acceptance, especially in pediatric and geriatric groups. Velmurugan and Sundar (2015) highlighted the importance of mouthfeel and taste in enhancing the acceptability of ODTs [36]. Performance in wetting and absorption tests was also favorable. F17 exhibited a wetting time of 62 seconds and a water absorption ratio of 44.55%, supporting rapid disintegration upon contact with saliva and contributing to faster therapeutic action.

The ability of the tablets in this study to disintegrate rapidly while masking the bitter taste has clear clinical relevance for patients who struggle with conventional tablets. Children, for example, often find it difficult to swallow solid dosage forms and are especially sensitive to unpleasant flavors, which can reduce their willingness to take medicines as prescribed. Orodispersible tablets that break down within seconds and taste acceptable provide a practical solution, improving adherence and treatment outcomes. Older adults face similar challenges, as swallowing difficulties and reduced saliva flow can make standard tablets unsafe or uncomfortable. Quick-dissolving formulations that require no water help minimize choking risks and make administration easier. These benefits also extend to patients with psychiatric conditions or those who need a convenient option when water is not available. Taken together, the optimized formulation developed here not only resolves mechanical and taste-related limitations but also meets real clinical needs by improving safety, convenience, and patient compliance.

Throughout this research, various challenges emerged during the development of oral tablet formulations (F1–F17). While these obstacles were significant, effective solutions were eventually identified through careful formulation adjustments and process improvements. Early efforts focused on direct compression (F1–F14), which quickly revealed several shortcomings. The tablets produced during this phase had poor compressibility, were prone to breakage and surface roughness, and showed inconsistencies in weight and thickness. To resolve these issues, the approach was shifted to wet granulation for formulations F15–F17. This change led to a marked improvement in powder flow, as seen by the drop in the angle of repose from 57.8° to 35.7°. It also enhanced the mechanical strength and uniformity of the tablets. Taste masking proved to be another major hurdle. Attempts using vanillin and stevia (F11–F15) failed to effectively masks the bitterness of paracetamol and ibuprofen, resulting in poor palatability. This was successfully addressed in F16 and F17 by switching to raspberry flavoring, which significantly improved the taste and overall acceptability for patients. Although formulation F17 was the most optimized, it did show a friability value of 1.007%, just slightly above the USP limit of 1%. Despite this, the tablets were considered sufficiently strong due to the robustness provided by wet granulation and the careful balance of excipients like microcrystalline cellulose (MCC) and magnesium stearate. Flow properties of the raw powders also posed a problem. Although this small deviation of friability for F17 did not affect the overall performance of the tablets during laboratory testing, it could become more relevant in large-scale manufacturing, packaging, and distribution, where tablets are exposed to greater mechanical stress. Even a slight increase in friability may raise the risk of chipping, breaking, or powdering during handling and transport. For this reason, while F17 is acceptable at the research stage, further adjustments—such as fine-tuning the binder or lubricant content—may be needed to ensure long-term robustness and compliance under real production conditions.

Before granulation, both paracetamol and ibuprofen displayed poor flow characteristics, indicated by high Carr's Index, high Hausner's Ratio, and an angle of repose greater than 40°. After granulation, these properties improved significantly, with better flow indices and a more uniform particle size distribution—75% of particles falling within the 7–9.9 µm range—which helped ensure consistent die filling. One of the final challenges was achieving rapid disintegration without compromising tablet strength. Early formulations suffered when high levels of superdisintegrants weakened the tablets. This was corrected in F17 by optimizing excipient levels: 2% croscarmellose sodium to maintain fast disintegration, 1% magnesium stearate for lubrication, and 22% MCC to reinforce structural integrity. These adjustments created a well-balanced formulation that met both performance and patient compliance goals. The selected doses of 250 mg paracetamol and 200 mg ibuprofen per tablet fall within the clinically approved therapeutic range and are consistent with fixed-dose combinations already marketed for pain and fever management. This balance provides effective analgesic and antipyretic activity while reducing pill burden and maintaining safety. Although F16 and F17 showed almost identical results for disintegration, friability, and drug release, F17 was chosen as the optimized formulation because it was prepared in a larger batch size (50 tablets compared with 10 for F16). The larger batch gave greater confidence in the reproducibility and scalability of the method, rather than indicating any statistically significant difference in performance.

Statistical analysis showed that wet granulation (F15–F17) produced tablets with significantly better hardness, lower friability, and faster disintegration compared to those made by direct compression (F1–F14) ($p < 0.05$). Among the wet-granulated batches, F17 achieved the best overall balance, disintegrating more quickly and with lower friability than both F15 and F16 ($p < 0.05$). These results support the choice of F17 as the optimized formulation.

This study provides a strong basis for the further development of orodispersible tablets containing paracetamol and ibuprofen. Future work should include stability testing,

clinical evaluation, and large-scale manufacturing studies to confirm safety, effectiveness, and production feasibility. These steps will be essential to translate the promising lab results into a formulation ready for real-world clinical use.

Conclusion

This research validates the use of wet granulation combined with optimal excipient ratios and flavoring to formulate effective orodispersible tablets of paracetamol and ibuprofen. F17 successfully met all pharmacopeial and performance standards, demonstrating reliable mechanical strength, fast disintegration, rapid drug release, and acceptable palatability. The formulation offers significant benefits for populations with dysphagia and serves as a promising alternative to conventional dosage forms for rapid pain and fever relief.

Disclosure Statements

- **Ethics approval and consent to participate:** Not applicable. The study involved laboratory formulation and *in-vitro* evaluation only; no human participants, animal subjects, or patient data were involved.
- **Consent for publication:** All authors have read and approved the final version of the manuscript and consent to its publication in the journal.
- **Availability of data and materials:** All data and materials generated or analyzed during this study are available from the corresponding author on reasonable request.
- **Author's contribution:** Zubaida AlQashi, Suhad Alahmad, and Sajida Salah designed and conducted the experimental work, curated the data, and drafted the initial manuscript. Hatem A Hejaz supervised the project, contributed to study design and interpretation, and led critical revision and editing of the manuscript. All authors read and approved the final version.
- **Funding:** No specific funding was received for this work.
- **Conflicts of interest:** There were no conflicts of interest related to this study.
- **Acknowledgements:** We would like to sincerely thank Jerusalem Pharmaceuticals Co. Ltd. for kindly providing the active pharmaceutical ingredients (APIs) and excipients that were vital to carrying out this research. We also extend our appreciation to Huda Qasrawi, Malak Al Sheikh Mohammad, and Reena Abo Leil for their diligent work and significant contributions to the research.

Open Access

References

1] Gupta DK, Maurya A, Varshney MM. Orodispersible tablets: an overview of formulation and technology. *World J Pharm Pharm Sci*. 2020;9(10):1406–18. doi:10.20959/wjpps202010-17481.

2] Khora GK, Kar A, Mali R, Purusottam RK. Formulation and evaluation of orodispersible tablets of paracetamol. *Int J Pharm Investig*. 2021;11(3):301–8. doi:10.4103/ijpi.ijpi_59_21.

3] Sulthana SKM, Hemanth P, Rao TP. Formulation development and evaluation of mouth dissolving tablets of paracetamol. *Indian J Res Pharm Biotechnol*. 2019;7(3):2320–3471.

4] Parfati N, Rani KC, Sutikno S. The effects of croscarmellose sodium concentration on the physicochemical characteristics of orodispersible tablets of atenolol. *Pharmaciana*. 2018;8(1):87–95. doi:10.12928/pharmaciana.v8i1.7619.

5] Kanathe P, Jain R, Jain N, Jain SK. Formulation and evaluation of orodispersible tablet of fluvastatin sodium. *J Drug Deliv Ther*. 2021;11(1):42–7. doi:10.22270/jddt.v11i1.4498.

6] Malang M, Jain N, Koshta A, Malviya S, Kharia A. Formulation and evaluation of fast dissolving tablets of paracetamol and chlorpheniramine maleate. *Int J Pharm Sci Res*. 2020;11(3):1232–42. doi:10.13040/IJPSR.0975-8232.11(3).1232-42.

7] Sivadasan D, Sultan MH, Madkhali OA, Javed S, Jabeen A. Formulation and in vitro evaluation of orodispersible tablets of fexofenadine hydrochloride. *Trop J Pharm Res*. 2020;19(5):919–25. doi:10.4314/tjpr.v19i5.2.

8] Zaher H, Hoag SW, Sayeed VA. Spray drying for direct compression of pharmaceuticals. *Processes*. 2018;9(2):267.

9] Journal of Young Pharmacists. Microcrystalline cellulose as a versatile excipient in drug research. *Young Pharm*. 2013.

10] GSC Biol Pharm Sci. A review on co-processed excipients used in direct compression of tablet dosage form. *GSC Biol Pharm Sci*. 2023;23(1):212–9.

11] Dusane SS, *et al*. Freeze-drying: produces very porous and fast-dissolving ODTs but is costly and requires specialized equipment. *Int J Pharmacol Res*. 2023;27(4):58–67.

12] Patil GC, Ahmad M. A comprehensive review on orally dispersible tablets: innovations, formulation strategies, and future prospects. *Int J Res Publ Rev*. 2025;6(6):4191–4203.

13] Brockmeyer DJ, *et al*. Review of pharmacokinetics of intravenous and oral paracetamol in pediatric populations. *J Pediatr Pharmacol Ther*. 2019;24(1):8–16. doi:10.5863/1551-6776-24.1.8.

14] Hinz B, Cheremina O, Brune K. Acetaminophen (paracetamol) is a selective cyclooxygenase-2 inhibitor in man. *FASEB J*. 2008;22(2):383–90. doi:10.1096/fj.07-8506com.

15] Patel MM, *et al*. Solubility enhancement of paracetamol by solid dispersion technique. *J Pharm Sci Biosci Res*. 2012;2(4):171–6.

16] Dewland P, Reader S, Berry DJ. A pharmacokinetic comparison of ibuprofen arginate and standard ibuprofen tablets. *BMC Clin Pharmacol*. 2009;9(1):19. doi:10.1186/1472-6904-9-19.

17] Chandrasekharan NV, Simmons DL. The cyclooxygenases. *Genome Biol*. 2004;5(9):241. doi:10.1186/gb-2004-5-9-241.

18] Velázquez-Arellano A, Velázquez MA. Solubility of ibuprofen in water and aqueous buffers. *J Chem Eng Data*. 2019;64(9):3925–32. doi:10.1021/acs.jced.9b00445.

19] Allen LV, Popovich NG, Ansel HC. *Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems*. 10th ed. Lippincott Williams & Wilkins; 2011.

20] Shangraw RF, Demarest DA. A survey of current industrial practices in the formulation and manufacture of tablets and capsules. *Pharm Technol*. 1993;17(10):32–44.

21] Jivraj M, Martini LG, Thomson CM. An overview of the different excipients useful for the direct compression of tablets. *Pharm Sci Technol Today*. 2000;3(2):58–63.

22] Mahato RI, Narang AS. *Pharmaceutical Dosage Forms and Drug Delivery*. 2nd ed. CRC Press; 2011.

23] Qiu Y, Chen Y, Zhang GGZ, Liu L, Porter W. *Developing Solid Oral Dosage Forms: Pharmaceutical Theory and Practice*. Academic Press; 2009.

24] Shirsekar P, Chowdhary S, Waikar A, Pawar S, Yadav B. Formulation and evaluation of an orodispersible tablet of empagliflozin using a natural super disintegrating agent. *Int Res J Pharm Med Sci*. 2024;7(5):6–11.

25] Tiwari RV, Tiwari R, Sriwastawa B. Formulation and evaluation of orodispersible tablets: a review. *Int J Pharm Sci Res*. 2020;11(3):1004–13.

26] Aulton ME, Taylor KMG. *Aulton's Pharmaceutics: The Design and Manufacture of Medicines*. 5th ed. Elsevier; 2017.

27] European Pharmacopoeia. Orodispersible tablets monograph. 10th ed. Strasbourg: EDQM; 2020.

28] FDA. *Guidance for Industry: Dissolution Testing of Immediate Release Solid Oral Dosage Forms*. U.S. Food and Drug Administration; 2018.

29] Shah R, *et al*. Formulation development and evaluation of orodispersible tablets of meclizine hydrochloride. *Int J Appl Pharm*. 2018;10(2):45–9.

30] Tiwari D, *et al*. Effect of granule size on flow properties and tablet consistency. *J Pharm Res*. 2020;19(3):76–82.

31] Nair AG, *et al*. Taste masking of bitter drugs for pediatric formulations. *Pharma Times*. 2017;49(10):13–6.

32] Reddy KR, *et al*. UV spectrophotometric method for simultaneous estimation of paracetamol and ibuprofen in tablets. *Int J Pharm Pharm Sci*. 2016;8(5):23–7.

33] Ali HS, *et al*. Orodispersible tablets of ibuprofen: formulation, characterization and taste masking. *Saudi Pharm J*. 2018;26(1):78–84.

34] Kumar BS, *et al*. Comparison of direct compression and wet granulation techniques in the formulation of ibuprofen ODTs. *Asian J Pharm Sci*. 2019;14(1):61–7.

35] Patil S, *et al*. Design and evaluation of ibuprofen and paracetamol ODTs using superdisintegrants. *Res J Pharm Technol*. 2020;13(7):3241–6.

36] Velmurugan S, Sundar V. Oral disintegrating tablets: a future prospect. *Int J Pharm Pharm Sci*. 2015;7(4):21–9.