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Original Article

Formulation and *in vitro* evaluation of medicated chocolate of ondansetron for pediatrics

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ABSTRACT

Managing oral drug administration in pediatrics faces significant compliance challenges due to the bitter taste of active pharmaceutical ingredients like ondansetron, which often leads to therapy rejection. This study designed, formulated, and evaluated a palatable, chocolate-based immediate-release oral delivery system to effectively mask drug bitterness and enhance patient adherence. Five distinct formulations (F1–F5) of ondansetron medicated chocolate were prepared by compounding uniform drug amounts (4 mg) with cocoa powder, milk powder, and sucrose syrup into a melted base containing varying concentrations of cocoa butter and lecithin powder. The resulting prepared formulations were thoroughly evaluated for physical appearance, weight variation, hardness, moisture content, disintegration time, and in-vitro drug release profiles. All batches exhibited a uniform dark brown color, smooth texture, pleasant odor, and zero blooming. The moisture content remained exceptionally low (<0.5%) across all formulations. Formulation F2, utilizing 0.47% moisture as a natural plasticizer, demonstrated superior quality with outstanding weight uniformity (0.31% RSD) and high mechanical strength (12.0 Kg/cm² hardness). Conversely, F3 failed standard weight variation criteria (9.00% RSD) due to poor pre-compression powder flowability. All formulations successfully passed immediate-release standards, completely disintegrating in under 6 minutes. Furthermore, in-vitro dissolution testing confirmed highly efficient profiles, with all five batches achieving 95% to 100% total drug release within 15 minutes. Formulation F2 was identified as the optimal candidate, successfully balancing excellent physical manufacturability, robust structural integrity for commercial shipping, and a rapid immediate drug release profile. Ultimately, medicated chocolate represents a highly promising, child-friendly delivery vehicle for masking bitter pediatric medications.

Keywords: Ondansetron, Chocolate, Pediatrics, Immediate-release, Dissolution

Introduction

The oral route is the most favored method for administering medication due to its versatility in dosage form design and high patient compliance. This popularity stems from its ease of administration, precise dosing, cost-effective production, and improved product shelf life [1]. Common oral forms include tablets, capsules, and liquids. Solid formulations like tablets are particularly economical as they do not require sterile production conditions [2]. Chewable tablets represent an advantageous modification designed to dissolve directly in the mouth upon consumption. They offer significant benefits over traditional tablets in manufacturing efficiency, precise dosing, portability, and shelf stability, while facilitating easier swallowing by breaking down into particles [3]. Because they require minimal or no water, chewable tablets are highly convenient for busy, traveling, or bedridden individuals, making them ideal for

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children and the elderly. Sweeteners play a crucial role in ensuring a pleasant taste for these formulations. Various natural, semi-natural, and chemical sweeteners are utilized, with sucrose frequently selected due to its quick absorption and energy-providing properties [4]. Despite these delivery advancements, pediatric patients are traditionally treated with off-label adult medications or extemporaneously compounded formulations, both of which pose concerns regarding safety and efficacy. Off-label drug use is especially challenging in neonates, children under two years old, and those with rare, chronic, or acute illnesses [5]. The Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA) were established to promote pediatric drug research, expand clinical testing, and ensure appropriate formulations reach the market. Nevertheless, children may reject medication regardless of tablet size if the flavor is unpleasant; for instance, the antiemetic drug ondansetron is characteristically bitter [6]. Vomiting, or emesis, is the forceful expulsion of stomach contents through the mouth, occurring as a complex reflex action involving multiple body systems. Its causes are multifaceted, relying on neural transmission pathways, neurotransmitters, and specialized receptors. The vomiting center is situated in the medulla oblongata, which includes the chemoreceptor trigger zone (CTZ) in the area postrema on the floor of the fourth ventricle and the nucleus tractus solitarius (NTS) in the lower brainstem [7]. The primary neural pathways stimulate the CTZ under the control of the vagus nerve. Lacking a complete blood-brain barrier, the area postrema receives stimuli from various chemicals, drugs, or metabolites in the blood and cerebrospinal fluid, triggering impulses to the NTS. Emesis results from continuous interaction between the gastrointestinal tract, enteric, central, and autonomic nervous systems [8]. Ondansetron is a commonly prescribed 5-HT3 receptor antagonist that suppresses these pathways centrally in the area postrema and peripherally on vagus nerve terminals. However, administering such bitter drugs to children is difficult and frequently causes medication non-adherence [9]. To overcome this, medicated chocolate has emerged as an accepted oral delivery system for pediatric cohorts, improving compliance by leveraging the unique taste, texture, and palatability of chocolate. Because numerous active ingredients possess an unpleasant taste, taste-masking using a chocolate base provides an ideal pediatric option [10]. Structurally, chocolate serves as an outstanding carrier; its lipid base (combining cocoa powder, cocoa butter, and sugar) forms a water-resistant medium that exhibits resistance to microbial growth and hydrolysis [11]. Furthermore, chocolate is a sophisticated, versatile food rich in polyphenols, saturated fats, aliphatic alcohols, and methylxanthines like caffeine and theobromine. It also contains phenylethylamine, a chemical linked to sensations of happiness and well-being. Since sweet is one of the most enjoyable fundamental flavors, incorporating medications into chocolate successfully masks bitterness. Consequently, this research aimed to develop and assess a novel chocolate-based oral delivery system for ondansetron, designed specifically to address the challenges of taste masking and ease of administration in pediatric patients [12].

Materials and Methods

Ondansetron, Cocoa Powder, Cocoa Butter, Lecithin Powder, Sucrose, Milk Powder, Sodium Benzoate, Chocolate Flavor

Method of preparation

All the ingredients were weighed accurately in one beaker. Sugar and water were taken, and sugar syrup was prepared on a heating mantle as shown in **Table 1**. Cocoa butter was heated in a separate beaker, then the powder mixture was added to the melted cocoa base and thoroughly combined to get a fine consistency. Further, soya lecithin as an emulsifier was added and mixed. Finally, Ondansetron was added to the prepared chocolate base. The flavoring agent was added before being set in molds. Then, the prepared chocolate containing the drug was poured into molds and kept in the freezer to set overnight, as shown in **Figure 1**.

Table 1. Formulations of ondansetron medicated chocolate.

Ingredient (mg)	F1	F2	F3	F4	F5
Ondansetron	4	4	4	4	4
Cocoa powder	400	400	400	400	400
Cocoa butter	340	350	360	370	380
Lecithin	60	50	40	30	20
Sucrose	85	85	85	85	85
Milk powder	100	100	100	100	100
Sodium benzoate	20	20	20	20	20
Chocolate flavour	0.001	0.001	0.001	0.001	0.001

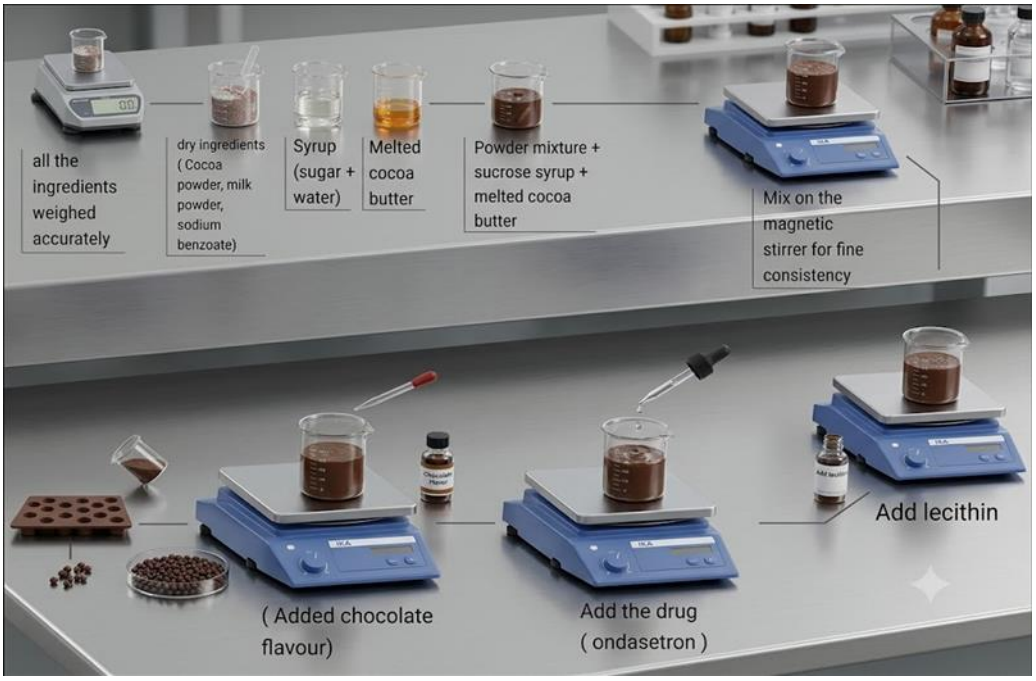

Figure 1. Illustration of the steps of the method of preparation.

In-vitro evaluation tests of medicated chocolate

General appearance

Tablets are assessed visually against color standards to detect color variance or mottling. Inspection ensures the surface is smooth and free from structural compression defects such as capping, lamination, chipping, picking, sticking, or cracking [13-15]. Embossed, debossed, or printed features (such as manufacturer logos, dose indicators, or score lines) are evaluated for legibility and sharpness. Odor and taste profiles are checked to verify palatability and detect potential chemical degradation [16].

Weight variation test

Select 20 tablets at random from a batch, weigh each tablet individually on an analytical balance, and compute the overall average mass [17-19].

Acceptance criteria (IP / BP / Ph. Eur. 2.9.5)

- ≤ 84 mg average weight: Maximum allowed deviation is $\pm 10\%$
- 84 mg to 250 mg average weight: Maximum allowed deviation is $\pm 7.5\%$
- > 250 mg average weight: Maximum allowed deviation is $\pm 5\%$

Acceptance criteria (USP standard)

- ≤ 130 mg average weight: Maximum allowed deviation is $\pm 10\%$
- 130 mg to 324 mg average weight: Maximum allowed deviation is $\pm 7.5\%$
- > 324 mg average weight: Maximum allowed deviation is $\pm 5\%$

The batch passes if no more than **2** of the 20 individual tablet weights exceed the allowed percentage deviation, and **zero** tablets deviate by more than double that percentage limit [20].

Hardness test

A sample set (typically 10 tablets) is tested individually after removing surface dust. The tablet is placed between two jaws (Monsanto tester) and compressive force is applied. Breaking force is expressed in Newtons (N) or kiloponds (kp or kgf). Conventional immediate-release compressed tablets generally target a hardness range of $4–10$ kp ($40–100$ N). Modified-release tablets often require higher strength (> 10 kp), whereas chewable or orally disintegrating tablets (ODTs) are engineered with lower force targets to facilitate easy mastication or rapid disintegration [21].

Friability test

For tablets with a unit mass ≤ 650 mg, a sample corresponding as closely as possible to 6.5 gis selected; for tablets with a unit mass > 650 mg, a sample of 10 whole tablets is used. The tablets are carefully de-dusted to remove loose surface powder and weighed on an analytical balance to determine initial mass (W_1). The weighed sample is tumbling-tested in the drum for

100 cycles (Roche friabilator). Tablets are removed, freed of any generated loose dust, and weighed to obtain final mass (W_2).

$$\text{Friability (\%)} = \left(\frac{W_1 - W_2}{W_1}\right) \times 100 \quad (1)$$

A maximum total weight loss of $\leq 1.0\%$ is considered acceptable across pharmacopeial guidelines [22-24]. The presence of visibly cracked, capped, cleaved, or broken tablets after tumbling constitutes an automatic failure, irrespective of percentage mass loss [25].

Moisture content

Pulverized tablet samples are heated in a hot-air oven at a designated temperature (typically 105 °C) until reaching a constant weight. Loss on Drying (LOD) measures total volatile mass loss, including surface moisture and trace organic solvents [26].

Disintegration test

A basket-rack assembly holding 6 open-ended cylindrical tubes (Erweka Disintegrator) fitted with a 10-mesh woven stainless steel screen (1.8–2.2 mm aperture) at the bottom. Purified water, simulated gastric fluid (0.1 N HCl), or simulated intestinal fluid (pH 6.8 phosphate buffer), as specified by the monograph. Maintained at 37 °C ± 2 °C to mimic physiological conditions. Vertical raising and lowering at a rate of 29 to 32 cycles per minute through a stroke distance of 50 to 60 mm (55 ± 2 mm) [27].

In-vitro drug release test

The test was performed using the Erewka dissolution apparatus, which is the most common standard for immediate-release and extended-release tablets. 900 mL of 0.1 N HCl (pH 1.2) was used as the dissolution medium with an agitation speed (50–100 rpm) at 37 ± 0.5°C. Analytical assay by UV-Vis Spectrophotometry [27].

Results and Discussion

General appearance

The general appearance of medicated chocolates of Ondansetron was studied, and the results are shown in **Table 2**. The evaluation of the general appearance (color, odor, taste, and texture) across all five formulations (F1 to F5) demonstrates complete uniformity in their macroscopic and organoleptic properties. All formulations achieved a semi-sweet taste and a pleasant odor. This is a major milestone for the study because the active pharmaceutical ingredient, ondansetron, is characteristically highly bitter. The combination of sucrose, milk powder, cocoa powder, and chocolate flavor successfully masked this bitterness, which is critical for ensuring patient compliance in pediatrics. Every batch maintained a smooth texture. A smooth texture indicates that the solid ingredients (cocoa powder, milk powder, and sucrose) were successfully reduced in particle size and uniformly dispersed within the melted cocoa butter matrix without forming gritty aggregates. It also proves that the mixing phase on the magnetic stirrer achieved an optimal, fine consistency. The dark brown color was perfectly uniform across all batches. This confirms that the cocoa powder was evenly distributed throughout the chocolate base and that no premature phase separation or visual irregularities occurred during the overnight freezing and setting process [9].

In this study, the concentrations of cocoa butter (varying from 340g to 380g) and the emulsifier lecithin (varying from 60g to 20g) were adjusted across the formulations. These results prove that altering the lipid-to-emulsifier ratio within this specific range does not negatively impact the outward aesthetic, mouthfeel, or palatability of the medicated chocolate. From a sensory and patient-acceptability standpoint, all five formulations are equally excellent. Because children judge oral medications primarily by flavor and texture, these results confirm that the chocolate matrix successfully transforms a bitter antiemetic into a highly palatable, smooth, and child-friendly dosage form [12].

Table 2. General appearance of formulation F1- F5.

Formulation	Color	Odor	Taste	Texture
F1	Dark brown	Pleasant	Semi-sweet	Smooth
F2	Dark brown	Pleasant	Semi-sweet	Smooth
F3	Dark brown	Pleasant	Semi-sweet	Smooth
F4	Dark brown	Pleasant	Semi-sweet	Smooth
F5	Dark brown	Pleasant	Semi-sweet	Smooth

Weight variation test

The weight variation of the medicated chocolates was studied, and the results are shown in **Table 3**. Formulation F2 is the most consistent by a significant margin. With an incredibly low SD of 0.0052 g and an RSD of just 0.31%, the manufacturing process for F2 is highly reproducible. F4 is also exceptionally stable (1.00% RSD). The powder or granular blends for F2 and F4 likely possess excellent flowability, ensuring consistent and uniform filling of the die cavity during compression. The particle size distribution, glidant, and lubricant concentrations in these batches are optimal. F1 (3.54% RSD) and F5 (4.16% RSD) show moderate variability. They may require minor optimization, such as slightly increasing glidant concentration or adjusting the granulation process to reduce fine powder. Formulation F3 shows a very high SD (0.1313 g), resulting in an average variability of 9.00%. Because this average deviation is so high, it is highly probable that individual tablets in this batch exceed the 10% maximum deviation limit, meaning F3 would fail standard pharmacopeial weight variation tests. F3 is suffering from significant powder flow issues. This erratic die filling is

typically caused by poor granulation, inadequate lubrication or glidant concentration, powder segregation in the hopper during the compression process, and high moisture content causing powder to stick to the punch faces or die walls [28]. F2 is the most robust formulation regarding weight uniformity.

Hardness test

The hardness of the formulations was studied, and the results are shown in **Table 3**. Keeping in mind the large size of tablets, the required hardness will naturally be higher than that of a standard small tablet to prevent breakage. Formulations F2 (12.0), F5 (10.5), and F3 (10.0) exhibit high mechanical strength. Pros: Given the large mass of these tablets, this high hardness is excellent for structural integrity. These tablets will easily survive the rigors of coating, blister-packing, bottling, and shipping without chipping, capping, or breaking. Cons: The primary risk with hardness values in this upper range is delayed disintegration and dissolution. High hardness usually means lower tablet porosity, making it harder for gastrointestinal fluids to penetrate the tablet matrix [29]. F2 has the highest hardness (12.0 Kg/cm²) and previously showed the best weight uniformity. This suggests it likely underwent a high compression force or contains a highly effective binder, resulting in a very dense, robust tablet. F1 (6.0) and F4 (7.5) sit in a more moderate range. For typical tablets, 4.0 to 8.0 Kg/cm² is the sweet spot for immediate-release profiles.

Friability test

F1 high risk of failure (>1% Weight Loss) as shown in **Table 3**, F1 exhibits the lowest hardness in the study at 6.0 Kg/cm^2 While a lower hardness allows F1 to achieve the fastest disintegration time (2.5 minutes), it severely compromises the tablet's structural integrity. For a large 1.660g tablet, this weak compaction force means the chocolate matrix is highly fragile. Under the continuous tumbling of a friability tester, F1 is highly likely to chip, cap, or shed edges, resulting in a failing weight loss exceeding 1%. F2 excellent pass (Very Low % Weight Loss), F2 has the most resilient friability profile. This batch achieved the highest hardness (12.0 Kg/cm^2) coupled with an exceptional weight uniformity of 0.31% RSD. This superior strength is driven by its 0.47% moisture content, which acts as a natural plasticizer to enhance particle-to-particle binding during formulation. F2 creates a highly dense, robust core that will easily resist friction and survive packaging or shipping without any visual or structural degradation. F3 passed with inconsistency; F3 possesses a solid average hardness of 10.0 Kg/cm^2, which should theoretically protect it from crumbling. The core issue with F3 is its severe pre-compression powder flow failure, yielding a highly erratic weight variation of 9.00% RSD. Because the individual tablet masses fluctuate wildly due to uneven die filling, the mechanical compaction across the batch is completely non-uniform. During a friability test, lighter or poorly compressed individual chocolates in this batch are highly susceptible to sudden capping or splitting, making the overall friability data highly unreliable. F4 balanced and successful pass (<1% Weight Loss). F4 strikes an outstanding compromise between mechanical durability and rapid drug delivery. With a moderate hardness of 7.5 Kg/cm^2 and a highly stable weight uniformity (1.00% RSD), the internal matrix contains enough porous void spaces to dissolve quickly but maintains enough structural cohesion to safely pass the 1% friability weight loss threshold. F5 dry but robust pass (<1% Weight Loss), F5 presents an incredibly dry matrix with a moisture content of just 0.17%. Normally, extreme dryness introduces static charge and causes tablets to split apart (lamination) during friability testing due to a lack of moisture-based binding [30].

Moisture content

Overall, all formulations have a moisture content of less than 0.5%, as shown in **Table 3**. Formulation F2 has the highest moisture content in the batch, yet it is still well under the typical 2-5% limit for most tablets. This slightly higher moisture level perfectly explains why F2 achieved the highest hardness (12.0 Kg/cm²) and the best weight uniformity (0.31% RSD). The trace amount of water acted as a natural plasticizer. It helped the particles bind together under compression (yielding higher hardness) and likely reduced static charge in the powder blend, allowing for smooth, uniform die filling (yielding excellent weight uniformity) [31]. If the Active Pharmaceutical Ingredient (API) is highly sensitive to moisture (prone to hydrolysis), these formulations will offer outstanding long-term chemical stability and extended shelf life. Extreme dryness can sometimes induce static electricity during the powder flow phase, which can cause erratic die filling. It can also lead to "capping" or lamination, where the tablet splits apart after compression because it lacks the binding property of water [32]. However, since F5 maintained a high hardness of 10.5 Kg/cm², your binder excipients are clearly strong enough to compensate for the lack of moisture. F3 sits near the average for moisture content. Because its moisture level is normal relative to the batch, we can rule out excessive moisture (which causes sticking/picking) or extreme dryness (which causes static/segregation) as the primary cause of F3's terrible weight variation (9.00% RSD). The flow failure in F3 is almost certainly due to particle size distribution or insufficient glidant, rather than moisture. The moisture content for all formulations is excellent for maximizing shelf life and API stability. Formulation F2 demonstrates that a very slight increase in moisture (closer to 0.5%) optimizes the mechanical strength and uniformity of this specific blend without threatening stability.

Disintegration test

All of the formulations easily pass this regulatory requirement, as shown in **Table 3**. Given that the tablets are quite large (averaging ~1.5 g), achieving complete disintegration in 6 minutes or less across the board is an excellent result. Because F1 and F4 have lower hardness levels (6.0 and 7.5 Kg/cm²), their

internal matrices are much more porous. High porosity allows the testing medium (water or simulated gastric fluid) to rapidly penetrate the tablet via capillary action, swelling the disintegrant particles and bursting the tablet apart quickly [33]. F4 continues to look like a fantastic formulation for an immediate-release drug. It has excellent weight uniformity, moderate hardness, and rapid disintegration. While F1 is the fastest, its low hardness means it still carries a high risk of failing friability testing. Formulations F2 and F5 had the highest hardness values (12.0 and 10.5 Kg/cm²). Consequently, they take the longest to disintegrate. The higher compression forces used (or the stronger binders) reduced the void spaces inside the tablets [34]. Because the tablet weights are wildly inconsistent, it is highly likely that individual disintegration times within batch F3 will also be wildly inconsistent.

Table 3. In-vitro evaluation and quality control parameters of tablet formulations.

Formula Code	Weight Variation (g) Mean ± SD	Hardness (Kg/cm²)	Friability (%)	% Moisture Content	Disintegration time (min.)
F1	1.660 ± 0.0588	6.0	High Risk of Failure (>1% weight loss)	0.26	2.5
F2	1.678 ± 0.0052	12.0	Excellent Pass (Very low % weight loss)	0.47	6.0
F3	1.459 ± 0.1313	10.0	Pass (Inconsistent)	0.36	4.5
F4	1.545 ± 0.0155	7.5	Pass (<1% weight loss)	0.28	3.5
F5	1.523 ± 0.0633	10.5	Pass (<1% weight loss)	0.17	5.0

Drug release test

All five formulations achieve nearly complete drug release (95% to 100%) within just 15 minutes, as shown in **Figure 2**. This definitively confirms the immediate release (IR) dosage form obtained. The release profiles in the graph align perfectly with the hardness and disintegration data. F1 is the fastest, releasing nearly 90% of its drug payload by the 5-minute mark and hitting 100% by 10 minutes. F4 follows closely behind, releasing about 80% in 5 minutes. F1 and F4 had the lowest hardness (6.0 and 7.5 Kg/cm², respectively) and the fastest disintegration times (2.5 and 3.5 minutes). Because their tablet matrices are softer and more porous, the dissolution medium rapidly breaks them apart and dissolves the active ingredient almost instantly [35]. F2 and F5 represent the lower curve of the graph. At the 5-minute mark, F2 has released about 45% of the drug, and F5 is at roughly 50%. By 15 minutes, they have both reached or exceeded 95% release. F2 and F5 had the highest hardness (12.0 and 10.5 Kg/cm²) and the longest disintegration times (6.0 and 5.0 minutes). Because these tablets are denser and more tightly compacted, it takes slightly longer for the fluid to penetrate, break down the tablet, and dissolve the drug. F3 sits squarely in the middle of the pack, reaching about 60% release at 5 minutes and nearly 100% by 15 minutes. This aligns with its moderate-to-high hardness (10.0 Kg/cm²) and 4.5-minute disintegration time. All five formulations display an excellent immediate-release profile. Even the "slowest" formulation (F2) releases approximately 95% of its active ingredient within 15 minutes, which is an outstanding result for an IR tablet. F2 remains the superior formulation. While F1 and F4 dissolve slightly faster, the speed difference (a few minutes) is negligible in a physiological context once ingested. F2 offers the distinct advantage of superior mechanical strength (12.0 Kg/cm² hardness) and excellent weight uniformity (0.31% RSD), meaning it will be robust during manufacturing and shipping while still delivering the drug rapidly and reliably to the patient.

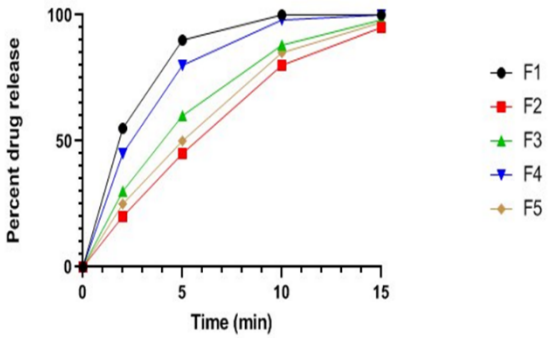

Figure 2. In vitro release profile of formulation F1-F5.

Conclusion

This research successfully designed, formulated, and evaluated a palatable chocolate-based immediate-release oral delivery system for ondansetron to overcome pediatric compliance challenges associated with bitter medications. Based on the experimental findings, all five formulations (F1–F5) achieved complete sensory uniformity, exhibiting a uniform dark brown color, pleasant odor, smooth texture, and semi-sweet taste. The moisture content across all formulations was exceptionally low (<0.5%), which is excellent for maximizing shelf life and active pharmaceutical ingredient (API) stability. F2 was identified as the optimal candidate for this pediatric delivery system, successfully balancing excellent physical manufacturability, robust structural core integrity, and a rapid drug release profile. Ultimately, incorporating medications into a chocolate base represents a highly promising and viable child-friendly strategy for masking bitter pharmaceutical ingredients and improving pediatric adherence.

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References

1. Bácskay I, Arany P, Fehér P, Józsa L, Vasvári G, Nemes D, et al. Bioavailability enhancement and formulation technologies of oral mucosal dosage forms: A review. Pharmaceutics. 2025;17(2):148. doi:10.3390/pharmaceutics17020148
2. Alqahtani MS, Kazi M, Alsenaidy MA, Ahmad MZ. Advances in oral drug delivery. Front Pharmacol. 2021;12:618411. doi:10.3389/fphar.2021.618411
3. Shingade SS, Mandhare TA, Kashid PS, Otari K. Chewable tablets: A comprehensive review. Asian J Pharm Res Dev. 2024;12(4):119-25.
4. Lopez FL, Ernest TB, Tuleu C, Gul MO. Formulation approaches to pediatric oral drug delivery: benefits and limitations of current platforms. Expert Opin Drug Deliv. 2015;12(11):1727-40.
5. AlAzmi A, Alasmari Z, Yousef C, Alenazi A, AlOtaibi M, AlSaedi H, et al. Off-label drug use in pediatric outpatient care: A multi-center observational study. Hosp Pharm. 2021;56(6):690-6. doi:10.1177/0018578720942226
6. Meyers RS. The past, present, and future of oral dosage forms for children. J Pediatr Pharmacol Ther. 2024;29(1):22-31.
7. Zhong W, Shahbaz O, Teskey G, Beever A, Kachour N, Venketaraman V, et al. Mechanisms of nausea and vomiting: current knowledge and recent advances in intracellular emetic signaling systems. Int J Mol Sci. 2021;22(11):5797. doi:10.3390/ijms22115797
8. van de Lisdonk D, Li B. The area postrema: A critical mediator of brain–body interactions. Genes Dev. 2024;38(17-20):793-7.
9. Khan S, Kataria P, Nakhat P, Yeole P. Taste masking of ondansetron hydrochloride by polymer carrier system and formulation of rapid-disintegrating tablets. AAPS PharmSciTech. 2007;8(2).
10. Al-Qinna N, Chachlioutaki K, Alhnan MA. In vitro and in vivo evaluation of dark chocolate as age-appropriate oral matrix. Eur J Pharm Sci. 2024;193:106646.
11. Yoo O, Tang E, Hossain ML, von Ungern-Sternberg BS, Sommerfield D, Heath C, et al. The development of a chocolate-based chewable tablet of prednisolone—enhancing the palatability of steroids for pediatric use. Pharmaceutics. 2024;16(8):1099.
12. Qureshi TY, Abbasi A, Padme K, Sawkare K. Novel approach to pediatric anti-nausea: formulating & evaluating ondansetron-infused chocolate. Int J Pharm Sci Med. 2024;9(9):29-42.
13. Alves R, Costa B, Martins H, Faria N. Federated learning framework for adverse drug reaction prediction from multi-institutional health records. Pharmacophore. 2026;17(1):1-11. doi:10.51847/f2RnAaSwj2
14. Schneider N, Frank T, Kramer J. Experiences of advance care planning among patients, family caregivers, and healthcare providers: A qualitative study. J Integr Nurs Palliat Care. 2026;7(1):16-29. doi:10.51847/Zv5HsDXVw5
15. Phan TAD, Tran HTT, Nguyen TTM, Nguyen TPT, Tran MD. Determinants influencing accountant staff's intention to pursue international professional accountant certifications: the case of Vietnam. J Organ Behav Res. 2025;10(2):83-99. doi:10.51847/BApjo0hA37
16. Allen LV, Ansel HC. Ansel's pharmaceutical dosage forms and drug delivery systems. 10th ed. Lippincott Williams & Wilkins; 2014.
17. Bukhary DM. Evaluation of complete denture impressions: implementing a numerical grading method. Ann Dent Spec. 2024;12(1):7-13. doi:10.51847/yczfxU5UcT
18. Al-Razem F, Shehadeh Y, Dandees D, Al-Kubaje S, Abo-Shakhdam S, Adm M. Association between Toll-like receptor 4 genetic variants and hyperlipidemia risk in Palestinian adults: A case-control study. J Biochem Technol. 2026;17(3):21-9. doi:10.51847/065SKANhhA
19. Obisesan OO, Egbetokun OA. Climate change impacts, food security, intra-Africa trade and sustainable land governance on food systems in Africa. World J Environ Biosci. 2024;13(3):39-50. doi:10.51847/ZFZDDD5lNJ
20. Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. 3rd ed. Lea & Febiger; 1986.
21. Aulton ME, Taylor K. Aulton's pharmaceutics: the design and manufacture of medicines. 5th ed. Elsevier; 2018.
22. Weber L, Janssen S, Richter J, Fischer E. Resilient herd health requires managing the next failure before it appears: A dynamic veterinary architecture integrating biosecurity, population immunity, pathogen pressure, production stress, detection capacity, response, and recovery. Int J Vet Res Allied Sci. 2026;6(1):55-65. doi:10.51847/fCTkjttmkQ
23. Alvarez JU, Clark J, Ferrari L, Weber PZ, Moore AI, Silva DK. Mechanisms of resistance to beta-cyfluthrin in the cigarette beetle, Lasioderma serricorne, and the effectiveness of imidacloprid space sprays. Entomol Res Lett. 2025;5(1):1-11. doi:10.51847/BZZSnkes0yq0
24. Petrova N, Dimitrov I, Stoyanova E. The interplay of spiritual insight, self-actualization, and educational excellence. J Appl Organ Syst Behav. 2025;5(2):22-4.
25. European Pharmacopoeia. Ph. Eur. 2.9.7: friability of uncoated tablets. European Directorate for the Quality of Medicines & HealthCare; 2023.
26. European Pharmacopoeia Commission. European Pharmacopoeia (Ph. Eur.): chapter 2.2.32 (loss on drying) and chapter 2.2.13 (water: micro-determination). Council of Europe; 2023.

27. European Pharmacopoeia. European Pharmacopoeia (Ph. Eur.). 11th ed. Council of Europe; 2022.
28. Morin G, Briens L. The effect of lubricants on powder flowability for pharmaceutical application. AAPS PharmSciTech. 2013;14(3):1158-68.
29. Donea C, Popa L, Lupuliasa D. Determination of the impact of the compression force by evaluating the mechanical and release properties of mesalazine tablets. Farmacia. 2022;70(5):964-75.
30. Suksawat T, Brniak W, Łyszczarz E, Wesoły M, Ciosek-Skibińska P, Mendyk A. Orodispersible dosage forms with Rhinacanthin-rich extract as a convenient formulation dedicated to pediatric patients. Pharmaceuticals (Basel). 2024;17(8):994. doi:10.3390/ph17080994
31. Sandler N, Reiche K, Heinämäki J, Yliruusi J. Effect of moisture on powder flow properties of theophylline. Pharmaceutics. 2010;2(3):275-90.
32. Suhag R, Kellil A, Razem M. Factors influencing food powder flowability. Powders. 2024;3(1):65-76.
33. Markl D, Zeitler JA. A review of disintegration mechanisms and measurement techniques. Pharm Res. 2017;34(5):890-917.
34. Pabari RM, Ramtoola Z. Effect of a disintegration mechanism on wetting, water absorption, and disintegration time of orodispersible tablets. J Young Pharm. 2012;4(3):157-63.
35. Costa P, Sousa Lobo JM. Modeling and comparison of dissolution profiles. Eur J Pharm Sci. 2001;13(2):123-33.