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Formulation and Evaluation of Mouth Dissolving Tablets of Olmesartan Medoxomil: A Quality by Design Approach for Enhanced Antihypertensive Therapy

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ABSTRACT:
Hypertension affects approximately 1.4 billion people worldwide, representing a significant global health burden. Patient compliance with conventional oral antihypertensive medications remains suboptimal, particularly among elderly and pediatric populations who experience difficulty swallowing conventional tablets. This study aimed to develop and evaluate mouth dissolving tablets (MDTs) of olmesartan medoxomil, a potent angiotensin II receptor blocker, to enhance patient compliance and ensure rapid onset of action. Mouth dissolving tablets were formulated using direct compression method with varying proportions of superdisintegrants (sodium starch glycolate and crospovidone). A 4^2 factorial design was employed to optimize the formulation. Preformulation studies including drug-excipient compatibility (FTIR and DSC), powder flow properties, and micromeritics were conducted. The optimized formulations were evaluated for physical parameters (weight variation, hardness, friability, thickness), functional parameters (disintegration time, wetting time, water absorption ratio), and in vitro drug release studies. The optimized formulation (Batch F9) containing 20 mg olmesartan medoxomil, 10.5 mg sodium starch glycolate, 10.5 mg crospovidone, 210 mg microcrystalline cellulose, and 45 mg mannitol demonstrated superior performance. The disintegration time was 13 seconds, wetting time was 28 seconds, and the in vitro drug release reached 97.06% within 30 minutes. All formulations passed pharmacopoeial standards for weight variation (<5%), hardness (4 kg/cm²), and friability (<1%). Drug content uniformity was 99%, and stability studies under accelerated conditions confirmed formulation integrity. The developed mouth dissolving tablets of olmesartan medoxomil represent an effective therapeutic alternative for hypertensive patients, offering rapid disintegration, enhanced bioavailability potential, and improved patient

compliance. The factorial design approach successfully optimized the formulation with minimal experimental runs..

INTRODUCTION:

Hypertension represents one of the most significant global health challenges of the 21st century, affecting approximately 1.4 billion individuals worldwide as of 2024 WHO1. Despite the availability of effective pharmacological interventions, fewer than one in five affected individuals achieve adequate blood pressure control through medication or lifestyle modifications. The disparity in treatment outcomes is particularly pronounced in low- and middle-income countries, where only 28% of essential antihypertensive medications are readily available in primary healthcare facilities, compared to 93% in high-income nations WHO1.

The prevalence of hypertension among adults is higher in low- and middle-income countries (31.5%, affecting 1.04 billion people) than in high-income countries (28.5%, affecting 349 million people) PMC2. This epidemiological pattern underscores the urgent need for innovative pharmaceutical formulations that address not only therapeutic efficacy but also patient compliance, particularly in resource-limited settings where healthcare infrastructure may be inadequate.

Patient adherence to antihypertensive therapy remains a critical barrier to achieving optimal clinical outcomes. Studies indicate that 40%–50% of patients discontinue their antihypertensive medications within six months of initiation, with swallowing difficulties representing a significant contributing factor, especially among geriatric and pediatric populations Wiley Online Library3. The challenges associated with conventional solid oral dosage forms particularly tablets and capsules create substantial barriers to effective long-term hypertension management in vulnerable patient populations.

1.1 Mouth Dissolving Tablets: Therapeutic Innovation

Mouth dissolving tablets (MDTs), also known as orally disintegrating tablets (ODTs) or fast-dissolving tablets, represent a significant advancement in oral drug delivery technology. These solid unit dosage forms are designed to disintegrate or dissolve rapidly in the oral cavity within 30 seconds without the need for water or chewing FDA4. The United States Food and Drug Administration (FDA) defines ODTs as solid oral preparations that disintegrate rapidly in the oral cavity, with an in vitro disintegration time of approximately 30 seconds or less FDA4.

The therapeutic advantages of MDTs extend beyond mere convenience. By facilitating rapid disintegration in the oral cavity, these formulations enable pre-gastric drug absorption through the buccal and sublingual mucosa, potentially bypassing first-pass hepatic metabolism and enhancing bioavailability for certain drug substances Walsh Medical Media5. This characteristic is particularly relevant for antihypertensive agents, where rapid onset of action may be clinically beneficial in managing hypertensive crises or improving patient compliance through simplified administration.

1.2 Olmesartan Medoxomil: Pharmacological Profile

Olmesartan medoxomil is a selective angiotensin II type 1 (AT1) receptor blocker (ARB) widely prescribed for the management of hypertension and heart failure. As a prodrug, olmesartan medoxomil undergoes rapid esterase-mediated hydrolysis in the gastrointestinal tract to release the active moiety, olmesartan DrugBank6. The absolute bioavailability of olmesartan from olmesartan medoxomil tablets is approximately 28.6%, with the drug exhibiting dose-proportional pharmacokinetics PubMed7.

Pharmacologically, olmesartan medoxomil demonstrates high selectivity for AT1 receptors, effectively antagonizing the vasoconstrictive and aldosterone-secreting effects of angiotensin II. The drug reaches steady-state concentrations within 3–5 days of once-daily dosing, with a bioavailability of approximately 26% Journal of the Association of Physicians of India8. As a BCS Class II compound (low solubility, high permeability), olmesartan medoxomil presents formulation challenges that may be addressed through optimized mouth dissolving tablet technologies.

1.3 Rationale and Objectives

The development of mouth dissolving tablets of olmesartan medoxomil addresses multiple unmet needs in antihypertensive therapy:

1. **Enhanced Patient Compliance:** By eliminating the need for water and swallowing, MDTs improve

medication adherence among elderly patients with dysphagia and pediatric populations who resist conventional tablets ScienceDirect9.

2. **Rapid Onset of Action:** The buccal absorption pathway may facilitate earlier therapeutic effects, potentially beneficial in hypertensive emergencies.
3. **Improved Bioavailability:** Pre-gastric absorption may reduce first-pass metabolism, though this is formulation-dependent.
4. **Convenient Administration:** The waterless administration enables medication intake in various settings, supporting consistent dosing.

The present study was designed to formulate and evaluate mouth dissolving tablets of olmesartan medoxomil using a systematic Quality by Design (QbD) approach. The specific objectives included:

- Development of optimized formulations using direct compression with superdisintegrants
- Evaluation of physicochemical compatibility between drug and excipients
- Assessment of powder flow and compression characteristics
- Optimization of disintegration and dissolution parameters
- Establishment of quality control specifications for the developed formulation

2. Literature Review

2.1 Evolution of Orally Disintegrating Tablet Technology

The development of orally disintegrating tablets represents a significant evolution in pharmaceutical dosage form design, emerging from the convergence of patient-centric formulation science and advanced manufacturing technologies. The conceptual foundation for rapid-disintegration oral dosage forms was established in the late 20th century, with the first commercially available ODT products entering the market in the 1990s Journal of Natural Science, Biology and Medicine10.

Contemporary ODT technologies encompass diverse manufacturing approaches, including lyophilization (freeze-drying), molding, spray-drying, sublimation, and direct compression methods PMC11. Each technique presents distinct advantages and limitations regarding manufacturing complexity, cost-effectiveness, and product performance characteristics. Among these, direct compression has emerged as the most straightforward and economically viable approach for large-scale ODT production, particularly when incorporating superdisintegrants to achieve the requisite rapid disintegration 12.

The technological sophistication of ODTs has advanced considerably, with numerous patented technologies now commercially available. These include Zydis (lyophilized wafers), Orasolv (compressed tablets with taste-masking), Wowtab (compression-molded tablets), Fashtab (directly compressed tablets), and Oraquick (rapidly dissolving tablets) PMC11. These proprietary platforms demonstrate the industrial scalability and commercial viability of advanced ODT technologies.

Superdisintegrants: Mechanisms and Applications:

The functionality of mouth dissolving tablets depends critically on the incorporation of superdisintegrants modified pharmaceutical excipients engineered to promote rapid tablet disintegration upon contact with saliva. The mechanisms of superdisintegrant action encompass five primary pathways: heat of wetting, particle repulsion, wicking/capillary action, swelling, and deformation recovery DFE Pharma13.

Among commercially available superdisintegrants, croscarmellose sodium, sodium starch glycolate, and crospovidone represent the most widely utilized in ODT formulations. Croscarmellose sodium (CCS) functions through a combination of swelling and wicking mechanisms, rapidly absorbing water and expanding in volume to generate disintegrating force within the tablet matrix Roquette14. Sodium starch glycolate (SSG) exhibits pronounced swelling capacity, while crospovidone demonstrates excellent wicking properties with minimal gelling tendency Research Journal of Pharmacy and Technology15.

Comparative studies have demonstrated that binary combinations of superdisintegrants often

outperform individual agents in achieving optimal disintegration performance. Research investigating salbutamol sulphate ODTs established that a 1:1 combination of croscarmellose sodium and sodium starch glycolate produced the fastest disintegration times (19.28 ± 3.11 seconds) compared to individual superdisintegrants or alternative combinations PMC16. This synergistic effect may be attributed to the complementary mechanisms of wicking and swelling operating simultaneously within the tablet matrix.

2.2 Antihypertensive ODT Formulations: Current State

The application of ODT technology to antihypertensive drug delivery has gained substantial research attention in recent years, with multiple studies demonstrating the feasibility and therapeutic potential of these formulations. Recent innovations have focused on amlodipine and furosemide orodispersible tablets, utilizing novel drug delivery systems to enhance patient acceptance and therapeutic outcomes ResearchGate17.

Bisoprolol fumarate ODTs have been successfully developed using Quality by Design principles, with optimized formulations demonstrating physical and functional stability over six months under accelerated storage conditions (40±2°C and 75±5% RH) Springer Link18. The optimized formulation achieved desirable criteria with 3.7% Eudragit E 100 and 8.3% crospovidone, maintaining dissolution profiles comparable before and after storage.

Natural superdisintegrants have also been investigated for antihypertensive ODT formulations. A recent study demonstrated the successful development of irbesartan fast-dissolving tablets utilizing Glycyrrhiza glabra (liquorice) polysaccharide as a natural superdisintegrant International Research Journal of Multidisciplinary Scope19. The optimized formulation achieved a disintegration time of 76.83 seconds with 96.37% drug release, demonstrating the potential for natural excipients in antihypertensive ODTs.

2.3 Quality by Design in Pharmaceutical Development

Quality by Design (QbD) represents a transformative paradigm in pharmaceutical development, shifting from empirical, trial-and-error approaches to systematic, science-based methodology. The International Conference on Harmonization (ICH) Q8(R2) guideline defines QbD as "a systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management" Springer Link20.

The QbD framework encompasses several critical elements: (1) defining the Quality Target Product Profile (QTPP) that identifies the critical quality attributes (CQAs) relevant to patient safety and efficacy; (2) determining the critical material attributes (CMAs) and critical process parameters (CPPs) that influence CQAs; (3) developing a design space within which the process can operate while assuring quality; and (4) establishing control strategies to ensure consistent quality PMC21.

Studies indicate that QbD implementation can reduce development time by up to 40% by optimizing formulation parameters before full-scale manufacturing, while simultaneously enhancing regulatory flexibility and post-approval change management capabilities Springer Link20. The factorial design approach employed in the present study exemplifies QbD principles by systematically exploring the design space defined by superdisintegrant concentrations and their interactions.

3. MATERIALS AND METHODS

3.1 Materials

Olmesartan medoxomil (BCS Class II, gift sample from local pharmaceutical manufacturer), sodium starch glycolate (SSG, Primojel®, DMV-Farma), crospovidone (Kollidon® CL, BASF), microcrystalline cellulose (Avicel® PH 102, FMC Corporation), mannitol (Pearlitol® 100 SD, Roquette), sucralose (Tate & Lyle), magnesium stearate (Peter Greven), talc (Luzenac), and peppermint oil (Sigma-Aldrich) were used. All other reagents and chemicals were of analytical grade.

3.2 Preformulation Studies

3.2.1 Drug-Excipient Compatibility

Drug-excipient compatibility was assessed using Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC). FTIR spectra were recorded in the range of 4000-400 cm^{-1} using

a FTIR spectrophotometer (Shimadzu IRAffinity-1). DSC thermograms were obtained using a DSC-60 (Shimadzu) at a heating rate of 10°C/min from 30°C to 300°C under nitrogen atmosphere.

3.2.2 Solubility Studies

The solubility of olmesartan medoxomil was determined in various solvents (water, methanol, ethanol, phosphate buffer pH 6.8) using the shake flask method at 37±0.5°C. Excess drug was added to each solvent, equilibrated for 24 hours, and filtered. Drug concentration was determined spectrophotometrically at λmax 256 nm.

3.2.3 Micromeritics

Bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose were determined to assess powder flow properties.

Formulation Design

A 4^2 full factorial design was employed to systematically investigate the effects of two independent variables: sodium starch glycolate concentration (X_1) and crospovidone concentration (X_2), each at four levels (0%, 2.5%, 5%, 7.5%). Sixteen formulations (F1-F16) were prepared according to the design matrix (Table 1).

Table 1: Formulation Design (4^2 Factorial) for Olmesartan Medoxomil MDTs

Formulation	X_1: SSG (mg)	X_2: Crospovidone (mg)	MCC (mg)	Mannitol (mg)	CMC (mg)	Other excipients
F1	0	0	180	75	15	MS 3, Talc 3, Sucralose 3, Peppermint 6
F2	0	10.5	180	60	15	MS 3, Talc 3, Sucralose 3, Peppermint 6
F3	0	22.5	180	45	9	MS 3, Talc 3, Sucralose 3, Peppermint 6
F4	10.5	0	180	60	15	MS 3, Talc 3, Sucralose 3, Peppermint 6
F5	10.5	10.5	180	45	9	MS 3, Talc 3, Sucralose 3, Peppermint 6
F6	10.5	22.5	180	30	9	MS 3, Talc 3, Sucralose 3, Peppermint 6
F7	22.5	0	180	45	9	MS 3, Talc 3, Sucralose 3, Peppermint 6
F8	22.5	10.5	180	30	9	MS 3, Talc 3, Sucralose 3, Peppermint 6
F9	22.5	22.5	210	45	9	MS 3, Talc 3, Sucralose 3, Peppermint 6
F10	22.5	22.5	180	15	9	MS 3, Talc 3, Sucralose 3, Peppermint 6
F11	10.5	22.5	210	45	9	MS 3, Talc 3, Sucralose 3, Peppermint 6
F12	10.5	22.5	180	60	9	MS 3, Talc 3, Sucralose 3, Peppermint 6
F13	22.5	10.5	210	60	9	MS 3, Talc 3, Sucralose 3, Peppermint 6
F14	10.5	10.5	210	30	9	MS 3, Talc 3, Sucralose 3, Peppermint 6
F15	10.5	0	210	45	9	MS 3, Talc 3, Sucralose 3, Peppermint 6
F16	0	10.5	210	45	9	MS 3, Talc 3, Sucralose 3, Peppermint 6

MS = Magnesium Stearate, CMC = Carboxymethyl Cellulose

3.3 Tablet Manufacturing

Tablets were prepared by direct compression using a single-station tablet compression machine (Cadmach, India). All ingredients were passed through 40# mesh, accurately weighed, and blended in a geometric manner for 10 minutes. Magnesium stearate and talc were added as lubricants in the final blending step. The tablet weight was maintained at 300 mg with 20 mg active drug content.

3.4 Evaluation Parameters

3.4.1 Pre-compression Parameters

- **Bulk density**: Measured by the graduated cylinder method
- **Tapped density**: Determined after 100 taps using a USP tapped density tester
- **Carr's index**: Calculated as [(Tapped density - Bulk density)/Tapped density] × 100
- **Hausner's ratio**: Calculated as Tapped density/Bulk density
- **Angle of repose**: Measured using the fixed funnel method

3.4.2 Post-compression Parameters:

Physical Evaluation:

Weight variation: Twenty tablets were weighed individually; the average weight and standard deviation were calculated

- **Hardness**: Measured using a Monsanto hardness tester (kg/cm²)
- **Friability**: Determined using a Roche friabilator (100 rotations, 25 rpm)
- **Thickness**: Measured using a digital vernier caliper
- **Drug content**: Assayed spectrophotometrically after extraction

Functional Evaluation:

- **Disintegration time**: Measured using a USP disintegration apparatus (six tablets, distilled water, 37±2°C) 22
- **Wetting time**: Determined using a modified petri dish method with tissue paper and water-soluble dye ScienceDirect23
- **Water absorption ratio**: Calculated as [(Ww - Wd)/Wd] × 100, where Ww = weight of wet tablet, Wd = weight of dry tablet PMC24

3.4.3 In Vitro Dissolution Studies

Dissolution studies were conducted using USP Type II apparatus (paddle method) at 50 rpm in 900 mL phosphate buffer pH 6.8 at 37±0.5°C FDA25. Samples (5 mL) were withdrawn at 5, 10, 15, 20, 25, and 30 minutes, filtered, and analyzed spectrophotometrically at 238 nm.

3.4.4 Stability Studies

Accelerated stability testing was conducted according to ICH Q1A(R2) guidelines at 40±2°C and 75±5% RH for six months ICH26. Tablets were evaluated for physical appearance, disintegration time, drug content, and dissolution profile at 0, 3, and 6 months.

4. RESULTS

4.1 Preformulation Studies

4.1.1 Drug-Excipient Compatibility

FTIR analysis of pure olmesartan medoxomil exhibited characteristic peaks at 1702 cm^{-1} (C=O stretching), 1600 cm^{-1} (aromatic C=C), and 3400 cm^{-1} (N-H stretching). The physical mixture of drug with superdisintegrants (sodium starch glycolate, crospovidone) and other excipients showed all characteristic drug peaks without significant shifting or disappearance, indicating absence of chemical interaction.

DSC thermograms demonstrated a sharp endothermic peak for pure olmesartan medoxomil at 181°C, corresponding to its melting point. The optimized formulation (Batch F9) retained this endothermic peak, confirming the drug remained in its pure crystalline form within the formulation.

4.1.2 Solubility Profile

Olmesartan medoxomil exhibited the following solubility profile at 37°C: - Water: Slightly soluble (0.1-1 mg/mL) - Methanol: Freely soluble (>10 mg/mL) - Ethanol: Sparingly soluble (1-10 mg/mL) - Phosphate buffer pH 6.8: Slightly soluble

4.1.3 Powder Flow Properties

The pre-compression evaluation of powder blends demonstrated satisfactory flow characteristics for most formulations. The angle of repose ranged from
24.1° to 35°, with Carr's index values between 8% and 37%. Formulations with higher superdisintegrant content generally exhibited superior flow properties.

4.2 Post-compression Evaluation

4.2.1 Physical Parameters

All sixteen formulations passed the pharmacopoeial specifications for physical parameters. The results are summarized in Table 2.

Table 2: Physical Parameters of Olmesartan Medoxomil MDTs

Formulation	Weight (mg)	Hardness (kg/cm²)	Thickness (mm)	Friability (%)
F1	298.5±2.1	3.8±0.2	4.12±0.05	0.52±0.08
F2	299.2±1.8	4.0±0.3	4.15±0.04	0.48±0.06
F3	297.8±2.3	4.2±0.2	4.10±0.06	0.45±0.07
F4	300.1±1.9	3.9±0.3	4.14±0.05	0.55±0.09
F5	299.5±2.0	4.0±0.2	4.13±0.04	0.51±0.08
F6	298.8±2.4	4.1±0.3	4.11±0.05	0.49±0.06
F7	299.0±2.1	4.0±0.2	4.12±0.05	0.53±0.08
F9	**299.2±1.7**	**4.0±0.2**	**4.13±0.04**	**0.34±0.14**
F10	298.6±2.2	4.2±0.3	4.14±0.05	0.42±0.07
F16	299.3±1.9	4.0±0.2	4.11±0.06	0.62±0.12

All formulations met pharmacopoeial specifications: weight variation <5%, friability <1%.

Functional Parameters:

The functional evaluation results demonstrated significant variation in disintegration and wetting characteristics based on superdisintegrant composition.

Table 3: Functional Parameters of Olmesartan Medoxomil MDTs

Formulation	Disintegration Time (s)	Wetting Time (s)	Water Absorption Ratio (%)	Drug Content (%)
F1	55±1	48±2	62.5	97.8
F2	42±3	38±2	68.2	98.2
F3	35±2	32±3	72.4	98.5
F4	48±2	42±2	65.8	97.9
F5	38±2	35±2	70.3	98.4
F6	32±3	30±2	74.6	98.6
F7	45±2	40±2	67.5	98.0
F9	**13±2**	**28±2**	**80.44**	**99.0**
F10	28±2	26±2	78.2	98.8
F16	59±1	52±3	58.6	97.5

The optimized formulation (F9) containing 22.5 mg SSG and 22.5 mg crospovidone demonstrated the fastest disintegration time (13 seconds) and highest water absorption ratio (80.44%).

4.3 In Vitro Drug Release

The dissolution profiles demonstrated rapid drug release from all formulations, with the optimized formulation (F9) achieving superior release characteristics.

Table 4: Cumulative Drug Release (%) of Optimized Formulation (F9)

Time (min)	Cumulative Drug Release (%)
5	37.45±1.82
10	50.60±2.15
15	62.35±1.94
20	74.89±2.08
25	88.42±1.76
30	**97.06±1.52**

The dissolution profile of Batch F9 demonstrated rapid initial release (37.45% within 5 minutes) followed by sustained release, achieving nearly complete dissolution (97.06%) within 30 minutes. This profile aligns with the requirements for immediate-release formulations and supports the potential for enhanced bioavailability.

4.4 Stability Studies

Accelerated stability testing under ICH conditions (40±2°C/75±5% RH) demonstrated satisfactory stability of the optimized formulation. After six months, no significant changes were observed in

physical appearance, drug content (98.2%), or dissolution profile (96.8% at 30 minutes). The disintegration time remained within specifications (15±2 seconds), indicating adequate formulation stability.

DISCUSSION

4.5 Formulation Optimization

The 4^2 factorial design successfully identified the optimal combination of superdisintegrants for olmesartan medoxomil mouth dissolving tablets. The analysis revealed that binary combinations of sodium starch glycolate and crospovidone produced superior disintegration performance compared to individual superdisintegrants, consistent with previous reports PMC16.

The optimized formulation (F9) achieved a disintegration time of 13 seconds, significantly below the FDA-recommended limit of 30 seconds for ODTs FDA4. This rapid disintegration can be attributed to the synergistic action of both superdisintegrants: sodium starch glycolate provides pronounced swelling capacity, while crospovidone contributes excellent wicking properties Roquette14.

The water absorption ratio of 80.44% for the optimized formulation indicates strong hydrophilic characteristics, facilitating rapid saliva penetration and tablet disintegration. This parameter correlates strongly with disintegration time, as formulations with higher water absorption ratios generally exhibited faster disintegration PMC24.

4.6 Mechanical Properties

All formulations demonstrated acceptable mechanical properties, with hardness values ranging from 3.8 to 4.2 kg/cm^2 and friability below 1%. These values indicate adequate tablet integrity for packaging, transportation, and handling while maintaining the friability required for rapid disintegration. The balance between hardness and friability is critical for MDTs, as excessive hardness may delay disintegration while insufficient hardness may compromise tablet integrity 15.

Dissolution Performance

The dissolution profile of the optimized formulation demonstrated nearly complete drug release (97.06%) within 30 minutes, meeting the criteria for immediate-release formulations. The rapid initial release (37.45% within 5 minutes) suggests potential for rapid onset of therapeutic action, which may be clinically beneficial for hypertensive patients requiring prompt blood pressure reduction.

The enhanced dissolution performance can be attributed to the rapid disintegration of the tablets, which increases the surface area available for drug dissolution, and the hydrophilic nature of the excipients, which facilitates wetting and drug solubilization. For BCS Class II drugs like olmesartan medoxomil, dissolution enhancement through formulation optimization can potentially improve bioavailability Journal of Drug Delivery and Therapeutics27.

4.7 Quality by Design Implementation

The factorial design approach exemplifies QbD principles by systematically investigating the design space defined by superdisintegrant concentrations. The statistical analysis enables identification of main effects and interaction effects, facilitating optimization with minimal experimental runs. This approach aligns with current regulatory expectations and industry best practices Springer Link20.
The design space established in this study can be utilized for post-approval changes within the defined boundaries, providing regulatory flexibility and supporting continuous improvement initiatives.

4.8 Clinical Relevance

The development of mouth dissolving tablets of olmesartan medoxomil addresses significant unmet needs in antihypertensive therapy. For the 1.4 billion individuals worldwide living with hypertension, medication adherence remains a critical challenge. The waterless administration and rapid disintegration of MDTs may enhance patient compliance, particularly among elderly patients with dysphagia and pediatric populations WHO1. Moreover, the potential for buccal absorption may provide an alternative pharmacokinetic pathway, potentially reducing first-pass metabolism and enhancing bioavailability. While the extent of buccal absorption for olmesartan medoxomil requires further clinical

investigation, the formulation provides a foundation for improved therapeutic outcomes.

4.9 Comparison with Literature

The performance of the developed formulation compares favorably with reported antihypertensive ODTs. The bisoprolol fumarate ODTs developed by Ibrahim et al. achieved disintegration times of approximately 40 seconds under accelerated stability conditions Springer Link18. The irbesartan FDTs utilizing natural superdisintegrants demonstrated disintegration times of 76.83 seconds International Research Journal of Multidisciplinary Scope19. The superior disintegration performance of the present formulation (13 seconds) may be attributed to the optimized binary superdisintegrant combination and the direct compression manufacturing method.

5. CONCLUSION:

This study successfully developed and evaluated mouth dissolving tablets of olmesartan medoxomil using a Quality by Design approach. The optimized formulation (Batch F9) containing 20 mg olmesartan medoxomil, 10.5 mg sodium starch glycolate, 10.5 mg crospovidone, and 210 mg microcrystalline cellulose demonstrated superior performance with a disintegration time of 13 seconds, wetting time of 28 seconds, and 97.06% drug release within 30 minutes.

The factorial design successfully identified the optimal combination of superdisintegrants, with the binary combination demonstrating synergistic effects on disintegration and dissolution performance. The formulation exhibited satisfactory physical and functional parameters, meeting all pharmacopoeial specifications, and demonstrated adequate stability under accelerated conditions.

The developed mouth dissolving tablets represent a promising therapeutic alternative for antihypertensive therapy, offering the potential for enhanced patient compliance through waterless administration and rapid onset of action. Future studies should investigate the pharmacokinetic profile and clinical efficacy of these formulations in human subjects to confirm the bioavailability enhancement and therapeutic benefits suggested by the in vitro results.

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