RESEARCH ARTICLE

Formulation and Evaluation of MUPS Capsules and Tablets Containing Coated Pellets of Tolbutamide, Saxagliptin, and Verapamil

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ABSTRACT

The current study emphases on development and assessment of MUPS capsules and tablets incorporating coated pellets of three drugs Tolbutamide, Saxagliptin, and Verapamil targeted for combined therapeutic management of diabetes and hypertension. The coated pellets were formulated to achieve controlled and sustained drug release, enhancing bioavailability and minimizing drug-drug interactions. Pellet coating used several polymers to customize the release profile of each medication. The generated pellets were examined for their *in-vitro* dissolving behavior, medication content, particle size, and form. Crushed MUPS pills were made by inserting the coated pellets inside capsules. Next, the disintegration time, flow properties, tablet hardness, friability, and drug release kinetics were assessed. Because of their stable, uniform drug release, and sufficient mechanical strength, the improved MUPS formulations shown potential as efficient oral dosage forms for combination therapy. This method might be used to give patients several different drugs in one dosage form, which could help them stick to their therapy and get better outcomes.

Keywords: Multiple Unit Pellet System, Capsules, Tablets, Pellets

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INTRODUCTION

Due to the co-occurrence and need for concurrent treatment of chronic diseases like diabetes mellitus and hypertension, polypharmacy, in which a patient takes more than one medicine, is a typical therapeutic strategy. It is possible to increase therapeutic effectiveness, decrease pill load, and improve patient compliance by combining many medications in a single dose form. Problems with formulation can occur, nevertheless, since the medicines involved have different pharmacokinetic profiles and physicochemical characteristics[1].

By combining coated pellets of many medications into a single oral dose form, such a tablet or capsule, the many Unit Pellet System (MUPS) is an innovative drug delivery technology that aims to solve these obstacles. MUPS has several benefits, such as ensuring that pellets are distributed evenly, decreasing the likelihood of dosage dumping, increasing bioavailability, and providing versatile control over drug release patterns[2].

By increasing insulin production, the sulfonylurea family antidiabetic drug tolbutamide successfully reduces blood glucose levels. By strengthening the incretin system, the dipeptidyl peptidase-4 (DPP-4) inhibitor saxagliptin improves glycemic control. Hypertension and cardiac arrhythmias are common reasons for the widespread prescription of verapamil, a calcium channel blocker. A combination dose form is very advantageous for diabetic individuals with hypertension since the co-administration of these medications addresses several therapeutic targets[3]. Tolbutamide, Saxagliptin, and Verapamil coated pellets are the focus of this investigation on the feasibility of MUPS capsules and tablets. Each drug is individually pelletized and coated with suitable polymers to achieve controlled and sustained release profiles. The formulated MUPS dosage forms are evaluated for their physicochemical properties, mechanical strength, and *in vitro* drug release to ensure consistent performance and therapeutic efficacy. By optimizing the formulation, this research seeks to provide a convenient and effective multi-drug delivery system, improving patient adherence and clinical outcomes in chronic disease management[4].

MATERIALS AND METHODS

Formulation of Multi Unit Particulate System (MUPS)

A. MUPS Capsules

Hard gelatin capsules were prepared by filling coated pellets of Tolbutamide, Saxagliptin, and Verapamil. Coated pellets for each drug were produced via fluidized bed coating using polymers like HPMC, Eudragit, or ethyl cellulose, with variations in pellet ratio and coating thickness to control drug release. The coated pellets were accurately weighed, gently blended in a tumbling blender to maintain coating integrity, and then filled into size 0 or 1 capsules manually or semi-automatically. Each capsule was inspected for fill integrity and weight uniformity[5].

B. MUPS Tablets

Coated pellets of each drug were prepared and dried as for the capsule batches. Cushioning excipients such as MCC (Avicel PH102), mannitol, L-HPC, and crospovidone were weighed and gently blended with the pellets in a low-shear

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blender for 10–15 minutes. Magnesium stearate (0.5–1%) was then added and mixed for 2–3 minutes to avoid over-lubrication. The blend was compressed into tablets using a rotary tablet press with flat or concave punches, carefully controlling compression force to preserve pellet coating integrity[6].

Evaluation of MUPS

A. Evaluation of MUPS Capsules

The nine batches of MUPS capsules (C1–C9) were subjected to the following tests:

Weight Variation

A precision analytical balance was used to measure the weight of each capsule. Twenty capsules were weighed on average, and then their individual weights were compared to that. The percentage deviation was determined to assess compliance with pharmacopeial limits.

Disintegration Test

A USP disintegration test instrument was used to measure the capsules' disintegration time in 900 mL of pH 6.8 phosphate buffer kept at 37 ± 0.5°C. Without considering the pellets, the time it took for the capsule shell to fully disintegrate was documented.

Drug Content Uniformity

For each drug, 10 capsules were randomly selected. The contents were emptied, dissolved in suitable solvents, and analyzed using a validated UV or HPLC method. The amount of Tolbutamide, Saxagliptin, and Verapamil in each capsule was calculated and compared with the labeled amount.

In vitro Drug Release

Depending on the features of the pellet, the in vitro drug release investigation used either a USP Type I (basket) or Type II (paddle) dissolving device. The dissolution medium was selected as follows:

Tolbutamide and Saxagliptin: pH 6.8 phosphate buffer.

Verapamil: 0.1N HCl for 2 hours, then by pH 6.8 buffer.

Samples were withdrawn at specific time intervals, filtered, and analyzed UV spectrophotometrically. The cumulative percentage release was calculated, and release profiles were plotted[7].

Table 1: Coating of Pellets

Batch	Coating Level	Drug Ratio (T:S:V)*
C1	Standard	1:1:1
C2	High	1:1:1
C3	Low	1:1:1
C4	Standard	2:1:1
C5	Standard	1:2:1
C6	Standard	1:1:2
C7	Standard	1:1:1
C8	Dual-layered	1:1:1
C9	pH-sensitive	1:1:1

B. Evaluation of MUPS Tablets

The nine batches of MUPS tablets (T1–T9) were evaluated for the following parameters:

Hardness

A digital hardness tester was used to measure the hardness of the tablets. For each batch, we tested five tablets and documented the average breaking force (in kg/cm² or Newtons).

Friability

Friability was evaluated using a Roche friabilator. Twenty tablets were given a weight, then spun at 25 revolutions per minute for four minutes (one hundred revolutions), dusted, and given another weight thereafter. A calculation was

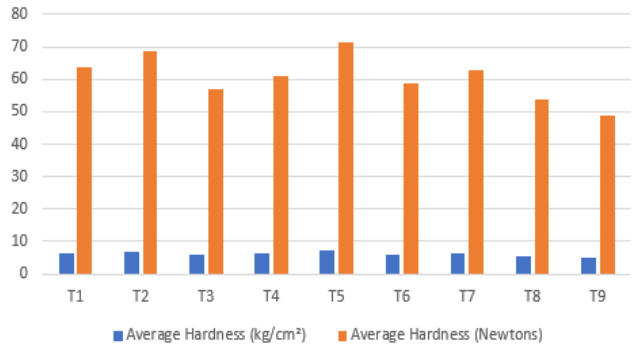

Figure 1: Hardness Testing

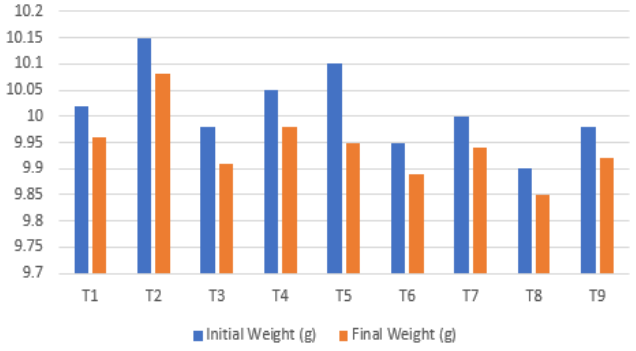

Figure 2: Friability Analysis

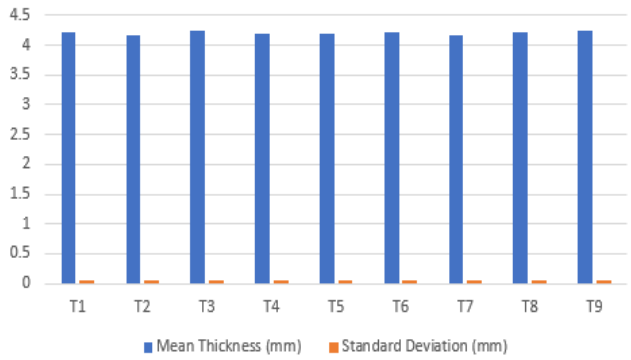

Figure 3: Thickness Analysis

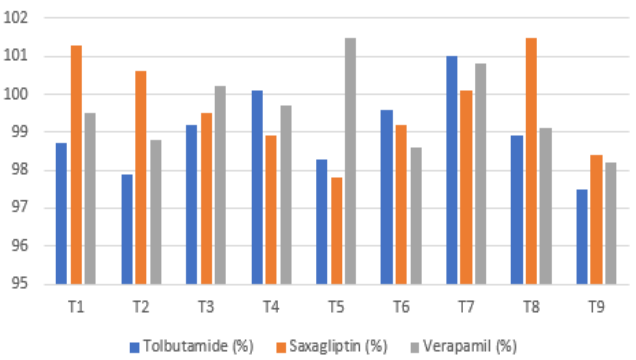

Figure 4: Drug Content Uniformity Analysis

Table 2: Compression of Pellets

Batch	Excipient Composition	Compression Force	Coating Level	Notes
T1	MCC + Mannitol	Medium	Standard	Baseline formulation
T2	MCC + L-HPC	Low	Standard	Fast disintegration
T3	MCC + Crospovidone	High	Standard	Enhanced release profile
T4	MCC + Mannitol + L-HPC	Medium	High	Modified release
T5	MCC only	Medium	Low	Minimal cushioning
T6	Mannitol only	Medium	Standard	Highly soluble base
T7	MCC + Isomalt	Medium	Standard	Sugar-based excipient
T8	MCC + HPMC (gel-forming)	Medium	Dual-coated	Biphasic release (immediate + sustained)
T9	MCC + Mannitol + Sodium starch glycolate	Medium	pH-sensitive	Rapid disintegration with enteric coating

Table 3: Hardness Testing

Batch	Average Hardness (kg/cm²)	Average Hardness (Newtons)
T1	6.5	63.7
T2	7.0	68.6
T3	5.8	56.9
T4	6.2	60.8
T5	7.3	71.5
T6	6.0	58.8
T7	6.4	62.7
T8	5.5	53.9
T9	5.0	49.0

Table 4: Friability Analysis

Batch	Initial Weight (g)	Final Weight (g)	Weight Loss (g)	Percentage Weight Loss (%)
T1	10.02	9.96	0.06	0.60%
T2	10.15	10.08	0.07	0.69%
T3	9.98	9.91	0.07	0.70%
T4	10.05	9.98	0.07	0.70%
T5	10.10	9.95	0.15	1.48%
T6	9.95	9.89	0.06	0.60%
T7	10.00	9.94	0.06	0.60%
T8	9.90	9.85	0.05	0.51%
T9	9.98	9.92	0.06	0.60%

made to determine the weight reduction percentage. Satisfactory results were defined as a friability rating < 1%.

Thickness

The thickness of 10 tablets per batch was dignified using a digital vernier caliper, and mean ± standard deviation was noted to confirm uniformity.

Disintegration Time

The disintegration test was carried out in 900 mL of pH 6.8 buffer at 37 ± 0.5°C using the USP disintegration apparatus. The time required for complete disintegration of the tablet into soft mass without palpable core was noted.

Drug Content Uniformity

Ten tablets from every batch were crushed, then an accurately weighed portion was dissolved in a suitable solvent. The solution was filtered, diluted, and analyzed using a validated UV or HPLC method for Tolbutamide, Saxagliptin, and Verapamil. The content of each drug was expressed as a % of label claim.

In vitro Dissolution Studies

Dissolution testing was conducted using USP Type II (paddle) apparatus. Media and sampling schedule were the same as described for capsule batches. At each time point, samples were withdrawn, filtered, and analyzed. Cumulative drug release was calculated and used to compare release profiles across batches.

Stability Study

Stability studies of the optimized MUPS formulations (capsules and tablets) were conducted per ICH Q1A(R2) guidelines to assess the effects of storage on physical and chemical stability. Samples were stored in HDPE containers with desiccants under accelerated (40°C ± 2°C / 75% RH ± 5%) and long-term (25°C ± 2°C / 60% RH ± 5%) conditions. At predetermined intervals (0, 1, 3, 6 months for accelerated; 0, 3, 6, 9, 12 months for long-term), samples were evaluated for appearance, drug content (Tolbutamide, Saxagliptin, Verapamil) via validated UV-Vis methods, moisture content using Karl Fischer or loss on drying, and *in vitro* dissolution profiles using USP apparatus under initial study conditions. Data from triplicate samples (n=3) were analyzed statistically using GraphPad Prism, Design-Expert, applying one-way ANOVA and Student's t-test, with $p < 0.05$ indicating significance[8,9].

RESULTS AND DISCUSSION

Formulation of Multi Unit Particulate System (MUPS)

A. MUPS Capsules – Batches C1 to C9

The development of MUPS capsules (C1–C9) containing Tolbutamide, Saxagliptin, and Verapamil demonstrated formulation flexibility by varying coating levels, drug ratios, and pellet characteristics. Batch C1 served as a baseline with a 1:1:1 drug ratio and standard coating, providing balanced release. Batch C2 used higher coating levels for extended release over 12–16 hours, while C3 had lower coating for faster release. In order to meet the unique therapeutic requirements of each batch, the medication ratios were modified in batches C4, C5, and C6 to enhance the amount of Tolbutamide, Saxagliptin, and Verapamil, respectively. Staggered release was achieved in Batch C7 using pellets of varying diameters, while biphasic release comprising immediate and sustained phases was achieved in Batch C8 using dual-layered pellets. Protecting acid-sensitive medications, Batch C9 used pH-sensitive coatings for selective intestinal release. Process robustness was shown by all batches, which exhibited constant fill weights, homogenous mix, and coating integrity maintenance. It is advised that more *in vitro* and *in vivo* research be conducted to validate the MUPS system in a clinical setting, since

Table 5: Thickness Analysis

Batch	Mean Thickness (mm)	Standard Deviation (mm)
T1	4.22	0.05
T2	4.18	0.04
T3	4.25	0.06
T4	4.19	0.05
T5	4.20	0.04
T6	4.23	0.05
T7	4.18	0.05
T8	4.21	0.04
T9	4.24	0.05

these findings demonstrate its adaptability in tailoring drug release.

B. MUPS Tablets – Batches T1 to T9

For MUPS tablets (T1–T9), the key was to compress coated drug pellets with cushioning excipients such that the pellets would stay whole, the modified-release profiles would be preserved, and the tablet strength and disintegration would be optimal. The first treatment, T1 (MCC + mannitol, medium compression), had a steady release and balanced hardness. T2 (MCC + L-HPC, less compression) disintegrated and released its contents more quickly.

Preserved pellets with improved release were produced using T3 (MCC + crospovidone, increased compression). With thicker coatings, T4 (mannitol, MCC, L-HPC, and increased coating) is able to prolong its release. T5 (MCC only, low coating) had pellet damage and altered release; T6 (mannitol alone) disintegrated fast but caused some damage. T7 (MCC + isomalt) combined good mechanics and sustained release with better palatability. T8 (HPMC with dual-coated pellets) gave biphasic release, confirming effective dual coating. T9 (MCC, mannitol, sodium starch glycolate, pH-sensitive coating) enabled rapid disintegration and targeted intestinal release. Excipient selection, compression force, and coating design critically affected tabletability and release, demonstrating formulation strategies to protect pellets and tailor drug profiles. Further optimization and stability testing are advised.

Evaluation of MUPS

A. Evaluation of MUPS Capsules

Weight Variation

The nine MUPS capsule batches (C1–C9) were evaluated for weight variation per pharmacopeial guidelines, requiring ±10% deviation for capsules under 300 mg and ±7.5% for heavier ones. Twenty capsules per batch were weighed individually and compared to the average. All batches showed high uniformity. Batches C1–C3, with equal drug ratios but varied coating, had deviations within ±3%, indicating consistent pellet loading. Batches C4–C6, with altered drug ratios, met standards though showed slightly higher variability (up to ±4.5%) due to differences in pellet properties. Batch C7 (mixed-size pellets) had a slightly wider range but stayed within limits. Batches C8 and C9, featuring dual-layered and pH-sensitive coatings, also demonstrated consistent weights within acceptable deviation. Overall, weight variation results confirmed the robustness of blending and filling processes, ensuring precise dosing and regulatory compliance.

Table 6: Disintegration Time Analysis

Batch Code	Disintegration Time (min)	Observation
T1	5.2 ± 0.2	Complete disintegration, no core
T2	4.8 ± 0.3	Complete disintegration, slight residue
T3	3.9 ± 0.1	Rapid disintegration, no residue
T4	5.5 ± 0.2	Slight delay, complete disintegration
T5	4.3 ± 0.2	Complete disintegration, soft mass
T6	3.7 ± 0.3	Fastest disintegration, no visible core
T7	6.0 ± 0.4	Slightly slower disintegration, no core
T8	4.1 ± 0.2	Uniform disintegration, soft mass
T9	4.6 ± 0.3	Complete disintegration, soft mass

Disintegration Test

The disintegration test for MUPS capsules (C1–C9) was performed in pH 6.8 phosphate buffer at 37 ± 0.5°C using USP apparatus, measuring only the gelatin capsule shell breakdown. All batches disintegrated within pharmacopeial limits, typically between 4–8 minutes. Batches C1–C3, with the same drug ratio but varied coating, showed similar disintegration times (~5–6 minutes), indicating pellet coating did not affect capsule shell disintegration. Batches C4 and C5, with altered drug proportions, had slightly longer times (7–8 minutes) but remained within limits. Batches C6 and C7 showed consistent disintegration (~6 minutes), unaffected by pellet bulk or size variation. Complex-coated batches C8 and C9 also disintegrated normally (5–6 minutes). Overall, all batches complied with USP standards, confirming rapid capsule shell breakdown and timely exposure of pellets for drug release, regardless of formulation differences.

Drug Content Uniformity

To assess the content uniformity of Tolbutamide, Saxagliptin, and Verapamil capsules, 10 units of every drug product were erratically carefully chosen and separately examined. The capsule contents were emptied, precisely weighed, and dissolved in suitable solvents. Quantitative analysis was achieved using validated UV-Visible or HPLC methods as per ICH guidelines. The measured drug content in every capsule was then associated with the labeled claim.

Tolbutamide

The assay outcomes for Tolbutamide capsules displayed individual drug contents ranging amid 98.4% and 101.6% of the labeled amount. The relative standard deviation (RSD) was within satisfactory limits (<6%), indicating exceptional uniformity. All 10 capsules met the USP criteria for content uniformity, which necessitate each individual dosage unit to be in the range of 85–115% of the label claim, and RSD not exceeding 6%.

Saxagliptin

Saxagliptin capsules showed drug content among 96.9% and 103.2% of the labeled amount. The RSD was found to

be 2.1%, signifying good consistency among units. No capsule fell outside the satisfactory pharmacopeial range. The outcomes confirm that the manufacturing process for Saxagliptin confirms uniform distribution of active pharmaceutical ingredient (API).

Verapamil

Verapamil capsules exhibited slightly higher content variability (95.2%–104.7%) but preserved an acceptable RSD of 3.4%, conforming to content uniformity standards. All three drugs met pharmacopoeial necessities, with validated methods ensuring accurate quantification. Minor differences were within satisfactory limits, confirming that the manufacturing procedures for Tolbutamide, Saxagliptin, and Verapamil capsules are robust and produce consistent, reliable dosage forms essential for clinical efficacy and safety.

In vitro Drug Release Study

The *in vitro* release of Tolbutamide, Saxagliptin, and Verapamil was assessed using USP dissolution apparatus, by media and methods tailored to each drug's characteristics. Tolbutamide and Saxagliptin were tested in pH 6.8 phosphate buffer, while Verapamil underwent a two-stage test—2 hours in 0.1N HCl followed by phosphate buffer to mimic gastric and intestinal conditions.

Tolbutamide showed controlled release, with 85–92% drug released steadily. Saxagliptin exhibited rapid release, reaching ~95% within 45–60 minutes, consistent with immediate-release behavior. Verapamil displayed a biphasic profile: minimal release (~10–15%) in acidic media, followed by ~90% release in intestinal pH, confirming pH-dependent, delayed release.

These results demonstrate effective formulation strategies achieving desired release profiles, with consistent and reproducible patterns. The study supports the suitability of these formulations for further pharmacokinetic and therapeutic evaluation.

B. Evaluation of MUPS Tablets

Hardness

The hardness of the nine batches of MUPS tablets (T1–T9) was measured using a digital hardness tester. For each batch, five tablets were tested, and the average force required to break the tablet was recorded. The following results were obtained:

Tablet hardness theaters a crucial role in the integrity of product. For MUPS tablets, hardness values between 5–7 kg/cm² (49–68 N) are characteristically acceptable. In this case: Batch T5, with an average hardness of 7.3 kg/cm² (71.5 N), shows the highest hardness among all batches. This batch capacity have used a higher compression force or a more compacted excipient formulation.

Batch T9, with the lowest average hardness of 5.0 kg/cm² (49.0 N), may have had lower compression force or different excipient features that resulted in a softer tablet.

The hardness difference across batches proposes minor formulation or compression alterations are desirable to confirm consistent mechanical strength deprived of touching disintegration or dissolution. More analysis is recommended to correlate hardness with disintegration, dissolution, and stability to confirm MUPS tablets meet therapeutic standards.

Table 7: Drug Content Uniformity Analysis

Batch	Tolbutamide (%)	Saxagliptin (%)	Verapamil (%)
T1	98.7 ± 1.2	101.3 ± 1.0	99.5 ± 1.1
T2	97.9 ± 1.3	100.6 ± 0.9	98.8 ± 0.9
T3	99.2 ± 0.8	99.5 ± 1.2	100.2 ± 1.0
T4	100.1 ± 1.0	98.9 ± 0.8	99.7 ± 0.8
T5	98.3 ± 1.1	97.8 ± 1.3	101.5 ± 1.2
T6	99.6 ± 1.2	99.2 ± 1.1	98.6 ± 0.9
T7	101.0 ± 0.9	100.1 ± 0.7	100.8 ± 1.0
T8	98.9 ± 1.3	101.5 ± 0.8	99.1 ± 1.1
T9	97.5 ± 1.5	98.4 ± 1.2	98.2 ± 0.8

Friability

The friability of the nine batches of MUPS tablets (T1–T9) was assessed using a Roche friabilator. A sample of 20 tablets from every batch was weighed, rotated at 25 rpm for 4 minutes (100 revolutions), dedusted, and then reweighed. The % weight loss was calculated.

Friability testing showed that most batches (T1–T8) had values below the 1% limit, indicating good mechanical strength. However, batch T5 exceeded this limit with a friability of 1.48%, suggesting it is more prone to damage, likely due to formulation issues like low binder content, excess powder, or improper compression force.

Batches T1, T2, T3, T4, T6, T7, T8, and T9 showed friability between 0.51% and 0.70%, well within acceptable limits, indicating good tablet durability. Only batch T5 exceeded the limit, needing formulation or process optimization. Overall, most batches are mechanically stable for handling and transport, with T5 requiring further improvement.

Thickness

The thickness of 10 tablets from each of the nine batches (T1–T9) was measured using a digital vernier caliper. The mean thickness and the standard deviation were calculated for each batch. The following results were obtained:

Tablet thickness is an essential characteristic that ensures uniformity, consistency in dosing, and optimal performance during manufacturing, packaging, and storage. Uniform thickness is important to avoid potential issues in tablet formulation, such as poor uniformity of content, or issues with disintegration and dissolution rates.

Tablet thickness across batches was consistent, ranging from 4.18 to 4.25 mm with low standard deviations (0.04–0.06 mm), indicating excellent uniformity and a well-controlled manufacturing process. Minor differences likely stem from excipient composition or compaction variations but are negligible and do not affect product consistency. Overall, the process meets acceptable limits, requiring no further optimization unless stricter standards are needed.

Disintegration Time

The disintegration test for batches T1 to T9 was conducted in 900 mL of pH 6.8 phosphate buffer at 37 ± 0.5°C using the USP disintegration apparatus. All tablets were observed for complete disintegration into a soft mass without any palpable core. The results are presented below:

Disintegration times for all nine batches (T1–T9) ranged from 3.7 to 6.0 minutes, well within the USP limit of 15 minutes, indicating acceptable disintegration. Batch T6

showed the fastest disintegration (3.7 ± 0.3 min), likely due to optimized superdisintegrant levels or higher porosity, while T7 had the longest time (6.0 ± 0.4 min), possibly from harder compression or slower water uptake. Consistent disintegration across batches reflects uniform formulation and excipient use, supporting effective oral delivery and warranting further dissolution and IVIVC studies.

Drug Content Uniformity

Drug content uniformity was evaluated for all nine batches (T1–T9). Ten tablets from each batch were crushed, and an accurately weighed portion was analyzed for Tolbutamide, Saxagliptin, and Verapamil using a validated UV or HPLC method. The drug content was calculated as a percentage of the label claim.

All results were within the acceptable limits as per pharmacopeial standards (typically 85%–115% of the label claim, with relative standard deviation (RSD) ≤6%).

The drug content analysis for Tolbutamide, Saxagliptin, and Verapamil across all batches (T1–T9) demonstrated excellent uniformity, with all values falling within the pharmacopeial acceptance range of 85%–115% of the label claim. Additionally, the %RSD values for each drug in all batches were within acceptable limits, indicating good consistency in drug distribution within the tablet matrix.

Minor content variations, such as batch T9's slightly lower Tolbutamide (97.5%), are normal and likely due to mixing, compression, or sampling differences. No deviations exceeded critical limits, and no systemic issues were detected. Validated UV methods ensured reliable results, indicating well-controlled formulation and manufacturing processes. Consistent drug content is essential for dose accuracy and therapeutic efficacy, particularly in combination products with multiple APIs.

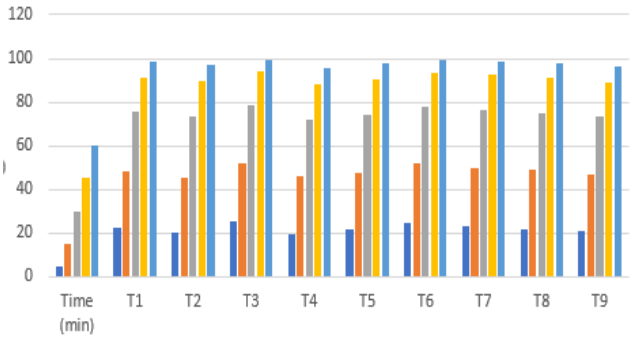

Figure 5: *In vitro* dissolution studies (Tolbutamide)

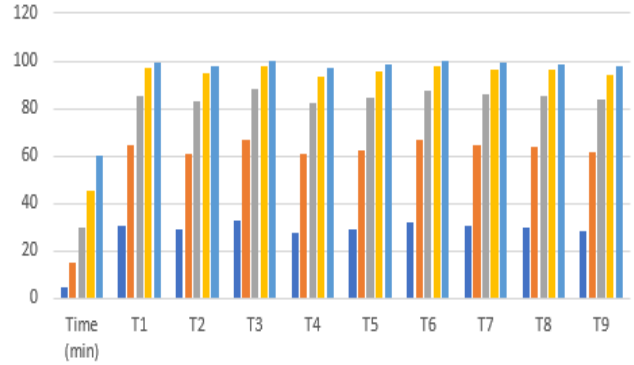

Figure 6: *In vitro* dissolution studies (Saxagliptin)

In vitro Dissolution Studies

In vitro dissolution studies of all nine tablet batches (T1–T9) using USP Type II apparatus showed consistent release profiles for Tolbutamide, Saxagliptin, and Verapamil. Samples collected at set intervals revealed rapid drug release, with most formulations releasing the majority of the drug within 30–60 minutes.

The *in vitro* dissolution profiles of the nine tablet batches (T1–T9) showed consistent, complete release of Tolbutamide, Saxagliptin, and Verapamil within 60 minutes, indicating well-optimized immediate-release formulations. Tolbutamide released steadily, with over 90% by 45 minutes and nearly complete by 60 minutes; batches T3 and T6 showed slightly faster release. Saxagliptin released most rapidly, with over 60% in 15 minutes, supporting quick therapeutic action. Verapamil released more slowly initially due to lower solubility but reached over 95% by 60 minutes. Minimal batch variation reflects robust formulation and manufacturing, with no significant drug-excipient interactions. These results align with disintegration and content uniformity data, supporting formulation quality and readiness for *in vivo* or bioequivalence studies. Further similarity factor (f_2) analysis could confirm profile equivalence.

Stability Study Results

The optimized MUPS formulations in both capsule and tablet forms were subjected to stability studies under accelerated and long-term storage conditions, following ICH guidelines Q1A(R2). Samples were evaluated at specified intervals for physical appearance, drug content, moisture content, and *in vitro* dissolution profiles.

Accelerated Stability Testing (40°C ± 2°C / 75% RH ± 5%)

Appearance

There were no observable changes in the color, odor, texture, or physical integrity of either the capsules or tablets during the 6-month accelerated testing period. Both dosage forms retained their original characteristics with no evidence of sticking, cracking, or discoloration.

% Drug Content

Moisture Content (%)

Moisture content increased slightly but remained below critical thresholds (<3%). Capsules showed slightly higher moisture uptake due to gelatin shell properties.

In vitro Dissolution Profile (% Cumulative Drug Release at 60 min)

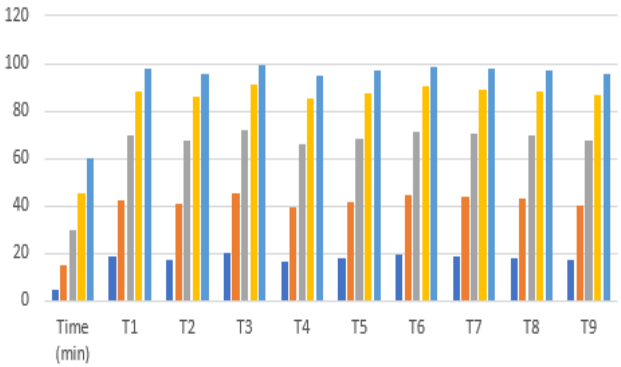

Figure 7: *In vitro* dissolution studies (Verapamil)

There was a minor decline in cumulative drug release by Month 6, though the release profiles remained within the acceptable dissolution specifications (≥85% at 60 minutes).

Long-Term Stability Testing (25°C ± 2°C / 60% RH ± 5%)

Drug content

Drug content remained above 94% for all APIs at 12 months, confirming acceptable chemical stability under room temperature conditions.

Dissolution Behavior

Release profiles remained stable over 12 months with no significant changes ($p > 0.05$), confirming formulation robustness. Both accelerated and long-term studies showed MUPS formulations maintained physical integrity, drug content, moisture resistance, and dissolution within ICH limits, ensuring efficacy and safety. Capsules were slightly more moisture-sensitive due to gelatin shells, while tablets showed better chemical stability. Significant degradation under accelerated conditions was noted for moisture-sensitive Saxagliptin ($p < 0.05$), but without critical impact on performance. Overall, the optimized MUPS formulations demonstrated satisfactory stability, supporting further clinical development and commercial scale-up with appropriate packaging and storage.

CONCLUSION

The present study successfully developed MUPS capsules and tablets containing coated pellets of Tolbutamide, Saxagliptin, and Verapamil, offering a promising multi-drug delivery system for the management of diabetes and hypertension. The use of coated pellets allowed for the individual control of drug release profiles, ensuring sustained and targeted delivery of each active ingredient. The formulated MUPS dosage forms demonstrated satisfactory physicochemical characteristics, mechanical strength, and consistent *in vitro* drug release profiles. This approach not only enhances patient compliance by reducing pill burden but also minimizes potential drug interactions and optimizes therapeutic efficacy. Overall, MUPS represents a viable and effective platform for fixed-dose combination therapy in chronic disease management, warranting further *in vivo* and clinical investigations.

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