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FORMULATION DEVELOPMENT AND IN-VITRO EVALUATION OF BILAYER TABLETS CONTAINING AMLODIPINE AND TOLBUTAMIDE FOR THE MANAGEMENT OF HYPERTENSION AND DIABETES MELLITUS

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ABSTRACT:

The present investigation was focused on formulation and in-vitro evaluation of a bilayer tablet of two different drugs like metaprolol and Tolbutamide working on metaprolol and Tolbutamide. The preformulation studies conducted on Amlodipine and Tolbutamide aimed to comprehensively assess various physicochemical properties and formulation considerations crucial for the development of effective pharmaceutical products. These studies encompassed organoleptic characterization, melting point determination, solubility studies, partition coefficient determination, FTIR spectroscopy analysis, and formulation studies. Organoleptic characterization revealed that both Amlodipine and Tolbutamide met the specifications outlined inthe Indian Pharmacopoeia (I.P.) monograph. They exhibited white to off-white crystalline powders with no discernible odor, ensuring their suitability for pharmaceutical use. The visual inspection of the drugs confirmed their physical attributes in alignment with industry standards. Melting point determination using the capillary fusion method provided valuable insights into the thermal behavior of the drugs. Amlodipine exhibited a melting point of 123°C, while Tolbutamide demonstrated a higher melting point of 169.5°C. These data are essential for understanding the drugs' behavior during formulation processes such as melting, solidification, and crystallization. Amlodipine and Tolbutamide's functional groups and molecular structures were clarified by FTIR spectroscopy research. The presence of distinctive peaks belonging toparticular functional groups was confirmed bythe spectra, assuring the identityand purity of the pharmaceuticals. The drug-excipient mixes' spectra showed no chemical interactions,indicatingthattheformulationswerecompatibleandthatthestabilityof the finished products was guaranteed. The development of Tolbutamide sustained- release tablets and Amlodipine immediate-release tablets was the main focus of formulation studies. For each formulation, a number of physical characteristics were assessed, including the bulk density, tapped density, Hausner ratio, Carr's index, and angleofrepose.Furthermore,researchonthedrugreleaseinvitroofferedinformation on the release characteristics of the tablets over time. All things considered, the preformulation research done on Tolbutamide and Amlodipine advances pharmaceutical science and creates novel drug delivery methods. To improve the formulations' stability, patient acceptance, and therapeutic efficacy, moreinvestigation and optimization work is necessary.

KEYWORDS: Amlodipine,Tolbutamide,Solubility,SustaindrugRelease

INTRODUCTION:

Hypertension and diabetes mellitus are among the most prevalent chronic diseases worldwide and frequently coexist in the same patient. The presence of both conditions significantly increases the risk of cardiovascular complications, including coronary artery disease, stroke, nephropathy, and other vascular disorders. Effective management of these comorbid conditions often requires the long-term administration of multiple medications, which may lead to poor patient compliance and reduced therapeutic outcomes.[1-4]

Bilayer tablet technology has emerged as a promising approach for the delivery of two drugs with different release characteristics within a single dosage form. This system enables the incorporation of an immediate-release layer and a sustained-release layer, thereby improving therapeutic efficacy, reducing dosing frequency, and enhancing patient adherence. Bilayer tablets are particularly beneficial in the treatment of chronic diseases that require combination therapy.[5-9]

Amlodipine, a calcium channel blocker, is widely prescribed for the treatment of hypertension due to its potent antihypertensive activity and favorable safety profile. Tolbutamide, a first-generation sulfonylurea, is used in the management of type 2 diabetes mellitus by stimulating insulin secretion from pancreatic β-cells. Combining these drugs in a single bilayer tablet offers a convenient strategy for the simultaneous management of hypertension and diabetes mellitus.[10-11]

In the present study, bilayer tablets containing immediate-release Amlodipine and sustained-release Tolbutamide were developed and evaluated. The objective was to formulate a stable and effective dosage form capable of providing rapid control of blood pressure along with prolonged glycemic management. The prepared formulations were subjected to pre-compression, post-compression, dissolution, compatibility, and stability studies to assess their pharmaceutical performance and suitability for combination therapy.

MATERIALS AND METHODS:

Materials:

Amlodipine and Tolbutamide were obtained from J.B. Chemicals Pvt. Ltd., Boisar. Different

grades of HPMC (E5, E6, E15, E50, K100M, and K4M), 2-hydroxypropyl β-cyclodextrin, sodium alginate, PEG 200, PEG 400, propylene glycol, and glycerol were used as excipients. Analytical-grade solvents and reagents, including methanol, ethanol, acetone, n-butanol, ethyl acetate, hydrochloric acid, sodium hydroxide, sodium chloride, phosphate salts, and other chemicals, were procured from reputed suppliers. All materials used in the study were of analytical grade and utilized without further purification.

Methodology:

Determination of Melting Point[12-14]

The melting points of Amlodipine and Tolbutamide were determined using the capillary method as per USP guidelines. A small quantity of each drug was filled into a sealed capillary tube and placed in a melting point apparatus. The temperature was gradually increased, and the temperatures at which melting started and completed were recorded.

Solubility Study[15-18]

The solubility of Amlodipine and Tolbutamide was evaluated in various organic solvents. Excess drug was added to 2 mL of each solvent and shaken at 37°C for 48 h. The samples were centrifuged, and the supernatant was diluted with methanol. Drug concentration was determined by UV spectrophotometry after scanning between 200–400 nm.

Determination of Partition Coefficient[19-22]

The partition coefficient of Amlodipine and Tolbutamide was determined using the shake-flask method with n-octanol and water as the organic and aqueous phases, respectively. The drug was equilibrated between the two phases at 37 ± 0.5°C. After separation of the layers, drug concentrations in each phase were measured using a UV-visible spectrophotometer. The partition coefficient (Log P) was calculated from the ratio of drug concentration in n-octanol to that in water.

Calibration Curve[23-28]

Selection of Wavelength

A standard stock solution of each drug was prepared in methanol and appropriately diluted to obtain working concentrations. The solutions were scanned in the UV region (200–400 nm) to determine the wavelength of maximum absorption (λmax).

Preparation of Standard Calibration Curve

Standard solutions of Amlodipine and Tolbutamide were prepared from the stock solution in the concentration range of 2–20 µg/mL. The absorbance of each solution was measured at the

respective λmax values, and calibration curves were plotted between concentration and absorbance to assess linearity.

Drug–Polymer Interaction Study[29-35]

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR analysis was performed to evaluate the compatibility between the drugs and excipients. Samples of pure drugs and drug–polymer mixtures were mixed with potassium bromide, compressed into pellets, and scanned over the range of 4000–400 cm^{-1} using an FTIR spectrophotometer. The obtained spectra were analyzed for any significant changes in characteristic peaks.

Differential Scanning Calorimetry (DSC)

DSC studies were carried out to investigate the thermal behavior and compatibility of Amlodipine, Tolbutamide, and their formulations. Approximately 5 mg of sample was sealed in an aluminum pan and scanned under a nitrogen atmosphere using a differential scanning calorimeter.

Formulation Development and Evaluation[36-45]

Formulation of Immediate-Release Amlodipine Tablets

Immediate-release Amlodipine tablets (F1–F9) were prepared by the direct compression method. The drug was blended with suitable excipients, including superdisintegrants, diluents, and lubricants, to obtain a uniform powder mixture. The blend was compressed into tablets using a tablet compression machine.

Formulation of Sustained-Release Tolbutamide Tablets

Sustained-release Tolbutamide tablets (F1–F12) were prepared by the wet granulation method. Tolbutamide was mixed with release-retarding polymers and excipients, followed by granulation using PVP K30 solution as a binder. The granules were dried, lubricated, and compressed into tablets. Different polymers and polymer combinations were evaluated to achieve the desired sustained-release profile.

Preparation of Bilayer Tablets[46-48]

The optimized immediate-release and sustained-release formulations were selected based on dissolution studies. Bilayer tablets were prepared by initially compressing the sustained-release Tolbutamide layer, followed by the addition of the immediate-release Amlodipine layer. Final compression was carried out to obtain bilayer tablets with adequate hardness and uniformity.

Pre-compression Evaluation of Powder Blend[49-51]

The prepared powder blends were evaluated for their flow and compression characteristics before tablet compression. Parameters such as bulk density, tapped density, Hausner's ratio, and angle of repose were determined using standard procedures. These studies were performed to assess the flowability and compressibility of the powder blends.

Post-compression Evaluation of Bilayer Tablets[51-58]

Hardness

The hardness of the bilayer tablets was determined using a Monsanto hardness tester. Tablets from each batch were randomly selected, and the crushing strength was recorded.

Friability

Friability was evaluated using a Roche friabilator. Pre-weighed tablets were subjected to 100 revolutions, and the percentage weight loss was calculated to assess tablet mechanical strength.

Weight Variation

Twenty tablets from each batch were individually weighed, and the average weight was calculated. The variation in tablet weight was determined according to pharmacopeial specifications.

Disintegration Study

The disintegration time of the immediate-release layer was determined using a USP disintegration apparatus operated at 37 ± 0.5°C in suitable dissolution media. The time required for complete disintegration was recorded.

***In-vitro* Dissolution Study**

The drug release behavior of the bilayer tablets was evaluated using a USP Type II (paddle) dissolution apparatus. Amlodipine release was studied in 0.1 N hydrochloric acid (pH 1.2), while Tolbutamide release was evaluated in phosphate buffer (pH 6.8) at 37 ± 0.5°C. Samples were withdrawn at predetermined intervals and analyzedspectrophotometrically to determine the cumulative drug release.

Stability Study

Accelerated stability studies were carried out to assess the physical stability and drug release characteristics of the optimized bilayer tablets. The formulations were stored at 40 ± 2°C and 75 ± 5% relative humidity for three months. Samples were periodically evaluated for hardness and *in-vitro* drug release to determine formulation stability.

RESULTS AND DISCUSSION:

Preformulation Studies

Preformulation studies were performed to evaluate the physicochemical properties of Amlodipine and Tolbutamide prior to formulation development. The melting point, solubility profile, partition coefficient, and UV spectroscopic characteristics were determined to confirm drug identity and suitability for bilayer tablet formulation.

Table 1: Preformulation Parameters of Amlodipine and Tolbutamide

Parameter	Amlodipine	Tolbutamide
Melting Point (°C)	123	169.5
Solubility in Water	Sparingly Soluble	Sparingly Soluble
Solubility in Ethanol	Soluble	Soluble
Solubility in Methanol	Soluble	Soluble
Solubility in Acetone	Soluble	Soluble
Solubility in Chloroform	Insoluble	Insoluble
Partition Coefficient (Log P)	1.56 ± 0.50	3.50 ± 0.10
λmax (nm)	224	308

The melting point values obtained for Amlodipine (123°C) and Tolbutamide (169.5°C) were found to be in agreement with the reported values, confirming the purity and identity of the drugs. Solubility studies revealed that both drugs were soluble in methanol, ethanol, and acetone, while exhibiting limited solubility in water and insolubility in chloroform. These findings aided in selecting suitable solvents for analytical and formulation studies.

The partition coefficient values indicated the lipophilic nature of both drugs, with Tolbutamide showing greater lipophilicity than Amlodipine. UV spectroscopic analysis showed maximum absorbance at 224 nm for Amlodipine and 308 nm for Tolbutamide, which were subsequently used for quantitative estimation during formulation evaluation.

Calibration Curve Studies

Calibration curves were constructed for both drugs in the concentration range of 2–10 µg/mL. A linear increase in absorbance was observed with increasing concentration, indicating compliance with Beer–Lambert's law.

Table 2: Calibration Data of Amlodipine and Tolbutamide

Concentration (µg/mL)	Amlodipine Absorbance	Tolbutamide Absorbance

0	0.000	0.000
2	0.050	0.045
4	0.099	0.088
6	0.139	0.133
8	0.193	0.185
10	0.248	0.245

The calibration plots of both drugs exhibited excellent linearity over the selected concentration range. Absorbance increased proportionally with concentration, confirming the suitability of the UV spectrophotometric method for quantitative drug estimation. The linear relationship obtained for both Amlodipine and Tolbutamide demonstrated the accuracy and reliability of the analytical method employed throughout the study.

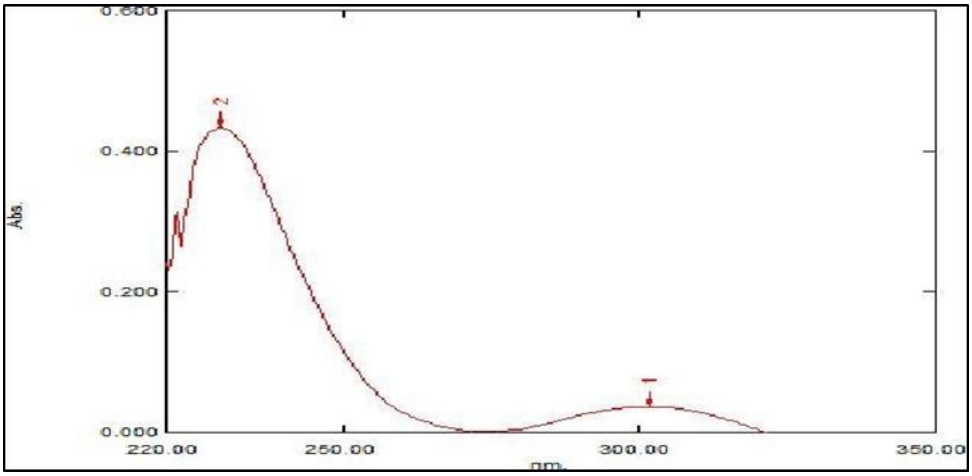

Figure 1: UV absorption spectrum of Amlodipine

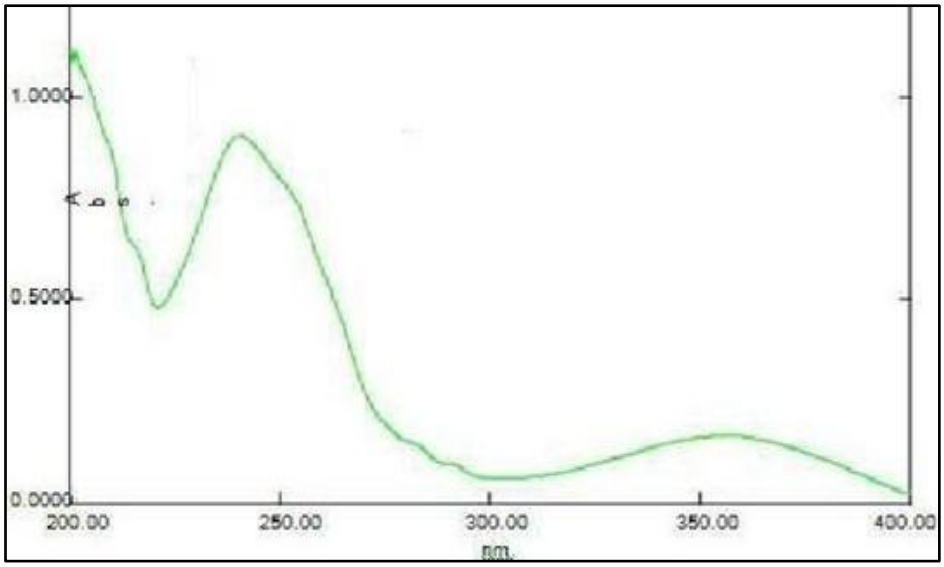

Figure 2: UV absorption spectrum of Tolbutamide

The results of the preformulation and analytical studies confirmed the purity, compatibility, and analytical suitability of both drugs for the development of bilayer tablets intended for the simultaneous management of hypertension and diabetes mellitus.

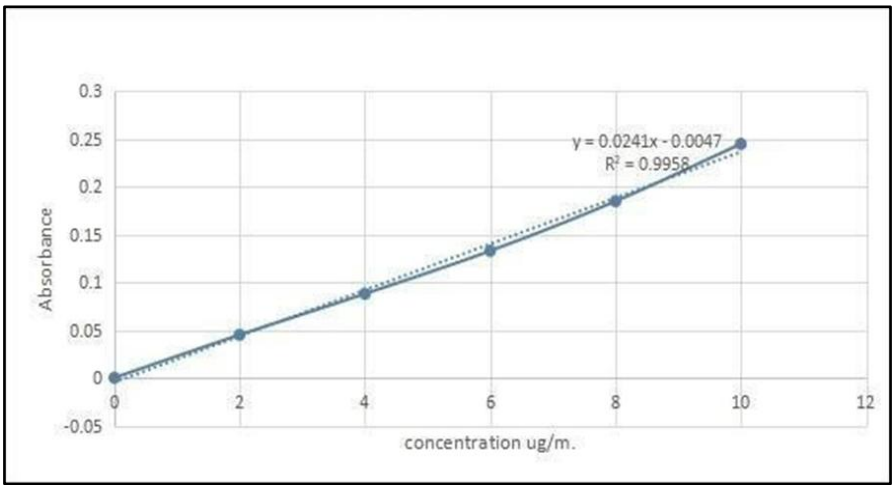

Figure3: calibrationcurve ofTolbutamide

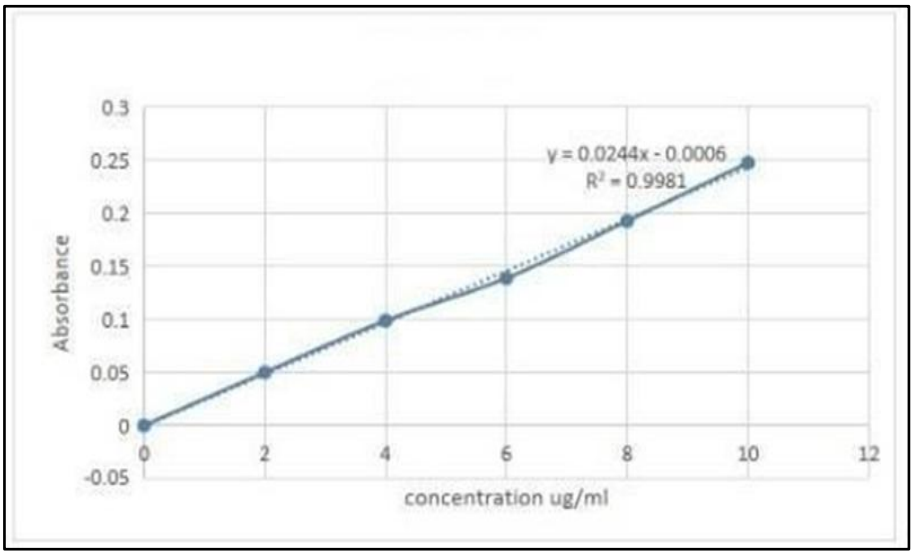

Figure4:calibration curveofAmlodipine

FT-IR Spectra:

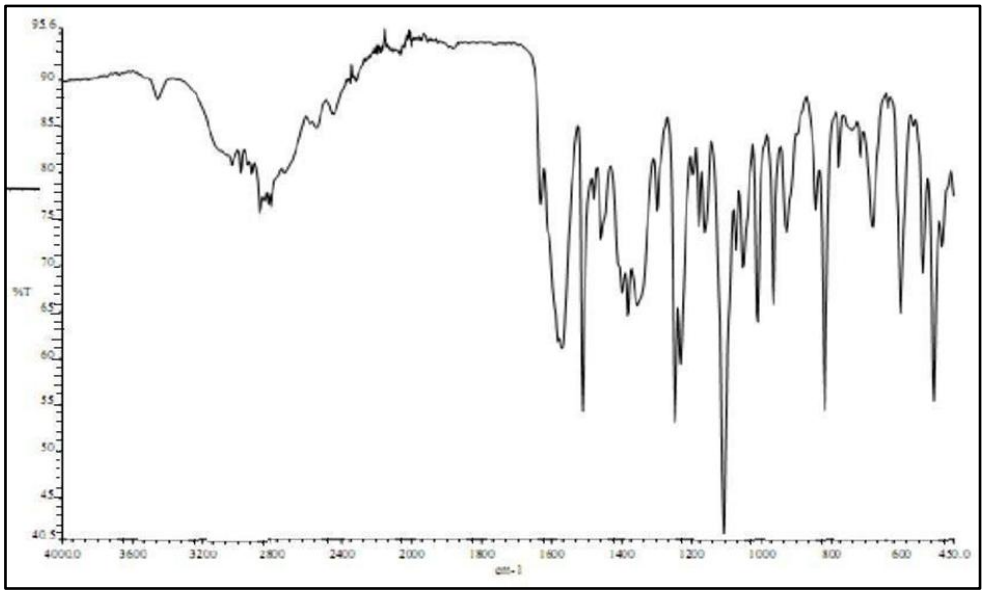

Figure5:FTIRSpectra ofPureAmlodipine

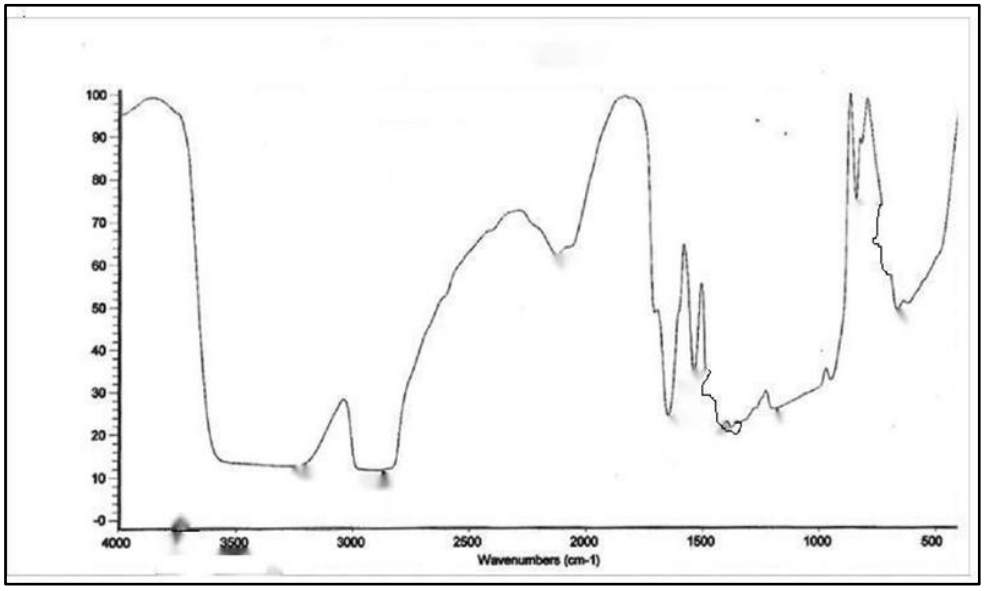

Figure6:FTIRSpectraofPureTolbutamide

Differential Scanning Calorimetry (DSC)

DSC analysis was performed to investigate the thermal behavior and compatibility of Amlodipine and Tolbutamide with the selected excipients. The thermogram of pure Amlodipine exhibited a sharp endothermic peak at approximately 123°C, corresponding to its melting point and confirming its crystalline nature. Similarly, pure Tolbutamide showed a characteristic endothermic peak at 172.99°C, indicating its crystalline structure and purity.

The DSC thermograms of drug-excipient mixtures displayed the characteristic melting peaks of both drugs with slight shifts and reduced peak intensity. No additional peaks or major

changes in thermal behavior were observed, indicating the absence of significant drug-excipient interactions. The results confirmed the compatibility of Amlodipine and Tolbutamide with the excipients used in the formulation.

Table 3: DSC Analysis

Sample	Endothermic Peak (°C)	Observation
Pure Amlodipine	123.0	Sharp characteristic melting peak observed
Amlodipine + Excipients	121.8–122.5	Slight peak shift with no significant interaction
Pure Tolbutamide	172.99	Sharp characteristic melting peak observed
Tolbutamide + Excipients	171.2–172.4	Minor peak shift with retained drug identity

The presence of characteristic melting endotherms of Amlodipine and Tolbutamide in the drug-excipient mixtures confirmed that both drugs remained stable during formulation. The minor shifts in peak temperature may be attributed to physical mixing and dilution effects of excipients rather than chemical incompatibility. Therefore, the DSC study demonstrated good compatibility between the drugs and selected formulation excipients, supporting their use in the development of bilayer tablets.

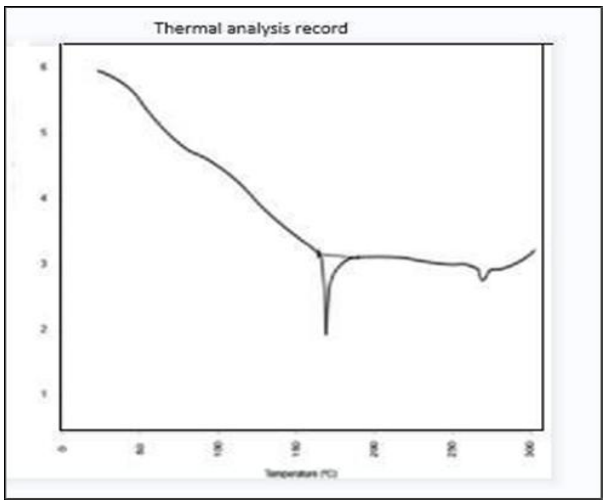

Figure7:DSCof Pure drugswithexcipients

Formulation Development of Amlodipine Immediate-Release Layer

Nine formulations (F1–F9) of the immediate-release Amlodipine layer were prepared by

direct compression using different superdisintegrants, namely crospovidone (CP), croscarmellose sodium (CCS), and sodium starch glycolate (SSG). The concentration of superdisintegrants was varied to evaluate their influence on tablet disintegration and drug release. Microcrystalline cellulose (MCC) was used as a diluent, magnesium stearate as a lubricant, and sodium lauryl sulfate (SLS) was incorporated in selected formulations to enhance wettability and dissolution. The total tablet weight was maintained at 150 mg for all batches.

Table4:CompositionofAmlodipine immediatereleasetablets(150mg)

IngredientinMg									
Batch Code	**Drug (mg)**	**MCC (mg)**	**CP (mg)**	**CCS (mg)**	**SSG (mg)**	**Mg. Stearate (mg)**	**SLS (mg)**	**Fe2O3 (mg)**	**Total**
F1	25	116	7.5	-	-	1.5	-	Qs	150
F2	25	108.5	15	-	-	1.5	-	Qs	150
F3	25	116	-	7.5	-	1.5	-	Qs	150
F4	25	108.5	-	15	-	1.5	-	Qs	150
F5	25	116	-	-	7.5	1.5	-	Qs	150
F6	25	108.5	-	-	15	1.5	-	Qs	150
F7	25	104.5	-	-	18.75	1.5	-	Qs	150
F8	25	116	-	-	7.5	1.5	0.3	Qs	150
F9	25	108.5	-	-	15	1.5	0.3	Qs	150

MCC: microcrystalline cellulose, CP: Crospovidone, CCS: Croscarmellose sodium, SSG:sodium starch glycolate, SLS: sodium lauryl sulfate

Different superdisintegrants were investigated to optimize the immediate-release behavior of Amlodipine. Formulations containing SSG and SLS were expected to exhibit faster tablet disintegration and improved drug dissolution due to enhanced swelling and wetting properties. The optimized formulation was selected based on subsequent post-compression and dissolution studies.

Formulation Development of Tolbutamide Sustained-Release Layer

The sustained-release layer containing Tolbutamide was developed using various hydrophilic polymers, including HPMC, guar gum, and xanthan gum, either alone or in combination. Ethyl cellulose was incorporated as a hydrophobic release-retarding polymer to prolong drug

release. Nine formulations (F1–F9) were prepared by varying the type and concentration of polymers while maintaining a constant tablet weight of 300 mg.

The sustained-release formulations were designed to evaluate the influence of different polymer matrices on the release profile of Tolbutamide. Increasing polymer concentration was expected to enhance matrix integrity and prolong drug release. Formulations containing a combination of HPMC and xanthan gum were anticipated to provide superior control over drug release due to synergistic swelling and gel-forming properties. The optimized formulation was selected based on dissolution performance and release kinetics studies.

Table 5:CompositionofTolbutamidesustainedreleasetablets

Ingredient in Mg											
Ingredient's	**Drug**	**HPMC**	**Guar Gum**	**X-Gum**	**EC**	**Mannitol**	**MCC**	**PV P**	**Mg. St.**	**Talc**	**TotalWt.**
F1	10	30	-	-	25	75	130	15	7.5	7.5	300
F2	10	45	-	-	25	75	115	15	7.5	7.5	300
F3	10	60	-	-	25	75	100	15	7.5	7.5	300
F4	10	-	30	-	25	75	130	15	7.5	7.5	300
F5	10	-	45	-	25	75	115	15	7.5	7.5	300
F6	10	-	60	-	25	75	100	15	7.5	7.5	300
F7	10	-	-	75	25	75	85	15	7.5	7.5	300
F8	10	-	-	75	25	75	85	15	7.5	7.5	300
F9	10	45	-	45	25	75	90	15	7.5	7.5	300

Evaluation of Pre-compression Parameters

The powder blends of Amlodipine and Tolbutamide formulations were evaluated for flow and compression characteristics before tablet compression. Parameters including bulk density, tapped density, Hausner's ratio, Carr's index, and angle of repose were determined. The results indicated satisfactory flowability and compressibility for all formulations, making them suitable for tablet manufacturing by direct compression.

Table 6: Pre-compression Parameters

Parameter	Amlodipine Blend (Range)	Tolbutamide Blend (Range)
Bulk Density (g/cm³)	0.34 – 0.60	0.32 – 0.63

Tapped Density (g/cm³)	0.55 – 0.76	0.52 – 0.75
Hausner's Ratio	0.91 – 1.27	0.89 – 1.28
Carr's Index (%)	11.05 – 16.35	10.97 – 16.27
Angle of Repose (°)	23.6 – 27.8	23.7 – 27.6

The angle of repose values below 30° and Hausner's ratio values close to 1.0 indicated good flow characteristics of the powder blends. Carr's index values were within acceptable limits, confirming satisfactory compressibility. Among the formulations, F5 exhibited the best flow properties for both drug blends, suggesting its suitability for uniform die filling and tablet compression.

Evaluation of Post-compression Parameters

The prepared bilayer tablets were evaluated for physical appearance, weight variation, hardness, thickness, friability, drug content, and disintegration time. All formulations complied with pharmacopeial requirements and demonstrated acceptable mechanical strength and uniformity.

Table 7: Post-compression Parameters of Bilayer Tablets

Parameter	Observed Range
Average Weight (mg)	299 – 305
Hardness (kg/cm²)	5.0 – 7.5
Thickness (mm)	3.5 – 5.2
Friability (%)	0.05 – 0.35
Drug Content (%)	95 – 104
Disintegration Time (min)	1.90 – 2.50

All formulations exhibited uniform tablet weight, indicating consistent die filling during compression. Hardness values were sufficient to withstand handling and transportation without compromising tablet integrity. Friability values remained below 1%, confirming excellent mechanical resistance. Drug content ranged from 95% to 104%, demonstrating uniform distribution of both drugs within the bilayer matrix. The disintegration time of all formulations was below 3 minutes, ensuring rapid release of the immediate-release layer.

Among the evaluated batches, formulation F6 demonstrated an optimal combination of hardness, friability, drug content, and rapid disintegration, while formulations F8 and F9 showed excellent drug content uniformity and satisfactory physical characteristics. Overall, the post-compression evaluation confirmed the successful development of bilayer tablets

possessing desirable pharmaceutical properties for the combined management of hypertension and diabetes mellitus.

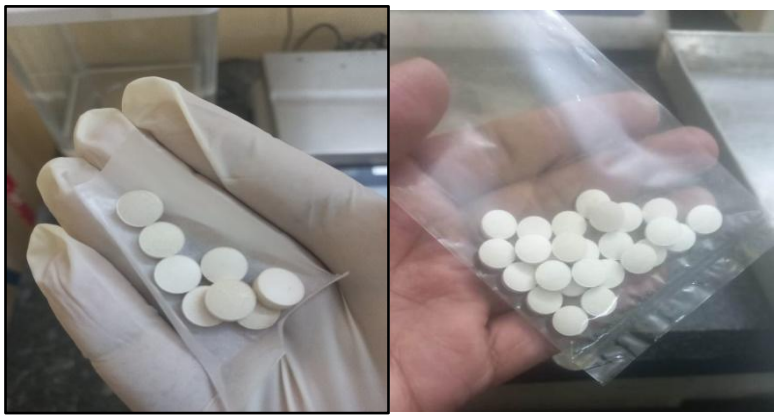

Figure 8: Prepared bilayer tablet containing Amlodipine and Tolbutamide.

***In-vitro* Drug Release Study of Amlodipine Immediate-Release Layer**

The in-vitro dissolution study of Amlodipine immediate-release tablets demonstrated rapid drug release from all formulations. Drug release increased progressively with time and exceeded 65% within 30 minutes for all batches, confirming the suitability of the formulations as immediate-release dosage forms.

Among all formulations, F6 exhibited the highest drug release (95.95%) within 30 minutes, followed by F1 (93.41%), F5 (90.57%), and F3 (90.54%). The enhanced release from F6 may be attributed to the optimized concentration of superdisintegrant, resulting in rapid tablet disintegration and dissolution. Formulations F2 and F7 showed comparatively slower release; however, they still met the requirements for immediate-release dosage forms. Based on the dissolution profile, formulation F6 was considered the optimized immediate-release layer for Amlodipine.

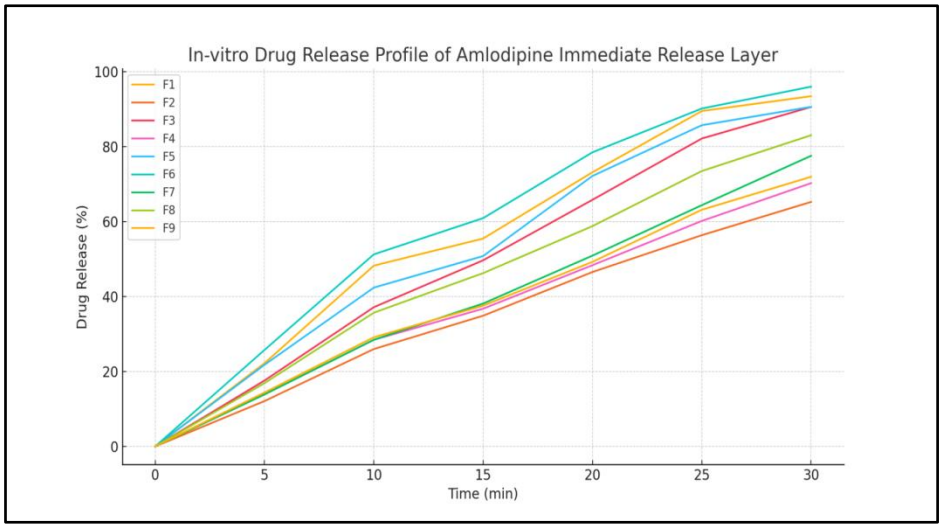

Figure 9:Comparative dissolution profile of Amlodipine immediate-release formulations

***In-vitro* Drug Release Study of Tolbutamide Sustained-Release Layer**

The dissolution study of the Tolbutamide sustained-release formulations was conducted over a period of 7 hours. All formulations exhibited a controlled and prolonged drug release pattern, indicating the effectiveness of the polymeric matrix system.

The sustained-release formulations successfully prolonged drug release over the study period. Formulations F9 and F2 exhibited the highest cumulative release (97%) at 7 hours, while F6 and F8 showed 96% release. The controlled release behavior can be attributed to the swelling and gel-forming properties of HPMC and xanthan gum, which effectively regulated drug diffusion from the matrix. Formulation F9, containing a combination of HPMC and xanthan gum, demonstrated the most desirable sustained-release profile and was selected as the optimized Tolbutamide sustained-release layer.

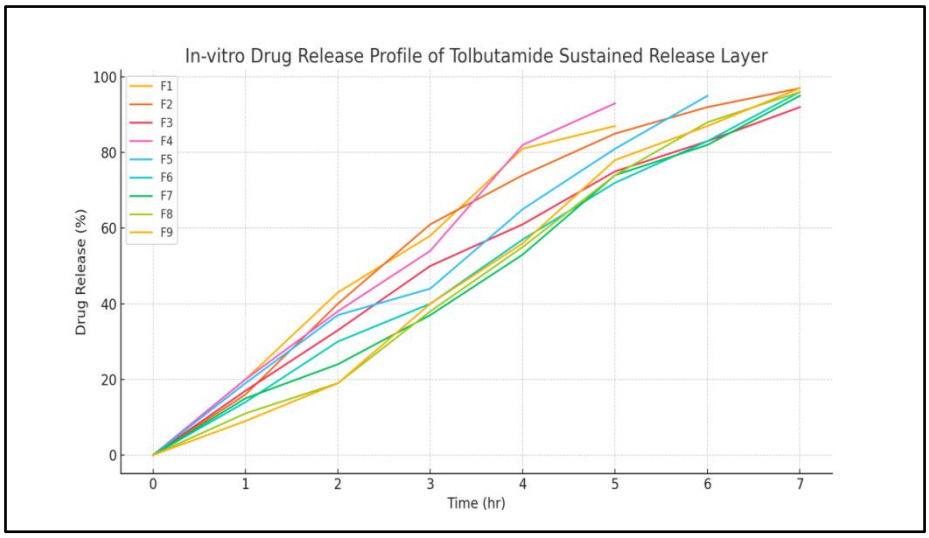

Figure 10:Comparative dissolution profile of Tolbutamide sustained-release formulations.

Stability Studies

The optimized bilayer tablets were subjected to accelerated stability studies to evaluate the effect of storage conditions on their physical properties and drug release behavior. The tablets were stored under specified temperature and humidity conditions and analyzed periodically for hardness, drug content, friability, and dissolution characteristics.

Table 8: Stability Study

Parameter	Initial	3rd Month
Hardness (kg/cm²)	5.16 ± 0.033	5.10 ± 0.019

Drug Content (%)	99.98 ± 0.50	98.86 ± 0.20
Friability (%)	0.24 ± 0.016	0.22 ± 0.012
Drug Release (%)	98.97	97.12

The stability study revealed no significant changes in the physical appearance, hardness, friability, drug content, or dissolution profile of the optimized bilayer tablets during the storage period. Drug content remained above 98%, while drug release was maintained above 97%, indicating excellent formulation stability. These findings confirm that the developed bilayer tablets retained their quality, efficacy, and performance throughout the study period and are suitable for long-term storage.

Overall, dissolution studies identified F6 as the optimized immediate-release Amlodipine formulation and F9 as the optimized sustained-release Tolbutamide formulation. The bilayer tablet prepared using these optimized layers demonstrated satisfactory stability and pharmaceutical performance for the combined management of hypertension and diabetes mellitus.

CONCLUSION:

The present study successfully developed and evaluated bilayer tablets containing Amlodipine and Tolbutamide for the simultaneous management of hypertension and diabetes mellitus. Preformulation studies confirmed the purity, compatibility, and suitability of both drugs for formulation development. FTIR and DSC analyses revealed no significant drug-excipient interactions, indicating the stability of the selected formulation components.The immediate-release layer of Amlodipine was successfully formulated using different superdisintegrants, while the sustained-release layer of Tolbutamide was developed using various polymeric matrices. All formulations exhibited satisfactory pre-compression and post-compression characteristics, including acceptable flow properties, hardness, friability, drug content uniformity, and disintegration time.Among the immediate-release formulations, batch F6 demonstrated the highest drug release (95.95% within 30 minutes) and was identified as the optimized Amlodipine formulation. For the sustained-release layer, formulation F9 containing a combination of HPMC and xanthan gum exhibited the most desirable controlled-release profile, achieving 97% drug release over 7 hours. The optimized bilayer tablet prepared using these formulations showed excellent physicochemical properties and satisfactory *in-vitro* performance.Furthermore, stability studies confirmed that the optimized bilayer tablets remained stable throughout the study period without significant

changes in hardness, friability, drug content, or dissolution behavior. Overall, the developed bilayer tablet offers a promising approach for combined therapy in patients suffering from both hypertension and diabetes mellitus by providing immediate antihypertensive action along with sustained antidiabetic drug release, potentially improving therapeutic efficacy, patient compliance, and treatment outcomes.

CONFLICTS OF INTERESTS:

All authors have declared no conflict of interest.

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