International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 22s, 2025
https://theaspd.com/index.php

Formulation and in Vitro Evaluation of Chlorpropamide Immediate-Release Tablets Using Superdisintegrants for Enhanced Glycemic Control in Type 2 Diabetes Mellitus

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Abstract

The present study focuses on the development and evaluation of immediate-release (IR) tablets of chlorpropamide, a first-generation sulfonylurea, aimed at achieving rapid glycemic control in patients with Type 2 Diabetes Mellitus (T2DM). Utilizing a 3×3 factorial design, nine formulations (C1–C9) were prepared using three different superdisintegrants sodium starch glycolate (SSG), croscarmellose sodium (CCS), and crospovidone (CP) each at varying concentrations (25, 50, and 75 mg). The formulations were evaluated for pre- and post-compression parameters including flow properties, hardness, friability, drug content uniformity, disintegration time, and in vitro drug release. Among all, formulation C4, containing 25 mg of CCS, demonstrated optimal performance with the shortest disintegration time (35 seconds) and the highest cumulative drug release (99.67%) at 60 minutes. FTIR studies confirmed the absence of chemical interactions between the drug and excipients. The calibration curve of chlorpropamide showed excellent linearity (R^2 = 0.999) at 240 nm in pH 6.8 phosphate buffer. The findings highlight the potential of CCS at optimal concentration in enhancing the performance of chlorpropamide IR tablets, thereby offering a promising approach for improved therapeutic management of T2DM.

Keywords: *Chlorpropamide; Immediate-release tablets; Superdisintegrants; Type 2 Diabetes Mellitus; In vitro drug release.*

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized primarily by insulin resistance and a progressive decline in pancreatic β-cell function, resulting in elevated blood glucose levels [1]. It represents a significant global health burden, accounting for the majority of diabetes cases worldwide. The prevalence of T2DM has surged due to sedentary lifestyles, unhealthy dietary habits, genetic predisposition, and aging populations [2]. Chronic hyperglycemia associated with T2DM can lead to serious microvascular complications such as nephropathy, neuropathy, and retinopathy, as well as macrovascular complications like cardiovascular disease and stroke [3]. Consequently, maintaining optimal glycemic control is essential not only for reducing symptoms and improving quality of life but

also for preventing or delaying long-term complications. Pharmacological intervention forms a critical part of diabetes management, especially when lifestyle modifications fail to maintain glycemic targets. Among the pharmacotherapeutic agents used for T2DM, chlorpropamide holds clinical significance as one of the first-generation sulfonylureas [4]. It functions by stimulating insulin secretion from the pancreatic β-cells, thereby lowering blood glucose concentrations. Chlorpropamide binds to the sulfonylurea receptor (SUR1) on the β-cell membrane, causing closure of ATP-sensitive potassium channels. This leads to cell membrane depolarization and subsequent opening of voltage-gated calcium channels, promoting calcium influx [5]. The increased intracellular calcium levels then trigger insulin granule exocytosis, enhancing insulin availability in the bloodstream. Although chlorpropamide is effective and has a long duration of action, its use has diminished in favor of newer agents due to its potential to cause prolonged hypoglycemia, especially in elderly patients [6]. Nonetheless, its pharmacodynamic profile makes it a suitable candidate for immediate-release (IR) formulations to ensure rapid therapeutic onset and minimize dosing-related complications. Despite the therapeutic benefits, conventional oral dosage forms of chlorpropamide often face limitations that compromise treatment outcomes. These include delayed drug release and absorption, leading to a slow onset of action and variable bioavailability [7]. In T2DM management, achieving a quick reduction in postprandial glucose spikes is crucial. Conventional tablets may not dissolve quickly enough to meet this pharmacokinetic need, especially in patients with delayed gastric emptying. Additionally, many traditional formulations require higher doses or frequent administration to achieve and maintain therapeutic levels, which can negatively impact patient compliance [8]. Non-adherence to prescribed therapy is a significant concern in chronic diseases like diabetes, often resulting from complex dosing regimens, tablet size, and delayed symptom relief. Therefore, innovations in drug delivery systems that enhance the speed and efficiency of drug release are crucial to address these challenges [9]. Immediate-release (IR) formulations are specifically designed to disintegrate and release their active pharmaceutical ingredients promptly after administration [10]. These dosage forms facilitate quick absorption in the gastrointestinal tract, offering faster onset of action compared to conventional tablets. In the context of chlorpropamide, developing an IR formulation can significantly enhance its therapeutic effect by enabling rapid control of blood glucose levels [11]. This is especially beneficial in situations where quick glycemic correction is required, such as after meals. Moreover, IR tablets can improve patient compliance by reducing dosing frequency and minimizing the risk of prolonged hypoglycemia associated with slow drug release. Formulating chlorpropamide as an IR tablet aligns with the broader goals of modern diabetes care, which emphasize personalized treatment, swift symptom control, and better adherence to therapy [12]. A critical factor in the success of IR tablets is the use of superdisintegrants specialized excipients that facilitate rapid tablet disintegration upon contact with gastrointestinal fluids. Superdisintegrants work primarily through three mechanisms: swelling, wicking (capillary action), and deformation [13]. Their inclusion in the tablet matrix allows the dosage form to break apart quickly, thereby increasing the surface area available for drug dissolution and absorption. In this study, three commonly used superdisintegrants sodium starch glycolate (SSG), croscarmellose sodium (CCS), and crospovidone (CP) are explored for their ability to enhance chlorpropamide tablet performance. SSG swells upon hydration, creating internal pressure that breaks the tablet apart. CCS employs both swelling and wicking mechanisms, allowing it to disintegrate tablets rapidly even at low concentrations [14]. CP, known for its porous structure, primarily acts through wicking and deformation, offering quick disintegration and minimal gelling effect. Each of these superdisintegrants offers unique physicochemical properties that can significantly influence tablet dissolution profiles, making their selection and optimization vital to the success of an IR formulation.

2.MATERIALS AND METHODS

2.1 Materials

The present study involved the formulation of immediate-release tablets of chlorpropamide using various pharmaceutical excipients, all of which were of analytical grade and used as received without further purification. Chlorpropamide, a first-generation sulfonylurea class antidiabetic drug, was employed as the active pharmaceutical ingredient (API) due to its potent insulin-secretagogue activity, making it suitable for managing type 2 diabetes mellitus. To achieve rapid tablet disintegration and drug release, three different superdisintegrants were incorporated in varying concentrations: Sodium Starch Glycolate (SSG), Croscarmellose Sodium (CCS), and Crospovidone (CP). These excipients were selected based on their distinct physicochemical properties and mechanisms of action swelling, wicking, and capillary

activity which are known to enhance the disintegration profile of oral solid dosage forms. Additional excipients used in the formulation included Avicel PH 102 (microcrystalline cellulose) as a direct compression filler and binder to improve tablet compressibility and mechanical strength. Mannitol, a non-hygroscopic polyol, was used as a diluent to provide bulk and improve the mouthfeel and solubility of the final dosage form. To ensure smooth processing during tablet manufacture, Magnesium Stearate was added as a lubricant, while Talc served as a glidant to improve powder flow properties. All materials were procured from reputed suppliers to ensure consistency and reliability in formulation development. Chlorpropamide was obtained from SURA LABS, Dilsukhnagar, Hyderabad. The superdisintegrants (SSG, CCS, and CP), as well as Avicel PH 102, mannitol, magnesium stearate, and talc, were all sourced from Merck Specialities Pvt. Ltd., India .

2.2Formulation Design

The immediate-release tablets of chlorpropamide were developed using the direct compression method, owing to its simplicity, cost-effectiveness, and suitability for moisture-sensitive drugs. To evaluate the effect of different superdisintegrants on disintegration and drug release, a total of nine formulations were designed based on a 3 × 3 factorial design**,** where three superdisintegrants Sodium Starch Glycolate (SSG)**,** Croscarmellose Sodium (CCS)**,** and Crospovidone (CP) were used individually at three concentration levels (25 mg, 50 mg, and 75 mg). This experimental design facilitated a systematic evaluation of how varying the type and concentration of superdisintegrant influenced the performance of the tablets.

All formulations were prepared by mixing the active pharmaceutical ingredient (chlorpropamide) with selected quantities of superdisintegrants, along with other common excipients such as Avicel PH 102 (binder), mannitol (diluent), magnesium stearate (lubricant), and talc (glidant). The powder blends were mixed uniformly and compressed into tablets of 250 mg each using a rotary compression machine under constant compression force[15]. The composition of the nine formulations (C1 to C9) is detailed in Table 1 below:

Table 1: Formulation Design for Chlorpropamide Immediate-Release Tablets Using Superdisintegrants

Formulation Code	**Chlorpropamide (mg)**	**SSG (mg)**	**CCS (mg)**	**CP (mg)**	**Avicel PH102 (mg)**	**Mannitol (mg)**	**Talc (mg)**	**Magnesium Stearate (mg)**	**Total Weight (mg)**
C1	50	25	–	–	12	151	6	6	250
C2	50	50	–	–	12	126	6	6	250
C3	50	75	–	–	12	101	6	6	250
C4	50	–	25	–	12	151	6	6	250
C5	50	–	50	–	12	126	6	6	250
C6	50	–	75	–	12	101	6	6	250
C7	50	–	–	25	12	151	6	6	250
C8	50	–	–	50	12	126	6	6	250
C9	50	–	–	75	12	101	6	6	250

2.3 Evaluation of Powder Blend (Pre-compression)

Prior to tablet compression, the prepared powder blends of all nine formulations (C1–C9) were subjected to pre-compression evaluation to assess their flow and packing properties, which are critical for ensuring uniform die filling and consistent tablet weight during the direct compression process. The evaluated parameters included angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio. These parameters provide insight into the flow characteristics and compressibility of the powder blend, both of which are essential for large-scale tablet manufacturing [16].

Angle of Repose (θ)

The angle of repose is an indirect measure of the flowability of the powder blend. It was determined by allowing the powder to flow through a funnel fixed at a constant height, forming a cone on a flat surface. The height (h) and radius (r) of the cone were measured, and the angle was calculated using the formula:

$$\theta = \tan^{-1}(h/r) \qquad \text{Eq.1}$$

An angle less than 30° indicates good flow, while angles above 40° suggest poor flowability.

Bulk Density and Tapped Density

Bulk density (ρb) was measured by gently pouring a known quantity of powder into a graduated cylinder and recording the volume occupied. Tapped density (ρt) was obtained by mechanically tapping the cylinder 100 times and noting the reduced volume. These densities are used to assess powder packing ability [17].

Bulk Density=Mass of Powder/Bulk Volume Eq.2

Tapped Density=Mass of Powder/Tapped Volume Eq.3

Carr's Index (%)

Carr's Compressibility Index is calculated from the bulk and tapped densities to evaluate compressibility:

Carr's Index=(ρt−ρb/ρt)×100 Eq.4

Values below 15% indicate excellent flow, while values above 25% suggest poor flow.

Hausner's Ratio

Hausner's Ratio is another index of powder flowability and is calculated as:

Hausner's Ratio=ρt/ρb Eq.5

A value between 1.0 and 1.25 indicates good flowability; values greater than 1.40 reflect very poor flow [18-20].

3.RESULTS AND DISCUSSION

3.1Pre-compression Parameters

The flow properties of all formulations (C1–C9) are summarized in **Table 2** below:

Table 2: Pre-compression Evaluation of Powder Blends (Formulations C1–C9)

Formulation Code	Angle of Repose (°)	Bulk Density (g/cm³)	Tapped Density (g/cm³)	Carr's Index (%)	Hausner's Ratio
C1	24.51 ± 0.34	0.516 ± 0.011	0.677 ± 0.005	23.80 ± 1.63	1.31 ± 0.03
C2	26.76 ± 0.31	0.510 ± 0.007	0.615 ± 0.012	17.01 ± 0.84	1.21 ± 0.01
C3	26.46 ± 0.36	0.492 ± 0.007	0.605 ± 0.001	18.63 ± 1.09	1.23 ± 0.02
C4	28.76 ± 0.77	0.504 ± 0.008	0.638 ± 0.015	21.01 ± 0.28	1.27 ± 0.00
C5	29.65 ± 0.44	0.385 ± 0.003	0.499 ± 0.004	22.82 ± 0.68	1.30 ± 0.01
C6	27.75 ± 0.30	0.366 ± 0.004	0.481 ± 0.004	23.81 ± 0.75	1.31 ± 0.01
C7	27.41 ± 0.33	0.436 ± 0.003	0.578 ± 0.003	24.67 ± 0.71	1.33 ± 0.01
C8	30.63 ± 0.21	0.328 ± 0.001	0.471 ± 0.005	20.80 ± 0.66	1.26 ± 0.01
C9	30.76 ± 0.32	0.353 ± 0.002	0.484 ± 0.004	27.16 ± 1.04	1.37 ± 0.02

1. Angle of Repose

The angle of repose for all nine formulations ranged from 24.51° (C1) to 30.76° (C9). Formulations C1 to C4 exhibited values below 30°, which indicates excellent to good flow properties, making them suitable for direct compression. However, C8 and C9 had angle values slightly above 30°, suggesting passable flow, which may require additional processing aids if scaled up. Overall, all formulations displayed acceptable flow behavior within pharmaceutically acceptable limits.

2. Bulk Density

Bulk density values ranged from **0.328 g/cm³ (C8)** to **0.516 g/cm³ (C1)**. Higher bulk density implies better packing ability. Formulations **C1 to C4** showed relatively higher bulk densities, indicating denser and more compactible powder blends, beneficial for uniform die filling. In contrast, **C8 and C9** had lower bulk densities, possibly due to the loose and porous nature of crospovidone at higher concentrations.

3. Tapped Density

Tapped density values were observed between **0.471 g/cm³ (C8)** and **0.677 g/cm³ (C1)**. Formulations with higher tapped density (e.g., **C1, C4)** tend to settle better during tapping, suggesting good compressibility. **C8 and C9**, with lower tapped densities, may be prone to inconsistent filling and require improved blend homogeneity or glidant optimization during scale-up.

4. Carr's Index

Carr's Index (Compressibility Index) values ranged from 17.01% (C2) to 27.16% (C9). Carr's Index below 20% generally indicates good compressibility and flow, while values above 25% suggest poor to fair flowability. Formulations C2, C3, and C4 showed excellent compressibility with values between 17–21%. In contrast, C9 displayed the highest Carr's Index at 27.16%, reflecting reduced flowability, which may be attributed to a higher amount of crospovidone, known for its elastic and bulky nature.

5. Hausner's Ratio

Hausner's Ratio values across the formulations ranged from 1.21 (C2) to 1.37 (C9). Values below 1.25 are indicative of excellent to good flow, while values above 1.30 suggest poor to marginal flowability. C2 and C3 had the most favorable Hausner's Ratios (1.21–1.23), reinforcing their suitability for direct compression. C9 showed the least favorable ratio at 1.37, again likely due to the cohesive and poorly flowing nature of crospovidone at a high concentration.

3.2 FTIR spectra

The FTIR spectra of pure chlorpropamide and the optimized formulation (C4) were analyzed to assess potential interactions between the drug and excipients used in the tablet formulation. In the spectrum of pure chlorpropamide, distinct and well-defined absorption peaks were observed at characteristic wavenumbers corresponding to specific functional groups. A broad peak around 3300–3400 cm^{-1} represents N–H stretching vibrations of the sulfonylurea moiety. A strong peak observed near 1700–1720 cm^{-1} corresponds to C=O stretching vibrations, while bands at 1150–1200 cm^{-1} are indicative of S=O stretching, confirming the presence of sulfonyl functional groups. These peaks are essential fingerprint regions for chlorpropamide. In the FTIR spectrum of the optimized formulation (C4), which contains chlorpropamide along with CCS, Avicel PH102, mannitol, talc, and magnesium stearate, all major characteristic peaks of the pure drug were retained with minimal to no shift in wavenumber and no disappearance of significant functional groups. This indicates the absence of any chemical interaction or incompatibility between the drug and the excipients. Additionally, no new peaks were observed in the C4 spectrum that would suggest the formation of degradation products or new chemical bonds. The similarity in spectral patterns confirms that the excipients used in the formulation are physically and chemically compatible with chlorpropamide. Hence, the FTIR analysis validates that chlorpropamide maintains its structural integrity in the final tablet formulation and is stable in the presence of selected excipients, supporting the overall safety and effectiveness of the developed immediate-release tablets.

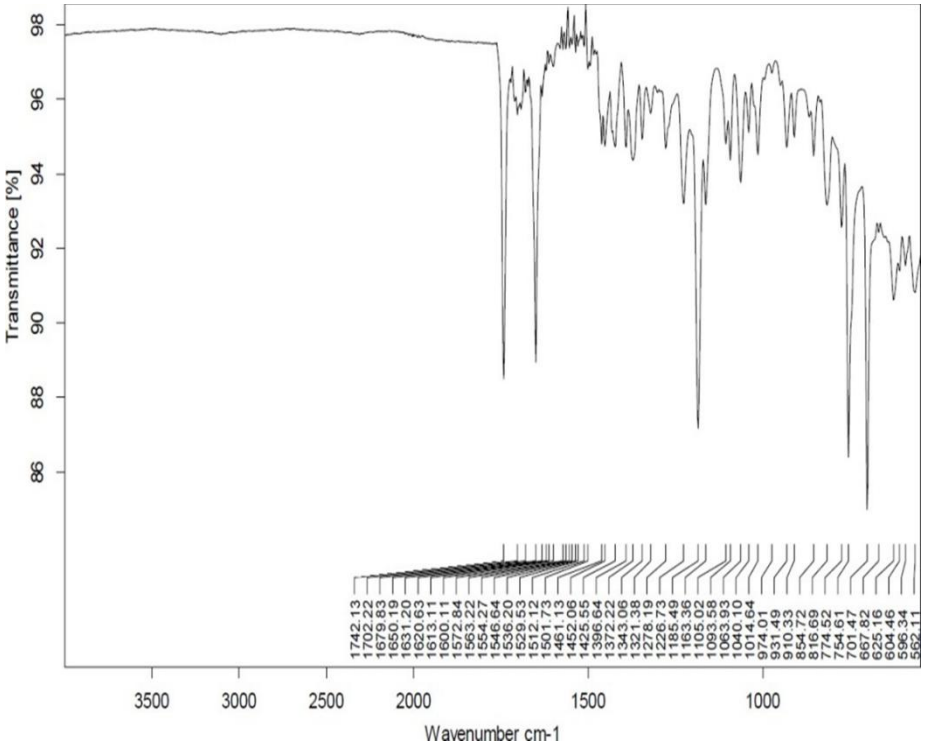

Figure 1: FTIR Spectrum of Pure Chlorpropamide

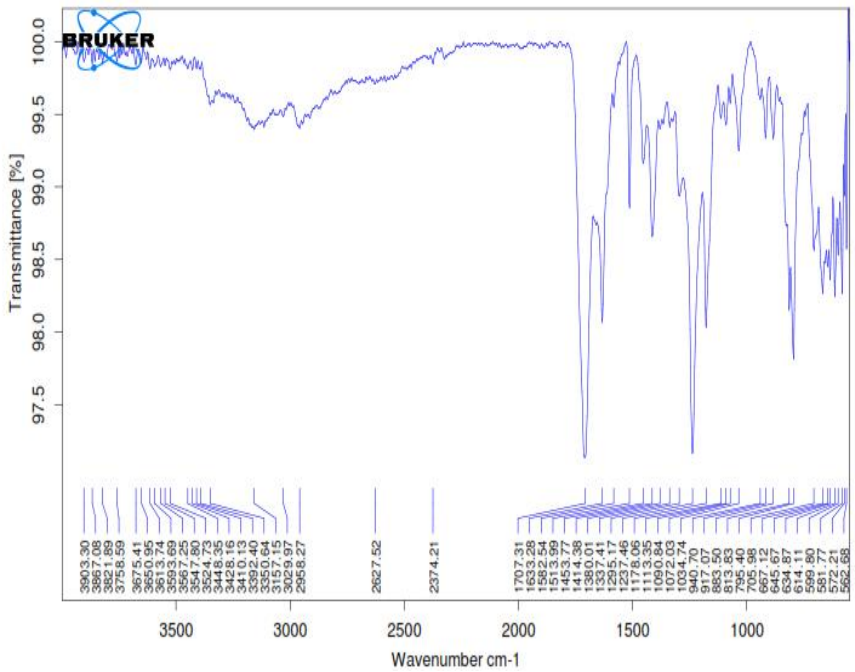

Figure 2: FTIR Spectrum of Optimized Formulation (C4)

3.3 Evaluation of Tablets (Post-compression)

All nine formulations (C1 to C9) of chlorpropamide immediate-release tablets were subjected to comprehensive post-compression evaluation to ensure they conformed to standard pharmacopeial specifications. The following parameters were assessed: weight variation, tablet thickness, hardness, friability, drug content uniformity, disintegration time, and in vitro drug release profile. These quality attributes are essential indicators of a tablet's mechanical integrity, uniformity, performance, and patient acceptability.

3.3.1 Physical Evaluation

The physical characteristics of the compressed tablets are summarized in **Table 3**.

Table 3: Post-compression Evaluation of Chlorpropamide IR Tablets (C1–C9)

Formulation Code	Weight Variation (mg)	Thickness (cm)	Hardness (kg/cm²)	Friability (%)	Drug Content (%)	Disintegration Time (sec)
C1	248.33	3.54	4.66	0.63	98.24	56
C2	247.68	3.68	4.59	0.49	99.35	49
C3	251.28	3.43	4.83	0.51	97.83	58
C4	250.89	3.12	3.72	0.44	99.75	35
C5	249.14	3.77	4.28	0.72	98.89	57
C6	247.89	3.26	4.53	0.53	97.35	52
C7	255.67	3.88	3.91	0.65	98.37	44
C8	251.39	3.57	4.12	0.53	99.12	53
C9	249.12	3.22	4.53	0.66	99.53	49

1. Weight Variation

The tablet weights for all nine formulations ranged between 247.68 mg (C2) and 255.67 mg (C7). These values fall within the permissible limits of ±5% for tablets weighing more than 250 mg, as per pharmacopeial guidelines. The minimal deviation in tablet weight across formulations indicates uniform die filling during compression, which is essential for dose accuracy and content uniformity. No formulation exhibited unacceptable weight fluctuation, confirming consistent powder flow and good compressibility of the blends.

2. Thickness

The thickness of the tablets varied from 3.12 cm (C4) to 3.88 cm (C7). Although slight variations were observed, they remained within acceptable pharmaceutical limits. The observed differences are likely due

to changes in powder bulk properties and the nature of the superdisintegrant used. For example, C4, which contained CCS (25 mg), produced the thinnest tablets, reflecting tighter packing. In contrast, C7, which included CP (25 mg), yielded thicker tablets, likely due to the porous nature of crospovidone affecting the blend's compressibility.

3. Hardness

Tablet hardness is critical for ensuring mechanical strength during handling, storage, and transportation. The hardness across formulations ranged from 3.72 kg/cm² (C4) to 4.83 kg/cm² (C3). All tablets exhibited sufficient hardness (≥3.5 kg/cm²), indicating they can withstand physical stress without breaking. Notably, C4 had the lowest hardness, which is favorable for fast disintegration and rapid drug release, aligning with its performance as the optimized formulation. In contrast, C3 (75 mg SSG) showed the highest hardness, which may have slightly delayed its disintegration.

4. Friability

Friability values ranged from **0.44% (C4)** to **0.72% (C5)**, all below the pharmacopeial limit of **1%**, demonstrating that the tablets possessed adequate resistance to abrasion and mechanical shock. The **lowest friability in C4** is particularly notable because it correlates with the shortest disintegration time and high dissolution, suggesting that **mechanical strength was achieved without compromising disintegration**. Even in formulations with higher concentrations of disintegrants (e.g., C3, C6, and C9), friability remained within acceptable limits, confirming the structural integrity of the tablets.

5. Drug Content Uniformity

The drug content in all formulations ranged from 97.35% (C6) to 99.75% (C4). According to pharmacopeial specifications, the acceptable range for content uniformity is 90% to 110%. All formulations complied with this requirement, indicating accurate dosing and homogeneous distribution of chlorpropamide in the tablet mass. Formulation C4 again emerged as the best, showing the highest drug content and minimal variation, which reflects good mixing efficiency and blend uniformity during pre-compression processing.

3.3.2 FTIR Compatibility Study

To assess the compatibility between chlorpropamide and the excipients used in the formulation, Fourier Transform Infrared (FTIR) spectroscopy was employed. This technique helps detect potential chemical interactions by identifying changes in the characteristic functional groups of the drug when combined with excipients. The analysis was performed using a Bruker FTIR spectrophotometer (Germany) via the potassium bromide (KBr) pellet method. Samples were prepared by mixing approximately 1–2 mg of chlorpropamide with 100–150 mg of dry, IR-grade KBr and compressing the mixture into a transparent pellet using a hydraulic press. Similar pellets were prepared for each individual excipient—Sodium Starch Glycolate (SSG), Croscarmellose Sodium (CCS), Crospovidone (CP), Avicel PH102, Mannitol, Talc, and Magnesium Stearate—as well as for the optimized formulation blend (C4). The spectra were recorded in the scanning range of 4000–400 cm^{-1} with a resolution of 4 cm^{-1}. The obtained FTIR spectra were then analyzed for characteristic peaks of chlorpropamide and checked for any significant shifts, disappearance, or appearance of new peaks, which would indicate possible physicochemical interactions. The absence of such changes would confirm the compatibility of the drug with the selected excipients.

3.3.3. Disintegration Time

Disintegration time is a key parameter for immediate-release formulations. It ranged from 35 seconds (C4) to 58 seconds (C3). C4, containing 25 mg of CCS, disintegrated the fastest, followed by C7 (44 sec) and C2 (49 sec). The superior performance of C4 can be attributed to croscarmellose sodium's dual mechanism swelling and wicking leading to rapid tablet breakup. On the other hand, C3, which had a higher concentration of SSG (75 mg), exhibited slower disintegration (58 seconds), likely due to the formation of a viscous gel barrier that temporarily delays tablet breakup despite high swelling.

3.3.4 Calibration Curve

To quantify the amount of chlorpropamide released during the in vitro drug release study, a standard calibration curve was constructed by measuring the absorbance of chlorpropamide at various known concentrations using a UV-Visible spectrophotometer.

3.3.5 Preparation of Standard Solution

A stock solution of chlorpropamide was prepared by dissolving 100 mg of chlorpropamide in a small volume of phosphate buffer (pH 6.8) and diluting it to 100 mL with the same buffer to obtain a concentration of 1000 µg/mL. From this stock, further serial dilutions were made to obtain working standard solutions in the concentration range of 0 to 25 µg/mL. The absorbance of each solution was

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 22s, 2025
https://theaspd.com/index.php

measured at a λmax of 240 nm using a UV-Visible spectrophotometer, with pH 6.8 phosphate buffer as the blank. The calibration data are shown in Table 5.

Table 4: Absorbance of Chlorpropamide at 240 nm in pH 6.8 Phosphate Buffer

Concentration (µg/mL)	Absorbance
0	0.000
5	0.111
10	0.225
15	0.339
20	0.452
25	0.558

3.3.5 Standard Graph of Chlorpropamide

The absorbance values obtained were plotted against their corresponding concentrations to generate a standard calibration curve. A linear relationship was observed, as represented in Figure 3.

- The regression equation was found to be:

$y=0.0223x+0.0019y=0.0223x+0.0019$

- With a correlation coefficient (R^2) of 0.999, indicating excellent linearity in the tested range.

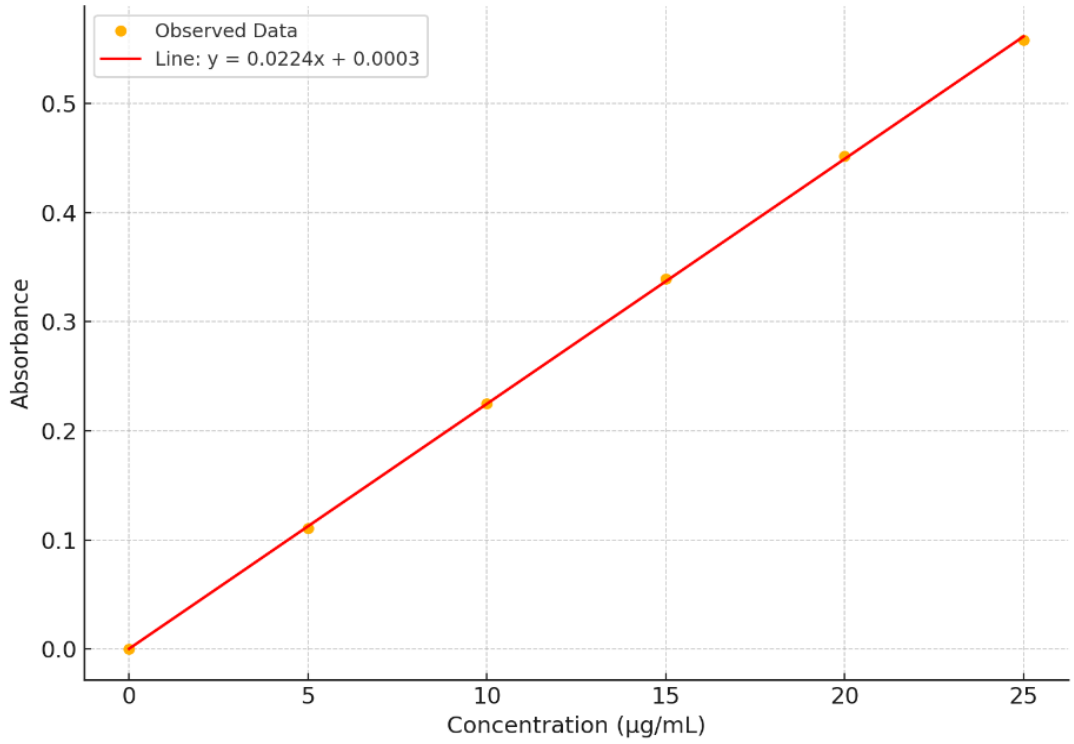

Figure 3: Calibration Curve of Chlorpropamide in pH 6.8 Phosphate Buffer at 240 n

3.3.6 In Vitro Drug Release

Table 4: In Vitro Drug Release Profile of Chlorpropamide IR Tablets (C1–C9)

Time (min)	C1	C2	C3	C4	C5	C6	C7	C8	C9
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5	22.32	33.84	28.08	33.62	26.48	33.92	42.02	38.45	41.82
10	35.15	48.62	42.31	51.42	38.63	45.88	56.69	48.88	63.13
20	46.68	67.93	56.82	64.93	51.89	58.62	61.23	57.22	72.05
30	55.89	77.36	69.73	75.17	66.41	72.25	78.55	68.75	88.14
45	63.27	83.12	81.54	91.88	86.39	82.92	88.96	76.32	92.06
60	89.53	92.73	95.12	99.67	92.51	87.44	93.15	91.39	97.48

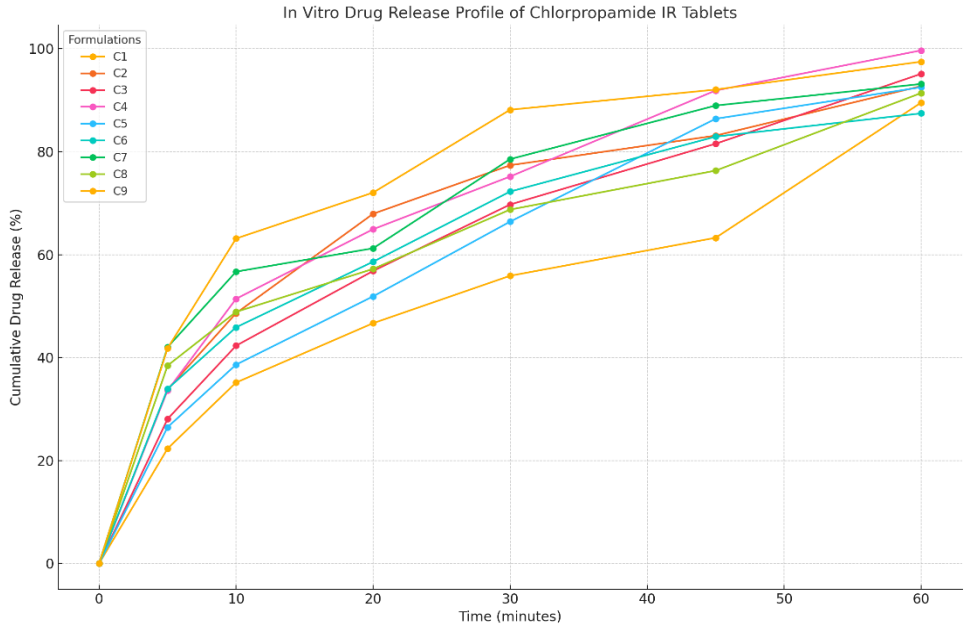

Figure 4: Comparative In Vitro Drug Release Profile of Chlorpropamide Immediate-Release Tablets (C1–C9) in pH 6.8 Phosphate Buffer

The in vitro drug release study was conducted using a USP Type II dissolution apparatus in pH 6.8 phosphate buffer to evaluate the drug release behavior of the formulated chlorpropamide immediate-release tablets. Samples were withdrawn at predetermined time intervals (0–60 minutes), and the percentage cumulative drug release was plotted for each formulation.

Formulations Containing SSG (C1–C3)

Formulations C1, C2, and C3 contained sodium starch glycolate (SSG) at increasing concentrations of 25 mg, 50 mg, and 75 mg respectively. Among these, C3 exhibited the highest drug release at 60 minutes (95.12%), followed by C2 (92.73%) and C1 (89.53%). The improvement in release profile with increasing SSG concentration can be attributed to its swelling property, which facilitates disintegration. However, the release did not reach 100%, possibly due to the formation of a gel-like barrier at higher concentrations, which can hinder further release.

Formulations Containing CCS (C4–C6)

C4, C5, and C6 utilized croscarmellose sodium (CCS) at 25 mg, 50 mg, and 75 mg respectively. C4, with 25 mg of CCS, demonstrated the highest cumulative drug release of 99.67% at 60 minutes and the shortest disintegration time (35 seconds). This performance can be attributed to CCS's dual mechanism rapid swelling and wicking which promotes efficient water uptake and tablet breakup. Interestingly, increasing CCS concentration beyond 25 mg (as in C5 and C6) did not enhance drug release proportionally, indicating that 25 mg is the optimal concentration for this formulation. C5 and C6 showed slightly lower release values of 92.51% and 87.44%, respectively, suggesting possible over-swelling and compact mass formation at higher concentrations.

Formulations Containing CP (C7–C9)

C7, C8, and C9 included crospovidone (CP) at 25 mg, 50 mg, and 75 mg respectively. Among them, C9 achieved 97.48% drug release, which was the second-highest among all batches, followed by C7 (93.15%) and C8 (91.39%). The superior performance of C9 is attributed to CP's capillary activity and porous structure, which facilitates water penetration and rapid disintegration. As seen with CCS and SSG, increasing CP concentration improved release up to a point, but extremely high levels may lead to bulkier tablets that reduce dissolution efficiency.

CONCLUSION

The present study successfully developed and evaluated immediate-release tablets of chlorpropamide using different superdisintegrants sodium starch glycolate (SSG), croscarmellose sodium (CCS), and crospovidone (CP) with the goal of enhancing glycemic control in patients with Type 2 Diabetes Mellitus (T2DM). A total of nine formulations (C1–C9) were prepared by direct compression and systematically assessed for their physicochemical properties, disintegration behavior, and in vitro drug release profile. Among the evaluated formulations, batch C4, containing 25 mg of CCS, exhibited superior performance, with the shortest disintegration time (35 seconds), optimal mechanical strength, and the highest cumulative drug release (99.67% within 60 minutes). The calibration curve constructed for chlorpropamide demonstrated excellent linearity with a correlation coefficient (R^2) of 0.999, ensuring accuracy in drug quantification. The FTIR compatibility study confirmed that no chemical interaction occurred between chlorpropamide and the selected excipients, indicating the formulation's stability. The study highlighted the critical role of the type and concentration of superdisintegrants in achieving desirable tablet performance. Notably, increasing the amount of superdisintegrant beyond an optimal level did not yield further enhancement and, in some cases, negatively impacted disintegration and dissolution characteristics.

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