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Formulation And In-Vitro Evaluation Of Gliclazide Oro-Dispersible Tablets

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ABSTRACT

Introduction:

Gliclazide is a second-generation sulfonylurea used for the management of type II diabetes mellitus. Due to its poor water solubility, the onset of action may be delayed. The primary objective of the present study was to formulate Gliclazide oro-dispersible tablets (ODTs) to enhance solubility and dissolution rate, thereby promoting a faster onset of therapeutic action.

Methods:

Gliclazide ODTs were formulated using the direct compression method with three different superdisintegrants: Crospovidone, Sodium Starch Glycolate (SSG), and Croscarmellose sodium. A total of nine formulations were developed. Differential Scanning Calorimetry (DSC) was performed to evaluate potential drug–excipient interactions. All formulations were assessed for physicochemical properties, in vitro drug release, and release kinetics. The optimized formulation was further subjected to a 6-month stability study under ICH-recommended conditions.

Results:

All formulations complied with pharmacopeia specifications. Among them, formulation F3 exhibited the fastest disintegration time (19.1 seconds) and achieved 99.31% drug release within 15 minutes, attributed to the efficient wicking and swelling properties of crospovidone. Based on disintegration time and drug release performance, F3 was identified as the optimized formulation. It remained physically and chemically stable over a 6-month period.

Conclusion:

Gliclazide ODTs were successfully developed using direct compression and superdisintegrants such as Crospovidone, SSG, and Croscarmellose Sodium. The optimized formulation (F3) demonstrated rapid disintegration, enhanced drug release, and stability over 6 months, indicating its potential for improved patient compliance and faster therapeutic onset in the treatment of type II diabetes..

Keywords: *Gliclazide, Diabetes mellitus, oro-dispersible tablets, superdisintegrants, in-vitro release..*

1. INTRODUCTION

The oral route is the most favorable and desirable mode of drug administration. However, one of the significant drawbacks of the oral dosage forms (viz., tablets and capsules) is their patient incompatibility due to swallowing problems, especially in the case of pediatric and geriatric patients [1]. The oro-dispersible tablets (ODTs) have gained increasing demand during recent years since they have had a marked influence on patient compliance. It disintegrates into minute granules and gets dissolved slowly in the mouth. The disintegration time of ODTs varies from a few seconds to a minute, depending on tablet size and dosage form. The faster the drug dissolves, the faster it is absorbed, and the faster the drug's effect occurs as the solution passes from the mouth, throat, and esophagus into the stomach. The bioavailability of the drug is relatively high in this dosage form compared to traditional dosage forms [2].Gliclazide is a second-generation anti-diabetic drug used for the treatment of type II diabetes. Chemically it is (1-(3-azabicyclo-[3, 3, 0]-oct-3-yl)-3-(p-tolylsulfonyl) urea). It is practically insoluble in water, which leads to poor solubility and low bioavailability, i.e., 42% [3]. Based on these characteristics,...

Gliclazide was chosen as the model drug in this work

2. MATERIALS AND METHODS

MATERIALS

Gliclazide was received as a gift sample from Aurobindo Pharma Limited, Hyderabad. Sodium Starch Glycolate, Crospovidone, and Croscarmellose sodium were obtained from Yarrow Chemicals and Pharmaceuticals, Mumbai, India. Magnesium Stearate, Microcrystalline Sodium, Talc, and all other ingredients were purchased from SD Fine-Chem Limited, Mumbai, India.

3. METHODS

Drug-excipient compatibility study

The Differential Scanning Calorimetry (DSC 4000, Perkin Elmer) was used to study the interaction between the drug and polymers. Approximately 5-15 mg of sample to be analyzed was placed in a pierced DSC aluminum pan and scanned over a temperature range of 50-300 °C. The heating rate was 10 °C/min.; nitrogen was used as purging gas, and the system was cooled down by liquid nitrogen.

Formulation development of Gliclazide ODTs

Gliclazide ODTs were prepared by the direct compression method. All the ingredients were passed through a #60 mesh sieve separately. The drug, mannitol, and selected superdisintegrants were passed through sieve 22 and mixed for 15 minutes. Microcrystalline cellulose (MCC) was mixed by adding a small portion of each at a time and blending it to get a uniform mixture, and kept aside. Then the other ingredients were mixed in geometrical order and the tablets were compressed using a 16-station rotary tablet press [4]. The composition of all the formulations is presented in Table 1.

Table 1: Composition of Gliclazide oro-dispersible tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Gliclazide	30	30	30	30	30	30	30	30	30
Microcrystalline cellulose	35	30	25	35	30	25	35	30	25
Crospovidone	5	10	15	-	-	-	-	-	-
Sodium Starch Glycolate	-	-	-	5	10	15	-	-	-
Croscarmellose sodium	-	-	-	-	-	-	5	10	15
Mannitol	20	20	20	20	20	20	20	20	20
Aspartame	5	5	5	5	5	5	5	5	5
Magnesium stearate	3	3	3	3	3	3	3	3	3
Talc	2	2	2	2	2	2	2	2	2
Total weight (mg)	150	150	150	150	150	150	150	150	150

Evaluation of Gliclazide ODTs

Weight variation

Weight variation was determined by taking twenty tablets and weighing them using an electronic balance to determine the average weight. At the end, the individual's weight was compared with the average weight [5].

Hardness

The Monsanto hardness tester was used to find out tablet hardness in kg/cm^2. It was measured to ensure the integrity and shape maintenance of the tablets, so that they could withstand the effects of transportation. Ten tablets were selected

randomly, and their average weight was calculated. The average of three values was determined.

Tablet thickness

The Verneir caliper was used to determine tablet thickness. The tablet was placed between the two arms of the caliper. The average of three values was calculated.

Friability

The friability of the tablets was determined using the Roche Friabilator. Twenty tablets were weighed and placed in the drum of the friabilator, and the speed was adjusted to 25 rpm. The tablets were allowed to revolve, fall from a height of six inches for 4 min. Then, the tablets were de-dusted and re-weighed. By using the following equation, the % friability was calculated.

% Friability = (loss in weight / Initial weight) x 100

Tablet disintegration

The tablet disintegration test apparatus was used to find the disintegration time. Six tablets were taken and placed individually in tubes and properly covered. The temperature of the medium was maintained at 37±2°. The time taken by the tablet to disintegrate completely was noted [6].

Wetting time

Ten milliliters of water-soluble dye (eosin) solution was added to the Petri dish. A tablet was carefully placed on the surface of the tissue paper. The time required for water to reach the upper surface of the tablet was noted as the wetting time.

Dissolution study

Dissolution studies of ODTs were performed on a USP type-II apparatus. The speed of the apparatus was set at 50 rpm. 900 ml of 0.1 N HCl solution was taken as the dissolution medium. The temperature of the dissolution medium was kept at 37±0.5°C. Samples (5 ml) were collected at predetermined time intervals (5,10,15,20,25, and 30 min), replaced with an equal volume of fresh medium, filtered through a Whatman filter paper, and analyzed with a UV–Visible spectrophotometer (UV 1700, Shimadzu, Japan) at 232 nm [7].

Drug release kinetics study

The mechanism and kinetics of drug release from the formulated tablets were evaluated using various mathematical models. The cumulative drug release data were fitted to Zero-order, First-order, Higuchi, and Korsmeyer–Peppas models to characterize the in vitro drug release behavior and to identify the underlying release mechanism [8].

Drug content uniformity

The tablets were assayed for drug content using methanol as the extraction solvent. Four tablets were accurately weighed and finely powdered in a mortar. A quantity of powder equivalent to 100 mg of Gliclazide was transferred into a 100 mL volumetric flask containing methanol. The solution was sonicated and filtered, then appropriately diluted. The drug content in the ODTs was estimated spectrophotometrically at 232 nm.

Stability studies

Stability studies of the optimized ODTs were carried out over a period of six months in accordance with ICH guidelines (International Conference on Harmonisation). The tablets were stored under accelerated conditions of temperature and humidity (35 ± 5°C and 75 ± 5% RH). At specified intervals, the tablets were evaluated for key quality parameters including hardness, friability, drug content, and in-vitro drug release [9].

4. RESULTS AND DISCUSSION

In the present study, Gliclazide ODTs were prepared by using Crospovidone, Croscarmellose sodium, and Sodium Starch Glycolate as superdisintegrants (Table 1). A total of nine formulations were prepared by the direct compression technique. All batches of the tablets were preliminarily evaluated for various physical parameters such as weight variation, hardness, friability, drug content, wetting time, disintegration, and dissolution, which are presented in Table 2

Table 2: Post-compression parameters of Gliclazide oro-dispersible tablets

Formulation Code	Weight Variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Wetting Time (sec)	Disintegration Time (sec)	Assay (%)
F1	149.2±0.11	3.51±0.1	5.2±0.04	0.25	55.04	63.1	93.2

F2	151.3±1.13	3.13±0.2	5.1±0.02	0.21	39.12	51.2	95.3
F3	150.2±0.22	3.48±0.1	5.0±0.01	0.13	22.01	19.1	99.5
F4	151.2±2.21	3.14±0.2	4.9±0.01	0.20	42.17	48.1	94.2
F5	149.1±0.01	3.22±0.1	5.2±0.13	0.19	31.23	34.2	94.6
F6	150.1±0.12	3.15±0.2	5.1±0.04	0.21	28.12	28.1	96.4
F7	148.2±0.03	3.13±0.1	5.3±0.01	0.28	66.02	45.2	94.3
F8	150.2±1.31	3.27±0.3	4.9±0.04	0.23	54.43	38.2	95.2
F9	151.1±1.04	3.53±0.2	5.2±0.01	0.17	49.12	29.3	96.1

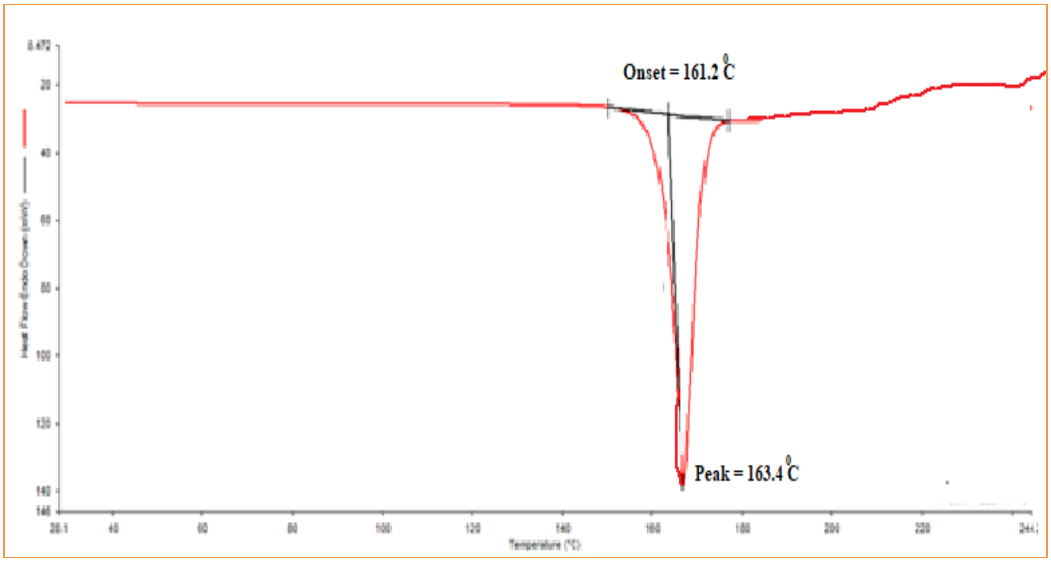

Fig 1: DSC thermogram of pure drug (Gliclazide)

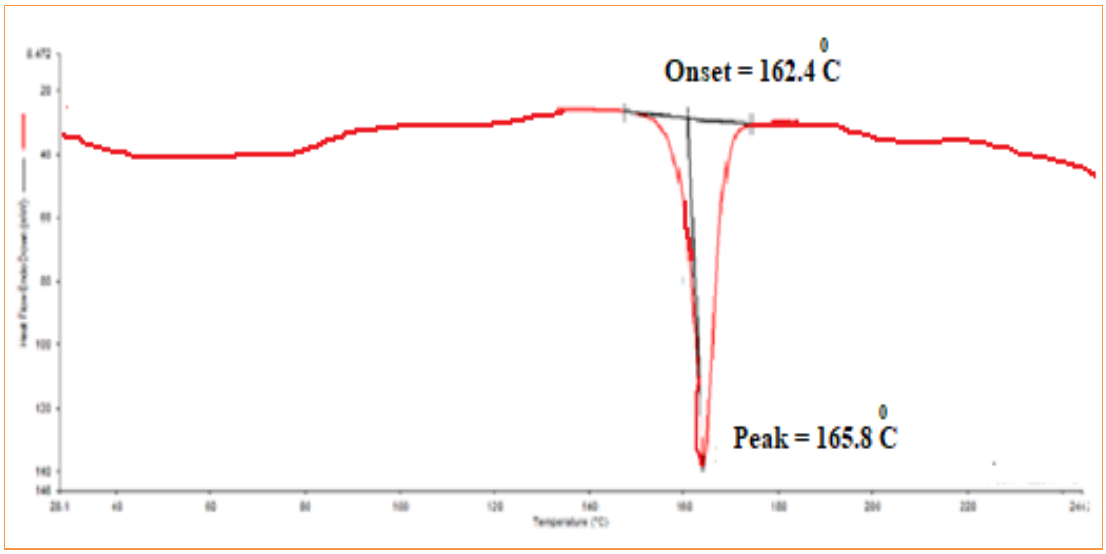

Fig 2: DSC thermogram of physical mixture

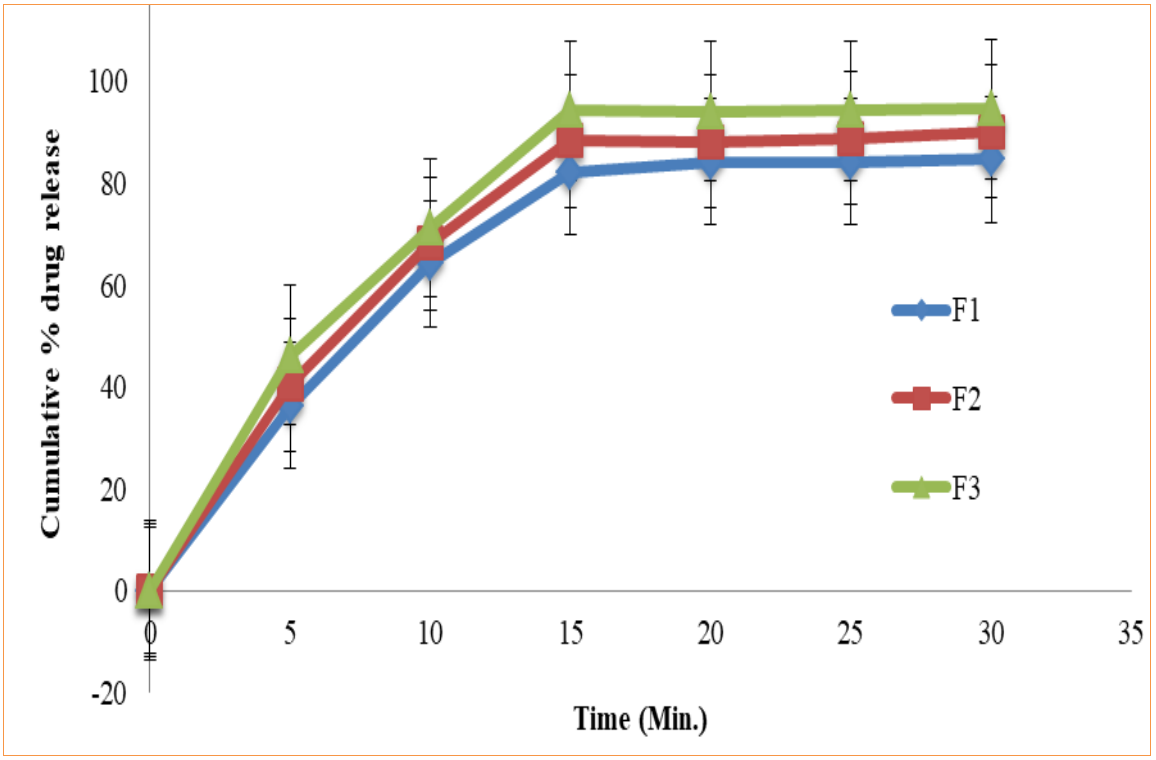

Fig 3: Dissolution profiles of Gliclazide prepared with Crospovidone (F1-F3)

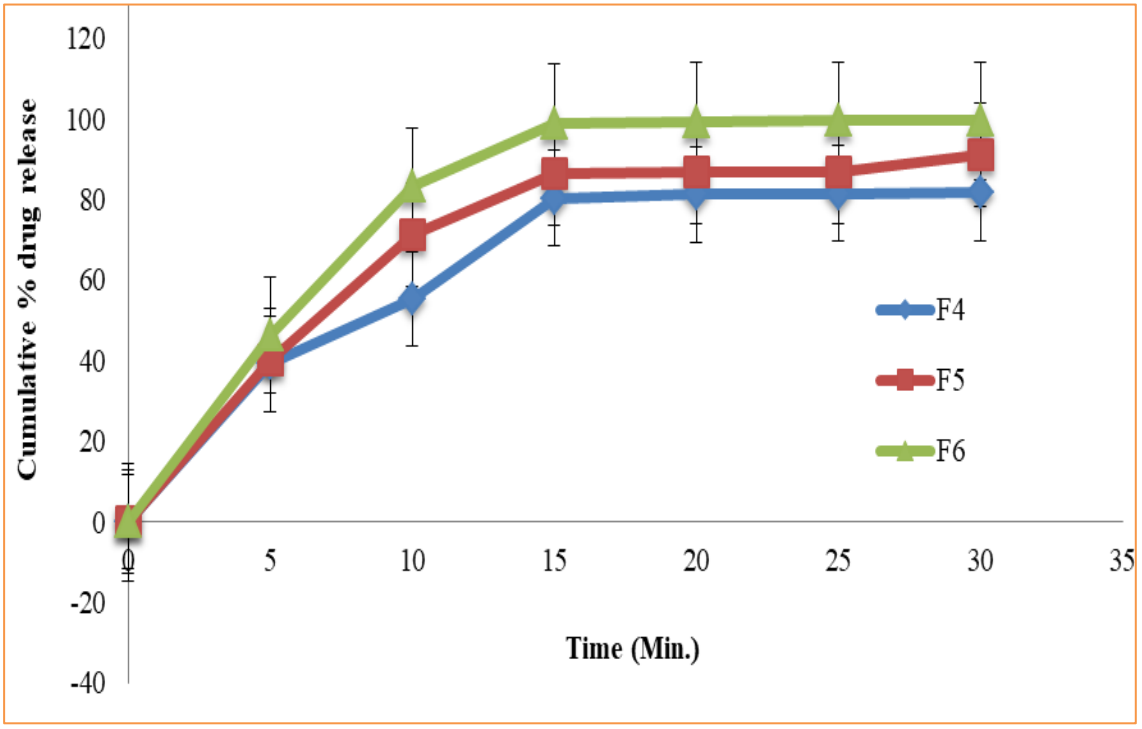

Fig 4: Dissolution profiles of Gliclazide prepared with Sodium Starch Glycolate (F4-F6)

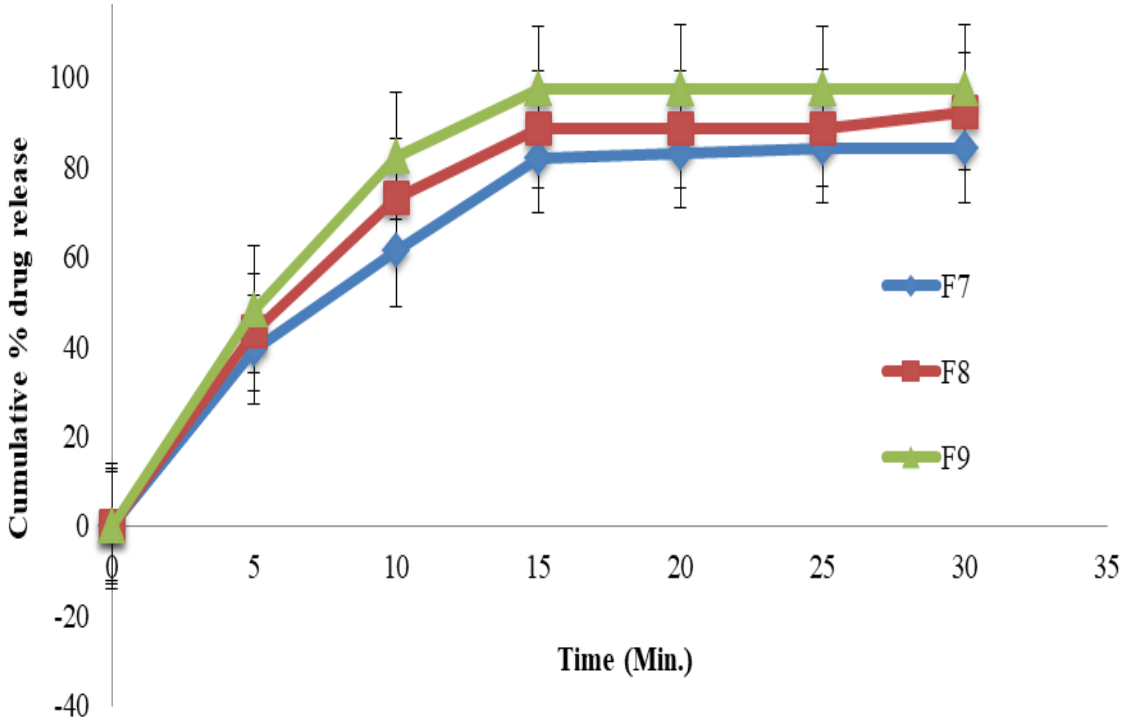

Fig 5: Dissolution profiles of Gliclazide prepared with Croscarmellose sodium (F7-F9)

Table 3: Drug release kinetics of all the developed Gliclazide ODTs

Formulation Code	Zero order	First order	Higuchi order	Peppas order
F1	0.8702	0.8901	0.9021	0.8231
F2	0.8413	0.8716	0.9124	0.8918
F3	0.9343	0.9121	0.9571	0.9213
F4	0.9021	0.8929	0.9223	0.8535
F5	0.9212	0.9013	0.9214	0.8351
F6	0.8941	0.8842	0.9365	0.8941
F7	0.9012	0.9010	0.9051	0.8613
F8	0.8746	0.9024	0.8921	0.8802
F9	0.9101	0.9031	0.9103	0.9031

A Differential Scanning Calorimetry (DSC) study was performed to assess the compatibility of the drug with the excipients. The pure drug exhibited a sharp endothermic peak at 163°C (Fig. 1), while the physical mixture showed a peak at 165°C (Fig. 2). This slight shift indicates the absence of significant interactions between the drug and the excipients, confirming their compatibility.

The weight variation among formulations ranged from 148.2 ± 0.03 mg to 151.3 ± 1.13 mg. Weight uniformity plays an important role in tablet manufacturing since it directly corresponds to a uniform drug dosage per unit. A low standard deviation indicates minimal variation in the weight of individual tablets from the average tablet weight. The weight of all the tablets was found to be uniform, with low standard deviation values, indicating efficient mixing of the drug, disintegrants, and other excipients [10]. Hardness values ranged from 3.13 ± 0.1 to 3.53 ± 0.2 kg/cm², indicating sufficient mechanical strength to withstand handling and transport stresses. Friability values ranged from 0.13% to 0.28%, all below the acceptable

limit of 1%, confirming good tablet integrity. The thickness of the tablets ranged from 4.9 ± 0.01 mm to 5.3 ± 0.01 mm across all formulations, demonstrating consistent tablet dimensions.

The F3 formulation exhibited the shortest disintegration time, 19.1 seconds, among all formulations. An inverse relationship was observed between the concentration of superdisintegrant and disintegration time, indicating that higher concentrations of superdisintegrant led to faster disintegration [11].

An assay was conducted on all the formulations to ensure the dose. It was proved that the drug content in all the formulations remained within the range of 93.2% to 99.5%. Thus, all formulations complied with the pharmacopeia limits.

The drug release studies were conducted for all the developed formulations using a USP type-II dissolution apparatus. Figures 3-5 represent the *in vitro* release profile of Gliclazide from different ODTs formulations. Formulations F1-F3 were developed with Crospovidone, and F4-F6 formulations were developed with SSG. F7-F9 formulations were developed with croscarmellose sodium. The results had shown that the drug release was in the range of 85 to 99 % for all 9 formulations in 15 min. From the *in vitro* dissolution data, it was found that the drug release from formulation containing high amount of Crosspovidone as a superdisintegrant (F3) was faster within 15 min and showed highest drug release 99.31% due to high capillary activity with pronounced hydration capacity of the Crospovidone when it comes in contact with aqueous fluids [12-13]. So, it can be concluded that Crospovidone is the strongest superdisintegrant among other superdisintegrants, resulting in faster disintegration and dissolution than Croscarmellose and SSG (Figures 3-5).

Drug release kinetics, such as Zero order, First order, Higuchi, and Peppas, were applied to all the formulations to determine the drug release pattern. The drug release kinetics model exhibiting the highest R^2 value was identified as the most suitable and best-fitted model. The results indicated that the best formulation (F3) followed Higuchi's diffusion model with the highest R^2 value (0.9571) compared to all other formulations. It occurs due to the quick diffusion of the drug through the porous structure of the tablets. The results are presented in Table 3.

Based on the disintegration time, wetting time, and drug release studies F3 formulation was selected as the optimized formulation, and further stability studies were conducted.

Table 4: Stability studies of optimized formulation (F3)

Time (Months)	Color change	Friability (%)	Hardness (Kg/cm^2)	Drug content (%)	Drug release (%)
0	No	0.13	3.48±0.1	99.5	99.31
1	No	0.13	3.48±0.2	99.3	99.12
3	No	0.14	3.49±0.1	99.2	98.90
6	No	0.13	3.47±0.3	99.4	99.13

The results clearly stated that no significant changes were observed in color change, friability, hardness, drug content, and *in vitro* drug release (Table 4). This study concluded that the optimized formulation F3 was stable under accelerated conditions of temperature and humidity.

5. CONCLUSION

Gliclazide ODTs were prepared by the direct compression method using Crospovidone, Sodium Starch Glycolate, and croscarmellose sodium. A total of nine formulations were developed. DSC study revealed that there was no interaction found between the drug and excipients. The best formulation (F3) was selected based on the disintegration time, wetting time, and dissolution study. A stability study was conducted on the optimized formulation and was found stable for a 6-month period of time.

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AUTHORS' CONTRIBUTIONS

All the authors have equally contributed to the article.

CONFLICT OF INTEREST

There is no conflict of interest

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