



Research and evaluation of Glimepiride Sustained release tablet formulation

¹Nishigandha S. Kharde, ²Pratik B. Bhanage, ³Megha T. Salve

^{1,2,3}Department of pharmacy, Shivajirao pawar college of pharmacy pachegaon 413721.

ABSTRACT:

The purpose of this effort is to construct a sustained release formulation of glimepiride, which is currently used to treat type 2 diabetes mellitus, and to examine how polymers affect the drug's release profile. The main goal of this project was to use the polymer ethyl cellulose to create a sustained release anti-diabetic pill. Using this polymer, wet granulation was used to produce sustained release glimepiride tablets in multiple trials with varying polymer concentrations. Pre-compression characteristics such as bulk density, tapped density, angle of repose, Hausner's ratio, and compressibility ratio were assessed for the prepared granules. Numerous physical parameter tests, such as those for weight variation, friability, hardness, thickness, and diameter, were performed on the produced tablets.

Keywords: Glimepiride, Sustained release tablet, Diabetes mellitus, Wet granulation method

Introduction:

The creation of oral sustained release formulations aims to regulate drug release from the gastrointestinal tract (GIT) and preserve a long-term, efficient drug concentration in the systemic circulation. Such a medication will remain in the stomach following oral administration, eventually releasing the medication in a regulated fashion to allow for continuous delivery of the medication to the GIT's absorption sites [1,2]. Reduced effectiveness of the administered dose results from partial drug release from the dosage form in the absorption zone.[3] The purpose of sustained release dosage type is to preserve therapeutic blood or tissue levels of the medicine over a extended duration.[4]

A person with diabetes mellitus has excessive blood sugar levels, which can be caused by either insufficient insulin production by the body or improper cell response to the insulin generated. The pancreas produces the hormone insulin, which allows body cells to absorb glucose and convert it into energy. The accumulation of glucose in the blood can result in vascular, nerve, and other issues if the body cells are unable to absorb it. According to recent estimates, there were 171 million diabetics worldwide in 2000; by 2030, that number is expected to rise to 366 million.[5] The main characteristic of diabetes is the degree of hyperglycemia that increases the risk of microvascular damage, including retinopathy, nephropathy, and neuropathy. It is linked to a lower life expectancy, substantial morbidity from certain microvascular consequences of diabetes, a higher risk of macrovascular complications (stroke, ischemic heart disease, and peripheral vascular disease), and a lower quality of life. According to the American Diabetes Association (ADA), the national costs of diabetes in the United States were projected to reach US\$132 billion in 2002 and US\$192 billion in 2020.[6]

Glimepiride is a third-generation sulphonylurea class oral blood glucose-lowering medication that is now prescribed to treat hyperglycemia in non-insulin-dependent diabetic mellitus (NIDDM). The biopharmaceutical classification system places glimepiride in class II.[7] The medication has a high permeability but is insoluble in water and an acidic environment. Oral bioavailability is almost 100%, and oral absorption is consistent and quick. Sustained release formulations, which are to be given once day for blood glucose monitoring, are supported by the pharmacokinetics and dose schedule, improving patient compliance and efficacy. The half-life is roughly five hours, and 99.5% of plasma proteins bind.[8]. The metabolic and endocrine disorder known as diabetes mellitus (DM) is typified by elevated triglyceridemia, cholesterol, and glucose levels. Diabetes mellitus affects about 200 million individuals globally and is brought on by either defects in insulin secretion, inadequate insulin secretion, or both. The hormone insulin, which is produced by the pancreas, facilitates the body's cells' absorption of glucose. If the cells are unable to absorb glucose from the body, it can result in serious consequences. [8,9].

1-[[p-[2-(3-ethyl-4-methyl-2-oxo-3-pyrroline-1-carboxamido) ethyl] phenyl] sulfonyl]-3-(trans-4-methylcyclohexyl) urea is the chemical name of Glimepiride.[10].It increases the amount of insulin secreted by the pancreatic β -cells by depolarizing the cell membrane and blocking potassium channels, which triggers the start of metabolic activities that produce insulin. The predicted water solubility of glimepiride, an off-white or white crystalline powder, is 1.6 $\mu\text{g/ml}$ ($\text{pKa}=6.2$), yet it is comparatively insoluble in water. This results in significant fluctuations in its bioavailability [11,12]. Additionally, the excipients may interact with the medicine and change its dissolving properties while it is being stored. Numerous publications indicate significant aging-related changes that negatively impact oral sulphonylurea medication solubility and, consequently, bioavailability [8, 9]. A number of strategies have been employed to get around these issues, including the creation of a complex between glimepiride and β -CD, hydroxypropyl- β -CD, or sulfobutylether- β -CD in the presence and absence of various water-soluble polymers.[11,13].

Material and Method:

Material: Glimepiride, ethyl cellulose, microcrystalline cellulose, povidone k30, magnesium stearate, starch, etc.

Pre formulation studies –

Angel of repose:

Both the fixed funnel and freestanding cone approaches use a funnel with its tip fixed at a specific height, h, maintained 2 cm above graph paper that is positioned on a level horizontal surface. Where r is the radius of the conical pile's base ,angle of repose can be calculated using the following formula

$$\phi = \tan^{-1} (h/r)$$

Where, ϕ is the angle of repose,

h is the pile's height, r is the pile's base radius.

Bulk density and Tapped density

The tapped bulk density as well as the loose bulk density were calculated. Two grams of granules from each recipe were added to a 10-milliliter measuring cylinder after being lightly shaken to break up any agglomerates that might have formed. The cylinder was allowed to descend its own weight from the hard surface at intervals of two seconds from a height of 2.5 cm in order to observe the initial volume. The tapping was kept up till the loudness didn't change any more.

The following formulas were used to determine LBD and TBD.

LBD: Powder weight divided by packing volume.

TBD: Powder weight divided by the packing's taped capacity.

Carr's index:

$$\text{Carr's index} = (\text{TBD} - \text{LBD}) * 100 / \text{TBD}$$

where ,LBD: is the powder's weight divided by the packing volume.

TBD: Powder weight divided by the packing's taped capacity.

Hausner's ratio:

The following formula can be used to calculate Hausner's ratio.

$$\text{Hausner's ratio} = \text{TBD} / \text{LBD}$$

Where, LBD stands for loose bulk densities and TBD for tapered bul densities.[6,14].

Formulation:

The matrix tablets were created using the wet granulation process. With the use of the granulating agent PVP K-30, the medication, Ethyl cellulose and microcrystalline cellulose were combined and granulated. After that, the moist substance was dried in an oven set to 50°C after passing through sieve number 44. Granules are sieved using sieve number 22 after drying. Talc and magnesium stearate were used to lubricate the grains. After that, a tablet punching machine was used to compress the tablets.[15,16]

Table-1: Formulation of Glimepiride sustained release tablet

	F1	F2	F3	F4	F5
Glimepiride	5	5	5	5	5
Ethyl cellulose	15	20	25	30	35
Microcrystalline cellulose	52	47	42	37	32
Povidone k-30	20	20	20	20	20
Magnesium stearate	5	5	5	5	5
Talc	3	3	3	3	3
Total	100	100	100	100	100

Evaluation of formulated tablet:

1. Weight variation:

At first, each of the twenty tablets was weighed separately. The standard deviation is determined after calculating the average weight of the tablets.

2. Thickness:

Density Vernier callipers (20 tabs) were used to measure each tablet's thickness.[8].

3. Hardness :

Hardness test Using a Monsanto Hardness tester, the tablets' hardness was assessed. Kg/cm² is the unit of measurement. The mean and standard deviation values were computed after six tablets were chosen at random from each formulation.[6].

4. Friability:

Twenty tablets were first weighed, put in the Roche friability device, and rotated for four minutes at 25 rpm. The tablets were cleaned and weighed once more following the revolutions. % Friability = $\{(\text{Initial weight}-\text{Final weight})/\text{Initial weight}\} \times 100$ was the formula used to measure it.[8].

5. In vitro dissolution study:

Glimepiride sustained release tablet dissolution studies were conducted using Hermann et al. (2005) methodology. Using phosphate buffer with a pH of 6.8, the experiment was conducted using the USP apparatus 2 (paddle method) for eight hours at 50 rpm and $37^\circ \pm 0.5^\circ \text{C}$. Using a UV spectrophotometer, released drug samples from the dissolution medium were measured at 228 nm.[1,17].

Result and Discussion:

Compatibility study using FTIR analysis:

None of the drug glimepiride's peaks appear or vanish in the physically mixed mixture. The slight variation in transmittance percentage could be the result of crystalline alteration. Thus, it demonstrates that the medication and polymer do not interact chemically.

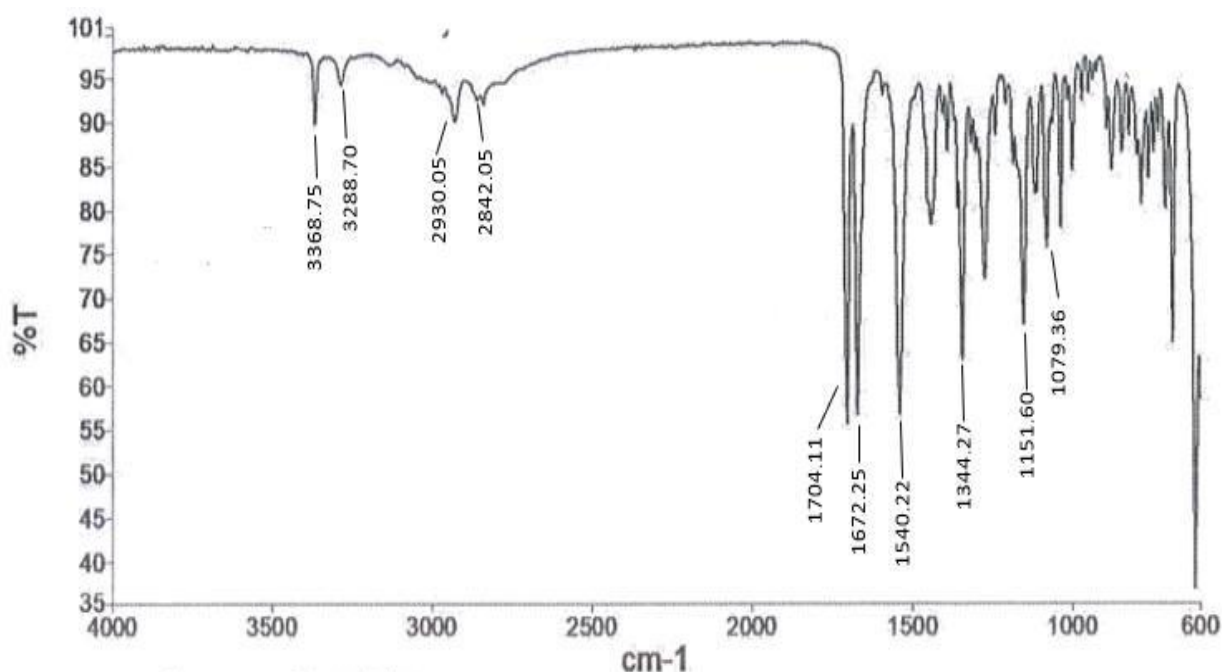


Fig.1: FTIR spectra of glimepiride drug

Table:2 Pre formulation study of glimepiride

Formulation	Angle of Repose (°)	Bulk Density (g/ml)	Tapped Density (g/ml)	Hausner's ratio	Car's index (%)
F1	29.74	0.465	0.540	1.17	14.8
F2	31.21	0.476	0.526	1.11	10.6
F3	29.054	0.444	0.555	1.26	20.72
F4	28.39	0.487	0.571	1.18	15.93
F5	30.46	0.454	0.512	1.13	12.10

Table -3 : Evaluation of prepared glimepiride sustained release tablet formulation

Formulation	Weight variation (mg)	Hardness (kg/cm ²)	Thickness (mm)	Friability
F1	99.8±0.91	3.34±0.10	2.07±0.06	0.40±0.08
F2	100.2±0.82	4.00±0.55	2.09±0.08	0.35±0.10
F3	100.1±0.12	3.20±0.40	2.11±0.07	0.24±0.12
F4	101.4±0.72	3.80±0.20	2.12±0.06	0.16±0.06
F5	99.3±0.58	4.05±0.20	2.16±0.11	0.27±0.15

Conclusion:

The Glimepiride Sustained Release Tablet formulation offers a promising approach for managing type 2 diabetes. By providing a sustained release of Glimepiride over an extended period, these tablets can:

- Improve patient compliance by reducing dosing frequency.
- Enhance glycemic control by maintaining therapeutic drug levels.
- Potentially reduce side effects associated with peak plasma concentrations.
- The formulation's success depends on optimizing the polymer blend, granulation process, and tablet compression parameters. Further studies, including in vivo evaluations, are necessary to confirm the formulation's efficacy and safety. Overall, the Glimepiride Sustained Release Tablets have the potential to provide a more convenient and effective treatment option for patients with type 2 diabetes.

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