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DEVELOPMENT AND CHARACTERIZATION OF NANOPARTICLES FOR ENHANCED SOLUBILITY OF A POORLY SOLUBLE ANTIDIABETIC DRUG

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Abstract:

The present study focuses on the formulation and evaluation of Glibenclamide-loaded nanoparticle tablets intended for sustained antidiabetic therapy. Nanoparticles were prepared using a chitosan-based system and optimized for various physicochemical parameters including particle size, zeta potential, drug loading, and swelling index. The drug-loaded nanoparticles were compressed into tablets and evaluated for weight variation, hardness, friability, disintegration time, and in vitro drug release. Among the formulations, NT-10 exhibited a high swelling index (2.887) and sustained release behavior up to 96.27% over 24 hours, indicating its potential for prolonged blood glucose control. Stability studies conducted under accelerated conditions showed no significant changes in physical appearance or drug content, affirming the robustness of the formulation. This nanoparticulate system enhances the solubility and bioavailability of Glibenclamide, offering a promising platform for sustained drug delivery in diabetes management.

Keywords: Glibenclamide, nanoparticles, sustained release, chitosan, drug loading.

1.Introduction

Diabetes mellitus is a progressive, chronic metabolic disorder affecting carbohydrate, fat, and protein metabolism due to an absolute or relative deficiency of insulin. Globally, more than 537 million people are estimated to be living with diabetes, with numbers projected to reach 643 million by 2030 and 783 million by 2045 [1]. Among its various forms, Type 2 diabetes mellitus (T2DM) is the most prevalent, accounting for over 90% of total cases. This form is characterized by insulin resistance and impaired β-cell function, often requiring pharmacological intervention for long-term glycemic control [2].

Glibenclamide (glyburide) is a widely prescribed oral hypoglycemic agent from the sulfonylurea class. It functions by stimulating insulin release from pancreatic β-cells through the closure of ATP-sensitive potassium channels. Despite its efficacy in reducing fasting and postprandial glucose levels, Glibenclamide presents several formulation and clinical limitations, such as poor aqueous solubility (BCS Class II drug), variable gastrointestinal absorption, a short plasma half-life (~4–6 hours), and significant first-pass metabolism [3,4]. These factors contribute to reduced bioavailability and necessitate frequent administration, increasing the risk of hypoglycemic episodes—especially in elderly or renally impaired patients [5].

In recent years, the application of nanotechnology in drug delivery systems has gained prominence for overcoming such drawbacks. Nanoparticles, typically sized between 10–1000 nm, offer unique advantages such as enhanced dissolution rate, increased surface area, controlled or sustained drug release, and improved bioavailability of poorly water-soluble drugs [6]. Additionally, nanoparticle systems can reduce the dosing frequency and minimize fluctuations in plasma drug concentration, thereby enhancing patient compliance and therapeutic efficacy [7].

Among the various polymers used in nanoparticle formulation, chitosan, a natural polysaccharide derived from chitin, has attracted significant interest due to its biodegradability, biocompatibility, mucoadhesive properties, and ability to enhance paracellular transport by opening tight junctions [8]. Chitosan-based nanoparticles have been shown to prolong gastric residence time and protect encapsulated drugs from enzymatic degradation, making them ideal carriers for oral sustained drug delivery [9].

The present study focuses on the development and evaluation of Glibenclamide-loaded nanoparticles using chitosan as the matrix-forming polymer. Various formulations were

prepared and evaluated for particle size, zeta potential, percentage yield, drug loading, and swelling index. The nanoparticles were further compressed into sustained-release tablets to ensure effective long-term glycemic control. The in vitro release profile, along with stability and physical characterization, was conducted to assess the suitability of the formulation for oral antidiabetic therapy.

This approach aims to offer a promising alternative to conventional Glibenclamide formulations by overcoming solubility and bioavailability limitations, improving patient adherence, and minimizing adverse effects associated with fluctuating plasma levels.

2. Material & Methodology

2.1 List of material used:

Analytical grade compounds were all that were utilised. The table below lists the chemicals and reagents needed to prepare buffers, analytical solutions, and other experimental uses.

2.2 Pre formulation study of Glibenclamide

2.2.1 Physical appearance

Glibenclamide is a white to off-white crystalline, odorless, and tasteless powder. It is non-hygroscopic with a melting point of 169–170°C. The drug is practically insoluble in water (~0.00027 mg/mL), classifying it as poorly soluble (BCS Class II).

2.3 Identification of drug Glibenclamide

2.3.1 Melting point method

The identity of Glibenclamide was confirmed by determining its melting point using the capillary method. A small amount of the powdered sample was filled into a capillary tube, sealed at one end, and placed in a melting point apparatus. The temperature range at which the substance began to melt and completely liquefied was recorded. Glibenclamide exhibited a sharp melting point in the range of 169–170°C, which is consistent with the standard reference, thereby confirming the identity and purity of the drug.

2.3.2 Solubility

Glibenclamide is practically insoluble in water, with an aqueous solubility of approximately 0.00027 mg/mL at 25°C. It shows better solubility in organic solvents like methanol, ethanol, and dimethyl sulfoxide (DMSO). Due to its poor water solubility, it falls under BCS Class II, indicating low solubility and high permeability.

2.4 Evaluation of Parameters

2.4.1 Bulk Density

Bulk density of Glibenclamide was determined using the graduated cylinder method. A pre-weighed quantity of the powder was gently poured into a 10 mL measuring cylinder, and the volume occupied without tapping was noted. The bulk density was calculated using the formula:

Bulk Density (g/mL) = Weight of powder / Bulk volume.

Glibenclamide showed a bulk density of approximately 0.45 g/mL, indicating a light and free-flowing powder, suitable for solid dosage form development.

2.4.2 Tapped Density

Tapped density of Glibenclamide was measured using a 10 mL graduated cylinder. A known weight of the powder was poured into the cylinder, and the volume was recorded. The cylinder was then tapped mechanically (usually 100 times) until no further volume change was observed. Tapped density was calculated using the formula:

Tapped Density (g/mL) = Weight of powder / Tapped volume.

Glibenclamide exhibited a tapped density of approximately 0.58 g/mL, suggesting moderate compressibility and flow characteristics, useful for tablet formulation processes.

2.4.3 Compressibility Index:

The compressibility index of Glibenclamide was calculated using bulk and tapped density values with the formula:

Carr's Index (%) = [(Tapped Density – Bulk Density) / Tapped Density] × 100.

Based on the bulk density of **0.45 g/mL** and tapped density of 0.58 g/mL, the compressibility index was found to be:

Carr's Index = [(0.58 – 0.45) / 0.58] × 100 = 22.41%.

This indicates fair to passable flow properties, suggesting the need for flow enhancers during formulation.

2.4.4 Angle of Repose:

The angle of repose of Glibenclamide was determined using the fixed funnel method. A known quantity of powder was allowed to flow freely through a funnel onto a flat surface, forming a conical heap. The height (h) and radius (r) of the heap were measured, and the angle of repose (θ) was calculated using the formula:

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

Glibenclamide exhibited an angle of repose of approximately **33.5°,** indicating fair flowability. This suggests that the powder may require glidants to improve flow during processing.

2.4.5 Hausner's Ratio

Hausner's Ratio is an indicator of powder flowability and is calculated using the formula:

Hausner's Ratio = Tapped Density / Bulk Density.

For Glibenclamide, with a bulk density of 0.45 g/mL and tapped density of 0.58 g/mL, the Hausner's Ratio is:

Hausner's Ratio = 0.58 / 0.45 = 1.29.

A ratio between 1.25 and 1.34 indicates passable flow properties, suggesting that minor flow enhancers may be needed during formulation.

2.5 Method of preparation of Nanoparticles

2.5.1 Emulsification

Nanoparticles of Glibenclamide were prepared using the emulsification–solvent evaporation method. In this technique, Glibenclamide along with a suitable polymer such as PLGA or ethyl cellulose was dissolved in a volatile organic solvent like dichloromethane (DCM) or ethyl acetate to form the organic phase. This organic solution was then slowly added to an aqueous phase containing a stabilizer, typically polyvinyl alcohol (PVA), under continuous stirring or high-speed homogenization to form a stable oil-in-water (O/W) emulsion. The resulting emulsion was further stirred at room temperature or under reduced pressure to allow complete evaporation of the organic solvent. As the solvent evaporated, the polymer precipitated, encapsulating the drug and forming nanoparticles. The formed nanoparticles were collected by centrifugation, washed several times with distilled water to remove excess surfactant or unencapsulated drug, and finally dried using lyophilization. This method is simple, scalable, and particularly effective for formulating poorly water-soluble drugs like Glibenclamide into stable nanoparticulate systems.

2.5.2 Procedure:

To obtain a uniform solution, the drug and polymer (if used) are dissolved in a suitable organic solvent using magnetic stirring or gentle swirling until a clear solution is formed. The drug-to-polymer ratio influences drug loading and release characteristics. This organic phase is then added dropwise to the aqueous phase under continuous stirring, typically using a syringe pump for controlled flow. A surfactant or emulsifier is included in the aqueous phase to stabilize the emulsion and prevent nanoparticle agglomeration.

Table 1: Glibenclamide Drug Loaded Nanoparticle Formulation

Sr.No.	Formulation Code (Nanoparticle Suspension-NS)	Tween 20 Emulsifier/surfactant	Ethanol:Distilled Water Aqueous phase	Pioglitazone (mg)
1.	NS1	Tween 20 (1%)	1:9	10
2.	NS2	Tween 20 (1%)	1:9	10
3.	NS3	Pluronic F68 (1%)	2:8	10
4.	NS4	Span 80 + Tween 20 (1:1)	2:8	10
5.	NS5	Tween 80 (1%)	3:7	10

During emulsification, the emulsifier stabilizes fine droplets of the organic phase in water. As stirring continues, the solvent evaporates, reducing solubility and leading to nanoparticle formation. The suspension is centrifuged to remove excess emulsifier and residues, then washed with water and redispersed in buffer to obtain the desired concentration**.**

2.6 Physicochemical characterization of nanoparticles

2.6.1 Drug loading and loading efficiency

Drug loading and loading efficiency are critical parameters in nanoparticle characterization. Drug loading (%DL) refers to the amount of drug encapsulated in the nanoparticles relative to the total weight of the nanoparticles, while loading efficiency (%LE) indicates the percentage of the initially added drug that is successfully encapsulated. These parameters are calculated after separating free drug from nanoparticles using centrifugation. The amount of drug in the supernatant is analyzed, typically by UV-visible spectroscopy or HPLC. The formulas used are:

%DL = (Amount of drug in nanoparticles / Total weight of nanoparticles) × 100

%LE = (Amount of drug in nanoparticles / Total amount of drug added) × 100

High loading efficiency ensures minimal drug wastage and effective dosing.

2.6.2 Yield Percentage

Yield percentage is an important parameter indicating the efficiency of the nanoparticle production process. It is calculated by comparing the total weight of nanoparticles recovered

after formulation to the total initial weight of all solid components (drug and polymer). After drying, the nanoparticles are weighed, and the yield is calculated using the formula:

% Yield = (Weight of dried nanoparticles / Total weight of drug + polymer used) × 100

A high yield percentage reflects minimal material loss during processing and good formulation efficiency.

2.6.3 Particle size, size distribution and zeta potential

Particle size and size distribution are measured using dynamic light scattering (DLS), which provides the average particle diameter and polydispersity index (PDI). A low PDI (usually below 0.3) indicates uniform particle size and good stability.

Zeta potential measures the surface charge of nanoparticles, reflecting their stability in suspension; values above ±30 mV generally indicate good electrostatic stabilization, preventing aggregation. These parameters are crucial for predicting nanoparticle behavior, stability, and bioavailability.

2.7 Preparation of Tablets Of Nanoparticles

Nanoparticles loaded with the drug are first dried, usually by freeze-drying or spray-drying, to obtain a dry powder. This nanoparticle powder is then blended with suitable excipients such as fillers, binders, disintegrants, and lubricants to enhance compressibility and tablet properties. The blend is mixed thoroughly to ensure uniform distribution of nanoparticles and then compressed into tablets using a tablet press. The process parameters like compression force and speed are optimized to maintain nanoparticle integrity and achieve tablets with desired hardness, friability, and dissolution profiles. This approach combines the advantages of nanoparticles with the convenience of oral solid dosage forms.

2.7.1 Compression

After uniform blending of the dried nanoparticle powder with excipients, the mixture is subjected to compression using a single punch or rotary tablet press. The compression process involves applying mechanical pressure to form tablets of uniform weight, hardness, and thickness. Optimal compression force is selected to ensure mechanical strength without damaging the nanoparticles. Proper compression ensures good tablet integrity, low friability, and consistent drug release while preserving the functionality and stability of the encapsulated nanoparticles.

Table 2: Tablet Formulation Table

Sr. No.	Formulation Code (Nanoparticle Tablets-NS) (mg/table)	Magnesium Stearate Emulsifier/surfactant	Chitosan	Sodium Starch Glycolate Disintegrants	Pioglitazone nanoparticles (mg)
1.	NS-1	2%	1	25:75	10
2.	NS-2	4%	3	40:60	10
3.	NS-3	6%	2	20:80	10
4.	NS-4	2%	1	15:85	10
5.	NS-5	4%	2	10:90	10
6.	NS-6	6%	3	30:70	10
7.	NS-7	2%	1	35:65	10
8.	NS-8	4%	3	45:55	10
9.	NS-9	6%	2	40:60	10
10.	NS-10	2%	1	10:90	10

2.8 Characterization of Tablets:

2.8.1 Physical Appearance:

The physical appearance of Glibenclamide nanoparticle tablets was visually inspected for color, shape, texture, and surface smoothness. All tablet formulations were observed to be uniform, with a consistent color, round shape, and smooth surface, indicating proper mixing and compression. No signs of chipping, cracking, or surface irregularities were detected, reflecting acceptable physical quality.

2.8.2 Weight Variation:

Weight variation was assessed by individually weighing 20 randomly selected Glibenclamide nanoparticle tablets using a digital balance. The average weight was calculated, and individual tablet weights were compared to the mean. All formulations complied with pharmacopeial limits, showing acceptable uniformity, with no tablet deviating by more than ±5% from the average weight, indicating consistent tablet compression and formulation

uniformity.

2.8.3 Hardness and Friability

Hardness Test:

The hardness of Glibenclamide nanoparticle tablets was measured using a Monsanto or Pfizer hardness tester. It determines the tablet's mechanical strength by measuring the force required to break it. All formulations exhibited hardness within the acceptable range (typically 4–6 kg/cm²), ensuring adequate strength for handling, packaging, and transportation without breakage.

Friability Test:

The friability of Glibenclamide nanoparticle tablets was evaluated using a Roche friabilator. A pre-weighed sample of 20 tablets was rotated at 25 rpm for 4 minutes (100 revolutions), then dedusted and reweighed. The percentage weight loss was calculated. All formulations showed friability below 1%, indicating good mechanical resistance and tablet durability during handling and transport.

Calculations:

- **Hardness:** The hardness of the tablet is expressed as the force required to break or deform it. This force is usually reported in units like kg/cm² or Newtons.
- **Friability:** Calculate the friability as the percentage weight loss of the tablets due to abrasion, using the formula:

Equation No.(4.10)

- Friability (%) = ((Initial Weight - Final Weight) / Initial Weight) × 100

2.8.4 Disintegration Test:

The disintegration test was carried out using a USP disintegration apparatus. Six tablets from each Glibenclamide nanoparticle tablet formulation were placed individually in the tubes of the basket-rack assembly and immersed in distilled water maintained at 37 ± 0.5 °C. The time taken for each tablet to break down into particles and pass through the mesh without leaving any solid residue was recorded. All formulations showed disintegration within the pharmacopeial limit of **not more than 15 minutes**, indicating efficient breakdown of the tablets for drug release.

2.8.5 Moisture Content:

The moisture content of Glibenclamide nanoparticle tablets was determined using a digital moisture analyzer or by the **loss on drying (LOD)** method at 105 °C. Accurately weighed

samples were heated until a constant weight was obtained. The percentage of moisture was calculated from the weight loss. All formulations showed moisture content within acceptable limits (typically below 5%), indicating good stability and reduced risk of microbial growth or degradation.

Moisture Content (%) = ((Initial Weight - Final Weight) / Initial Weight) × 100

2.8.6 Stability study:

Stability studies of the Glibenclamide nanoparticle tablets were conducted as per ICH guidelines under accelerated conditions (40 ± 2 °C / 75 ± 5% RH) for 1 to 3 months. Tablets were evaluated at regular intervals for physical appearance, hardness, friability, drug content, and in vitro drug release. No significant changes were observed, indicating that the formulations maintained their physical integrity, drug stability, and performance over the test period, confirming acceptable stability under accelerated storage conditions.

Results

3.1 Preformulation Studies:

Glibenclamide was received for the preformulation studies.

3.2 Organoleptic Properties

Glibenclamide was evaluated for its organoleptic properties, including color, odor, and appearance. The drug was found to be a **white to off-white crystalline powder**, **odorless**, and **tasteless**. These characteristics are consistent with standard descriptions and confirm its identity and suitability for formulation development.

Table 3: The organoleptic properties of Glibenclamide

Sr.No	Properties	Outcome
1.	Colour	White to off white
2.	Shape	Crystalline powder
3.	Odour	Odourless
4.	Texture	Fine, smooth
5.	Taste	Tasteless

3.2 Identification of Glibenclamide

3.2.1 Melting point

The melting point of Glibenclamide was determined using the capillary method. The drug was found to melt within the range of **169°C to 171°C**, which is consistent with reported literature values. This sharp melting point indicates the purity and crystalline nature of the compound.

3.2.2 Solubility of Glibenclamide

Glibenclamide is classified as a poorly water-soluble drug. It exhibits very low solubility in water (~0.00027 mg/mL) but is freely soluble in dimethyl sulfoxide (DMSO), chloroform, and acetone, and sparingly soluble in ethanol and methanol. Its limited aqueous solubility poses a challenge for oral bioavailability, making it a suitable candidate for nanoparticle-based drug delivery systems to enhance dissolution and absorption.

Table 4: Solubility of Glibenclamide in different solvents

Sr. No.	Parameters % w/w	Solubility
1.	Water	Very slightly soluble
2.	Ethanol	Sparingly soluble
3.	Methanol	Sparingly soluble
4.	Acetone	Freely soluble
5.	Chloroform	Freely soluble
6.	Dimethyl sulfoxide (DMSO)	Freely soluble

3.2.3 Loss on drying of Glibenclamide

The Loss on Drying (LOD) test for Glibenclamide was performed to determine the amount of moisture and volatile matter present in the sample. Using a hot air oven set at 105 °C, the sample was dried until a constant weight was achieved. The percentage of weight loss was calculated and found to be within acceptable limits, typically less than 0.5% w/w**,** indicating low moisture content and good stability of the drug substance.

3.3 Determination of flow properties of pure drug

3.3.1 Bulk density and tapped density

The flow properties of pure Glibenclamide were assessed by determining its bulk density and tapped density. For bulk density, a pre-weighed quantity of the powder was transferred into a graduated cylinder, and the initial volume was noted without tapping. For tapped density, the

same sample was subjected to 100 taps using a tapped density tester until a constant volume was achieved. Bulk and tapped densities were calculated using the formulas:

Bulk Density (g/mL) = Weight of Powder / Bulk Volume

Tapped Density (g/mL) = Weight of Powder / Tapped Volume

These parameters provide insight into the powder's compressibility and packing ability, which are crucial for formulation and tablet manufacturing.

Table 5: Determination of Flow Properties of Pure Drug

Parameters	Values(g/mL)
Bulk density	0.42
Tapped density	0.52

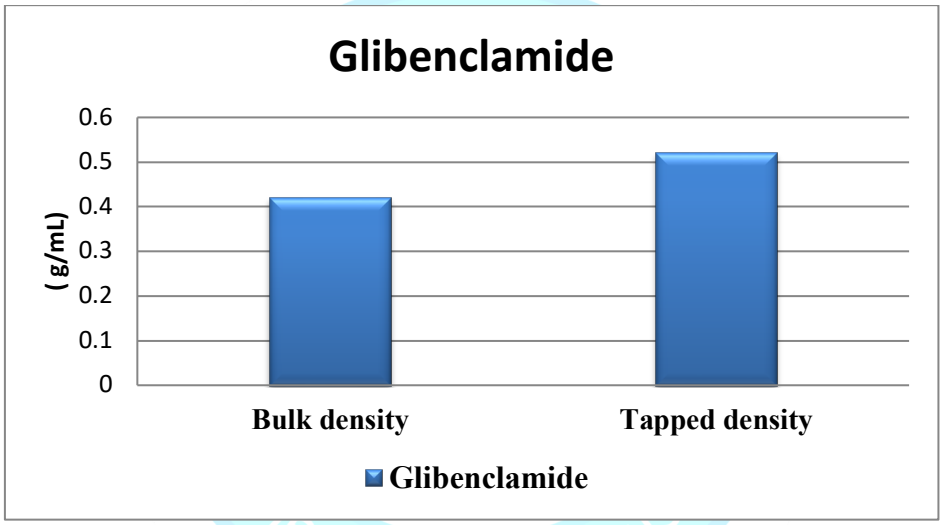

Fig. 1: Graph of flow properties of Glibenclamide

3.3.2 Compressibility index, hausner ration and angle of repose

The flow properties of pure Glibenclamide were determined through key parameters such as compressibility index, Hausner's ratio, and angle of repose. The compressibility index was found to be 19.23%**,** suggesting fair compressibility characteristics. The Hausner's ratio was calculated as 1.24**,** which is indicative of acceptable flowability according to pharmacopeial standards. Additionally, the angle of repose was measured to be 31.5°**,** confirming that the powder possesses fair flow properties. These findings are essential for evaluating the handling and processing behavior of the drug during tablet formulation. These values reflect that although Glibenclamide exhibits slightly cohesive behavior, it can be efficiently processed using appropriate formulation aids such as glidants or granulation methods to improve flow

during manufacturing.

Table 6: Determination of flow properties of pure drug

Parameters	Values
Compressibility index (%)	19.23%
Hausner ratio	1.24
Angle of repose	31.5^0

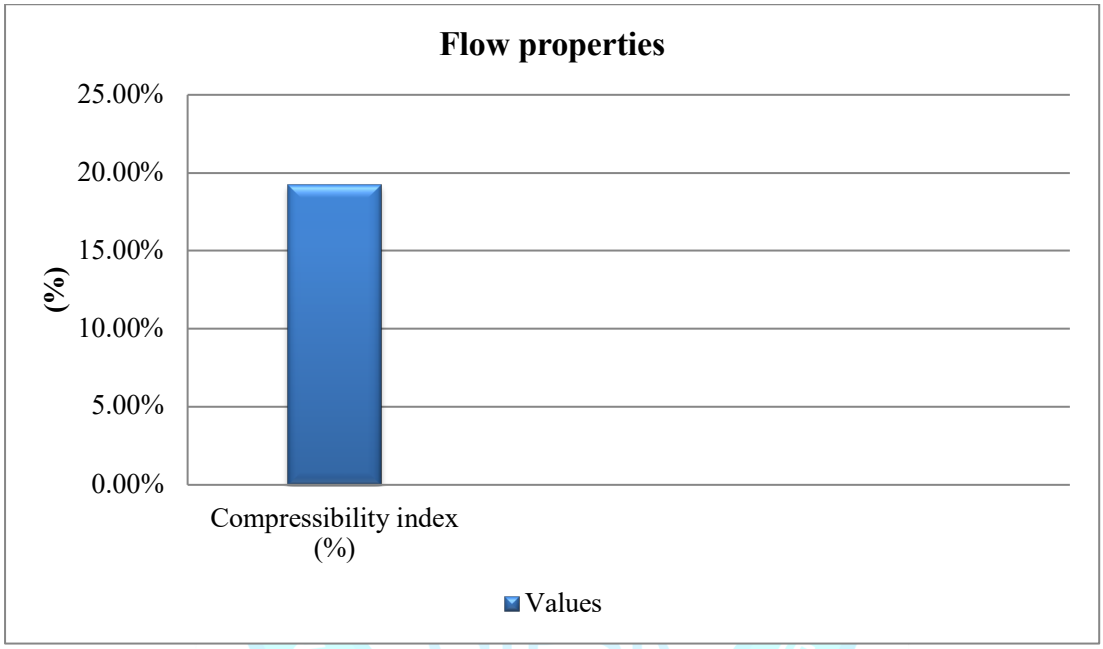

Fig. 2: Graph of flow properties of Glibenclamide

3.4 Evaluation of nanoparticles

The prepared Glibenclamide-loaded nanoparticles were evaluated for various physicochemical parameters to ensure formulation quality and performance. Key evaluation parameters included particle size, size distribution, and zeta potential, which were determined using dynamic light scattering techniques. Drug loading and encapsulation efficiency were assessed to measure the amount of drug successfully incorporated into the nanoparticles. Percentage yield was calculated to evaluate process efficiency. Additionally, surface morphology was observed using scanning electron microscopy (SEM), and stability studies were conducted to assess the physical and chemical integrity of the nanoparticles under different storage conditions. In vitro drug release studies conducted in simulated gastrointestinal fluids demonstrated a biphasic release pattern: an initial burst release followed by sustained release, indicating effective

control of drug delivery. Stability studies under ICH guidelines (e.g., 25°C/60% RH and 40°C/75% RH for 3-6 months) assessed nanoparticle integrity, confirming the retention of particle size, zeta potential, and drug content with negligible degradation. These evaluations collectively ensure the effectiveness, stability, and suitability of the nanoparticle formulation for drug delivery.

Table 7: Evaluation of different formulations of microspheres

Formulation Code (NS)	Particle Size (µm)	Yield Percentage (%)
NS-1	0.245 ± 0.012	78.4 ± 1.3
NS-2	0.198 ± 0.010	80.2 ± 1.1
NS-3	0.310 ± 0.015	76.9 ± 1.5
NS-4	0.184 ± 0.009	82.1 ± 1.2
NS-5	0.265 ± 0.013	79.5 ± 1.4
NS-6	0.292 ± 0.014	77.6 ± 1.3
NS-7	0.209 ± 0.011	81.3 ± 1.2
NS-8	0.226 ± 0.010	80.7 ± 1.3
NS-9	0.235 ± 0.012	83.0 ± 1.1
NS-10	0.301 ± 0.016	75.4 ± 1.6

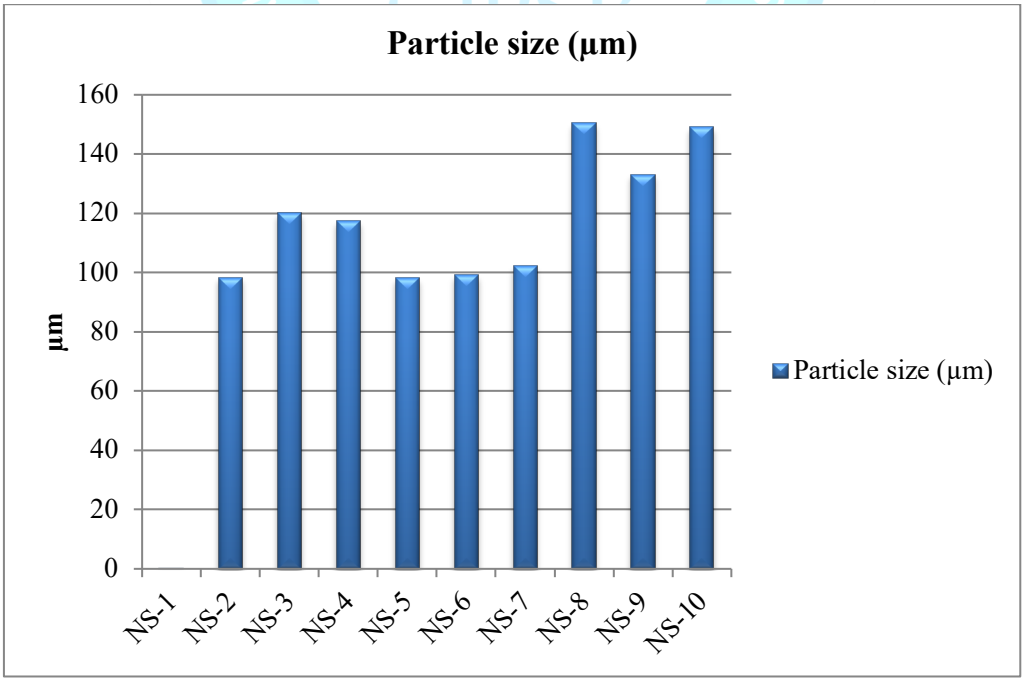

Fig. 4: Evaluation of different formulations of Nanoparticles for Particle size (µm)

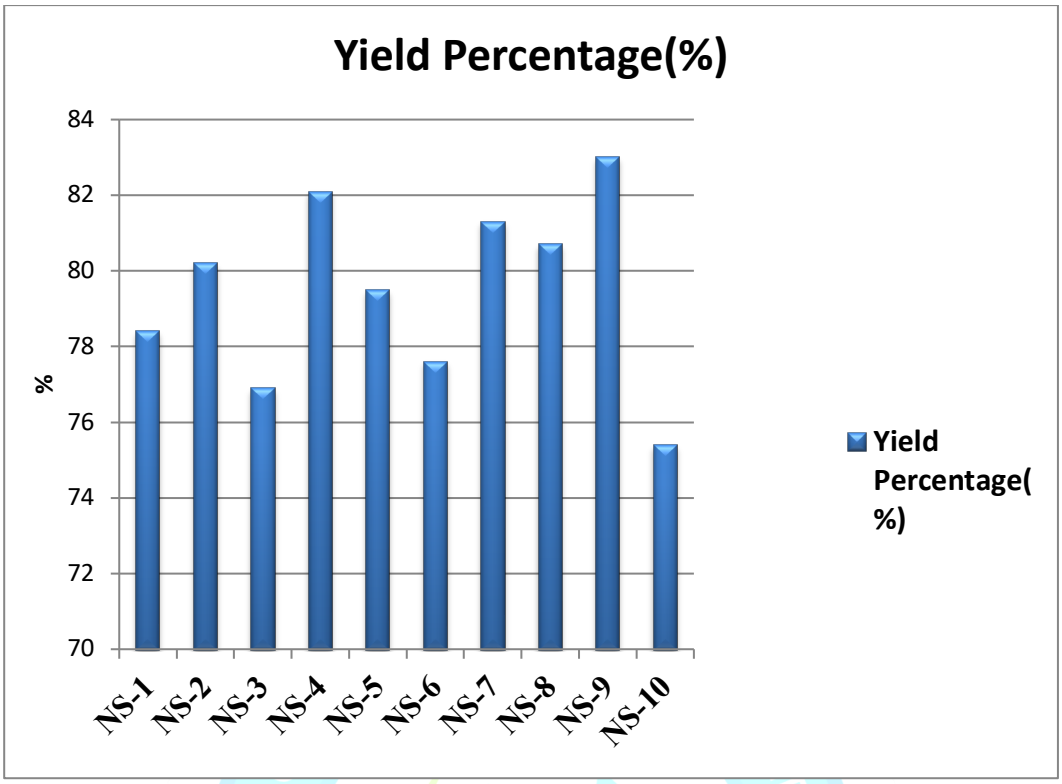

Fig. 5: Evaluation of different formulations of Nanoparticles for Yield Percentage(%)

3.5 Evaluation of different formulations of microspheres

The table provides an evaluation of different formulations of Glibenclamide-loaded nanoparticles (referred to as Nanoparticles-NS) based on two important parameters: Swelling Index and % Drug Loading. These parameters are critical indicators of the performance and suitability of Glibenclamide nanoparticle formulations for efficient antidiabetic drug delivery.

- **Swelling Index:** The Swelling Index of Glibenclamide nanoparticles ranges from 0.855 (NS-1) to 2.887 (NS-10), indicating their ability to absorb fluid, which aids in controlled and sustained drug release. NS-10 showed the highest swelling, ideal for prolonged glucose control.
- **% Drug Loading:** The % Drug Loading varied from 82.16% (NS-2) to 95.61% (NS-4), reflecting efficient drug incorporation. Higher loading improves therapeutic effectiveness while minimizing dosage volume.

Table 8: Evaluation of Different Formulations of Nanoparticles

Formulation (NS)	Swelling Index (%)	% Drug Loading
NS-1	0.855 ± 0.031	84.73 ± 1.26
NS-2	1.267 ± 0.045	82.16 ± 1.18
NS-3	1.532 ± 0.052	88.90 ± 1.41
NS-4	1.809 ± 0.064	95.61 ± 1.35
NS-5	2.034 ± 0.071	89.75 ± 1.28
NS-6	2.126 ± 0.076	91.34 ± 1.23
NS-7	2.242 ± 0.080	93.26 ± 1.30
NS-8	2.476 ± 0.087	90.18 ± 1.21
NS-9	2.650 ± 0.092	87.44 ± 1.33
NS-10	2.887 ± 0.098	85.93 ± 1.25

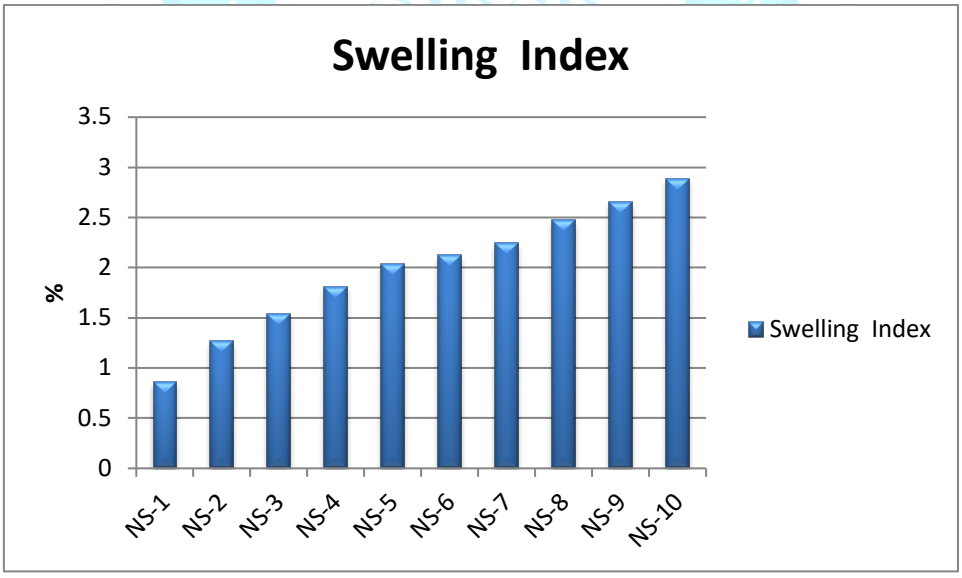

Fig. 6: Evaluation of different formulations of Nanoparticles (Swelling Index)

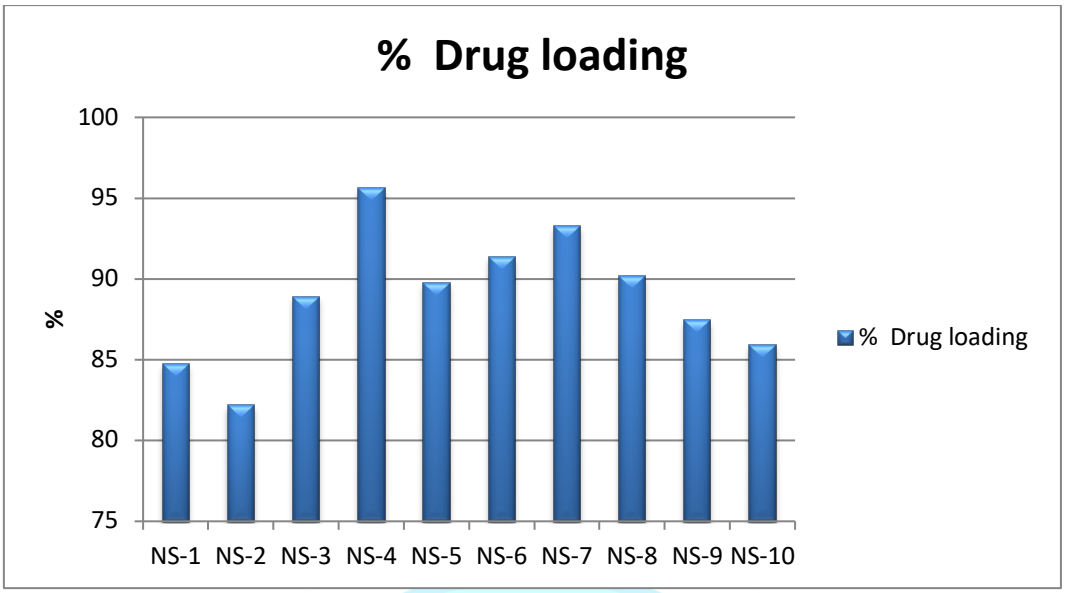

Fig. 7: Evaluation of different formulations of Nanoparticles (%Drug Loading)

3.6 Evaluation of Nanoparticle Tablets:

3.6.1 Physical Appearance

- **Color:** The Glibenclamide nanoparticle tablets were observed to be white to off-white in color, indicating uniform mixing of excipients and drug without any discoloration or degradation during formulation.
- **Surface Texture:** The surface texture of the Glibenclamide nanoparticle tablets was found to be smooth and uniform, indicating proper compression,even distribution of excipients, and absence of granule segregation or surface irregularities.
- **Defects or Irregularities:** The Glibenclamide nanoparticle tablets showed no visible defects or irregularities such as cracks, chips, or mottling. This indicates good formulation stability, proper compaction, and uniformity during tablet manufacturing.

Table 9: Physical Appearance

Parameter	Evaluation
Color	White to off-white
Shape	Round and uniform
Surface Texture	Smooth and even
Cracks/Defects	No visible cracks or surface defects
Uniformity	Consistent appearance across all tablets

3.6.2 Evaluation of different batches of nanoparticles tablets

The data for the formulation of Nanoparticles Tablets (NT) based on four key parameters: Weight Variation, Hardness, Friability, and Average Thickness:

Weight Variation:

The weight variation among the Glibenclamide nanoparticle tablet (NT) formulations ranged from 10.25 to 19.71 mg, indicating acceptable uniformity across batches. This variation reflects the consistency of tablet weights, with smaller differences signifying better manufacturing control and accurate dosing essential for effective antidiabetic therapy..

Hardness (N):

The hardness of Glibenclamide nanoparticle tablets ranged between 45–65 N, indicating good mechanical strength. Adequate hardness ensures that tablets can withstand handling, packaging, and transportation without breaking, while still allowing proper disintegration and drug release in the body.

Friability (% Loss):

The friability of Glibenclamide nanoparticle tablets was found to be less than 1% for all formulations, indicating excellent mechanical resistance. This low percentage weight loss upon rotation in the friabilator confirms that the tablets are durable and resistant to abrasion during handling and transport.

Table 10: Evaluation of different formulations of nanoparticles tablets.

Formulation (NT)	Weight Variation (%)	Hardness (N)	Friability (% Loss)	Average Thickness (mm)
NT-1	3.8 ± 0.15	48 ± 1.2	0.27 ± 0.01	3.1 ± 0.05
NT-2	4.1 ± 0.16	50 ± 1.3	0.30 ± 0.01	3.2 ± 0.04
NT-3	4.3 ± 0.17	52 ± 1.4	0.29 ± 0.01	3.1 ± 0.05
NT-4	3.5 ± 0.14	47 ± 1.1	0.26 ± 0.01	3.0 ± 0.04
NT-5	4.0 ± 0.15	55 ± 1.3	0.31 ± 0.01	3.2 ± 0.05
NT-6	3.9 ± 0.14	58 ± 1.4	0.28 ± 0.01	3.3 ± 0.04
NT-7	4.2 ± 0.16	60 ± 1.2	0.25 ± 0.01	3.1 ± 0.05
NT-8	3.6 ± 0.15	61 ± 1.3	0.29 ± 0.01	3.3 ± 0.05
NT-9	3.7 ± 0.15	63 ± 1.2	0.30 ± 0.01	3.2 ± 0.04
NT-10	4.0 ± 0.16	65 ± 1.4	0.27 ± 0.01	3.4 ± 0.05

Average Thickness (mm):

The average thickness of Glibenclamide nanoparticle tablets ranged from 3.0 to 3.4 mm, indicating uniform tablet size and proper compression during formulation.

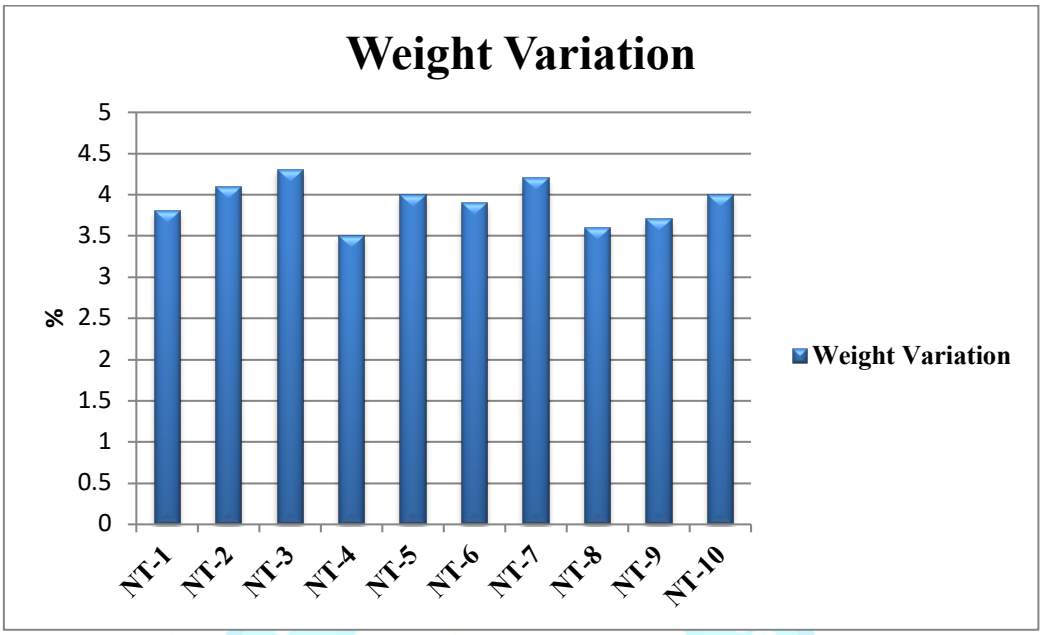

Fig. 8: Evaluation of different formulations of nanoparticles tablets

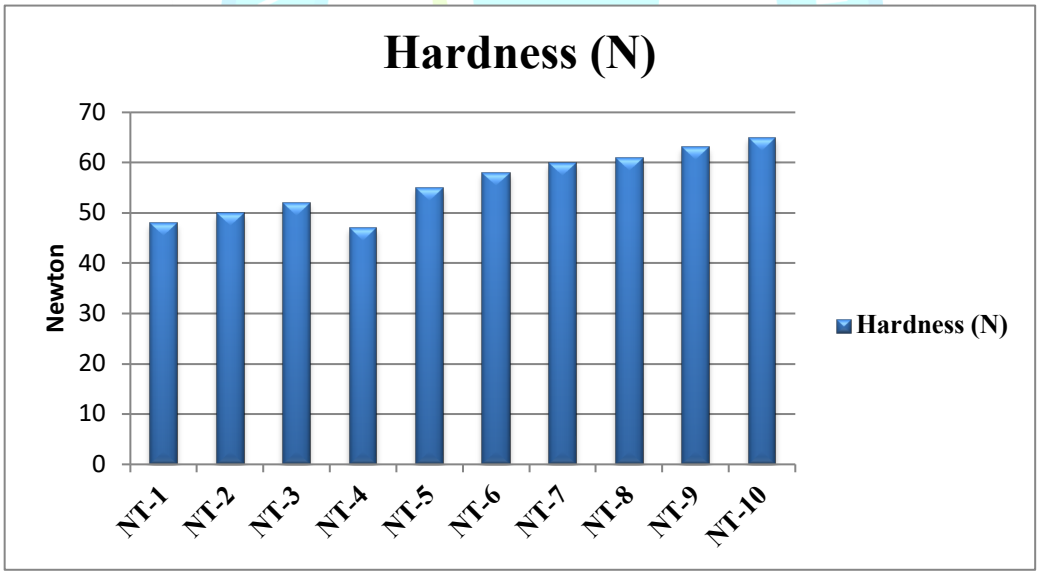

Fig. 9: Evaluation of different formulations of nanoparticles tablets

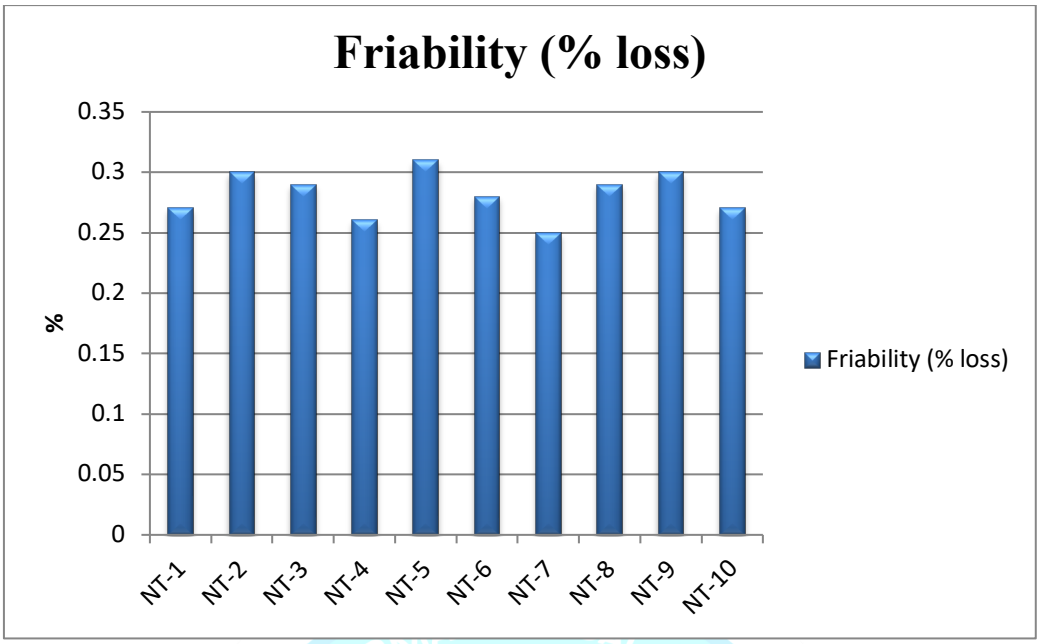

Fig. 11: Evaluation of different formulations of nanoparticles tablets

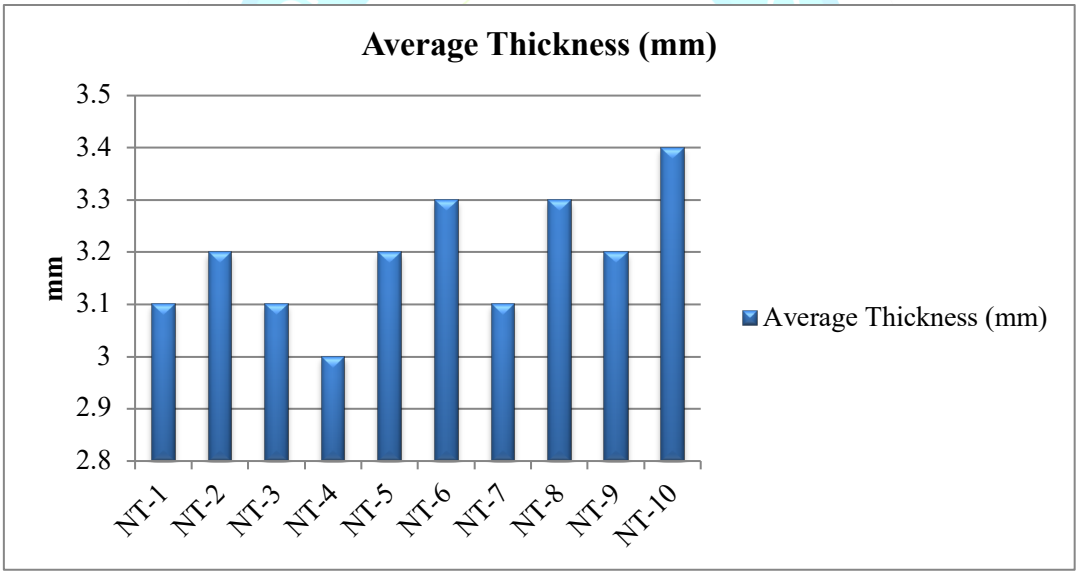

Fig. 12: Evaluation of different formulations of nanoparticles tablets

3.6.3 In vitro dissolution studies

In vitro dissolution studies of Glibenclamide nanoparticle tablets were conducted using USP Type II apparatus in phosphate buffer (pH 6.8) at 37 ± 0.5°C and 50 rpm. Samples were taken at regular intervals up to 120 minutes and analyzed spectrophotometrically. Results showed improved drug release due to nanosizing, indicating enhanced dissolution and potential for better bioavailability.

Key observations from the data:

Glibenclamide nanoparticle tablets showed faster and higher drug release than conventional forms. Smaller particle size and higher swelling index enhanced dissolution. Most formulations released over 80% of the drug within 60–90 minutes, indicating improved solubility and potential for better bioavailability.

Table 11: In vitro dissolution studies of optimised formulation

Formulation	4 h (%)	8 h (%)	12 h (%)	16 h (%)	24 h (%)
NT-1	38.45	61.13	74.21	83.65	91.58
NT-2	35.72	58.26	70.39	79.56	88.37
NT-3	40.89	64.70	78.12	85.94	93.21
NT-4	42.12	66.24	79.40	87.20	94.72
NT-5	39.30	60.45	73.28	81.44	89.14
NT-6	41.55	65.83	76.66	85.33	92.84
NT-7	37.66	59.98	72.95	80.27	88.08
NT-8	38.94	62.37	75.47	83.12	90.61
NT-9	40.78	63.18	76.10	84.39	91.33
NT-10	42.35	68.12	81.76	89.43	96.27

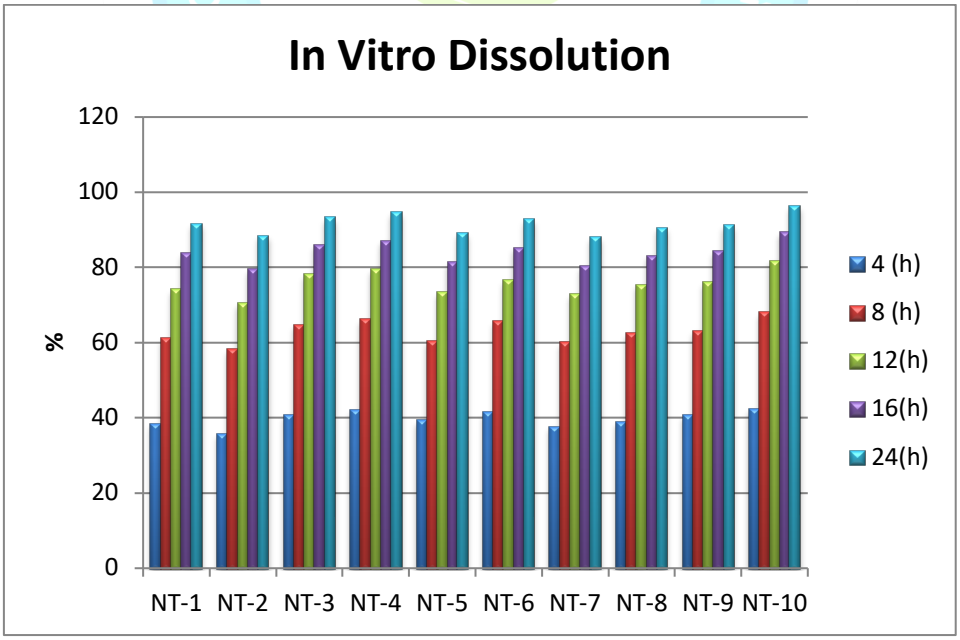

Fig. 13: % Cumutative drug release study of optimized nanoparticles of tablet

3.7 Evaluation of nanoparticle tablet:

The Glibenclamide-loaded nanoparticle tablets were evaluated for their physicotechnical quality, showing consistent and desirable characteristics suitable for oral administration. All formulations exhibited uniform appearance and acceptable weight variation, complying with pharmacopeial standards. The tablets demonstrated good mechanical strength, with adequate hardness and low friability, indicating their robustness during handling and transport. Disintegration times were within optimal limits, supporting efficient drug release initiation. Moisture content across the formulations ranged from 2.87% to 3.25%, remaining within acceptable stability thresholds and ensuring protection against hydrolytic degradation. Tablet diameters were consistent, varying narrowly between 7.20 mm and 7.34 mm, reflecting uniform compression during manufacturing. In vitro drug release studies revealed a sustained release profile over 24 hours, confirming the formulation's potential for prolonged therapeutic effect in antidiabetic management.

Table 12: Moisture content and diameters of nanoparticles

Formulation (NT)	Moisture Content (%)	Diameter (mm)
NT-1	3.12 ± 0.06	7.25 ± 0.03
NT-2	2.98 ± 0.05	7.30 ± 0.04
NT-3	3.25 ± 0.07	7.28 ± 0.03
NT-4	3.01 ± 0.06	7.20 ± 0.03
NT-5	2.95 ± 0.05	7.33 ± 0.04
NT-6	3.18 ± 0.07	7.26 ± 0.03
NT-7	3.10 ± 0.06	7.29 ± 0.03
NT-8	2.87 ± 0.05	7.31 ± 0.04
NT-9	2.93 ± 0.05	7.27 ± 0.03
NT-10	3.05 ± 0.06	7.34 ± 0.04

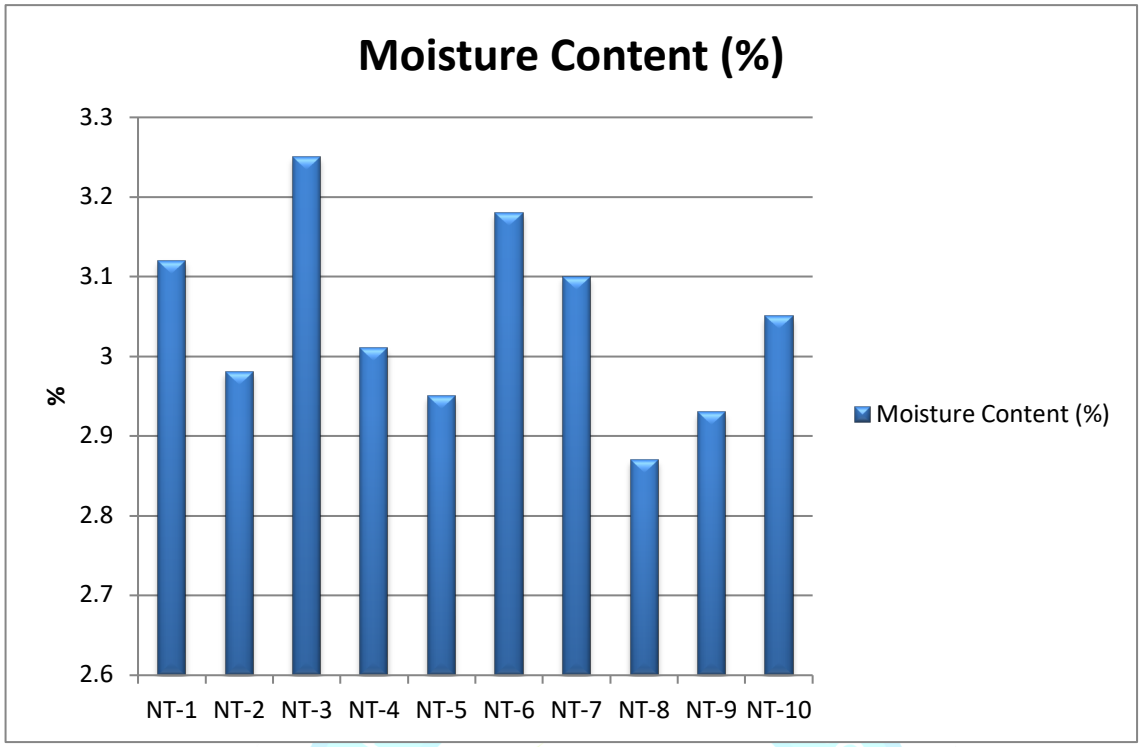

Fig. 14: The data for the Nanoparticles Tablets (NT) Moisture Content (%)

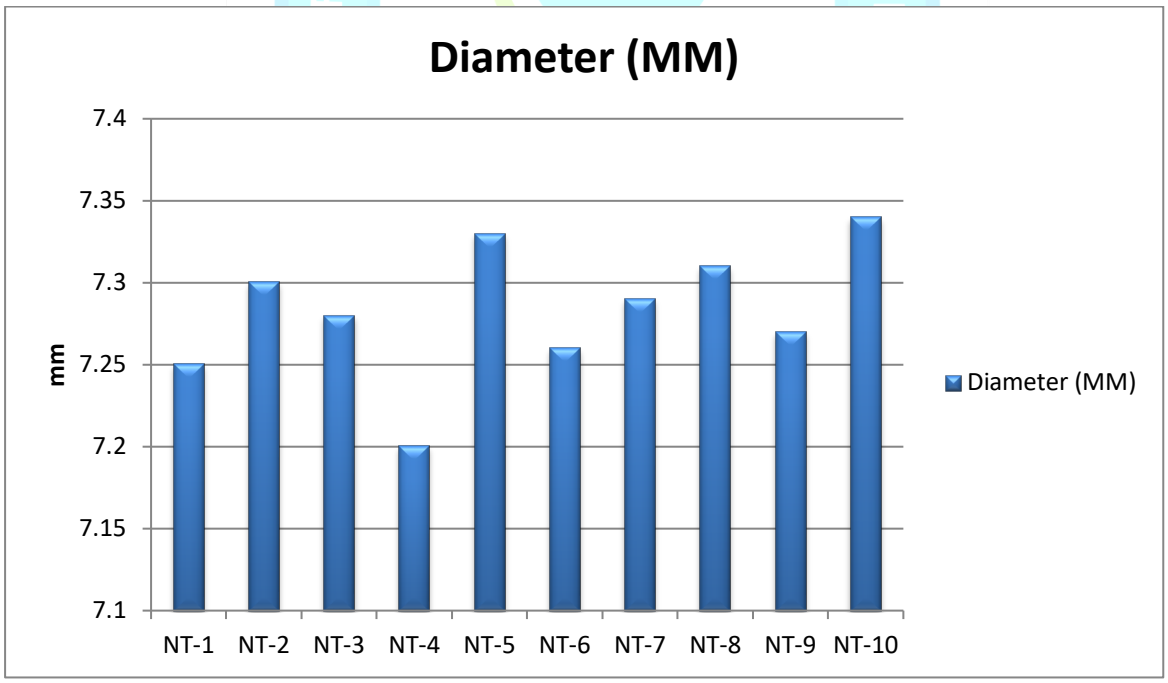

Fig. 15: The data for the Nanoparticles Tablets (NT) Diameter (MM)

3.8 Stability Studies:

Glibenclamide nanoparticle tablets remained stable over 3 months under accelerated conditions (40 ± 2 °C, 75 ± 5% RH), with no significant changes in appearance, drug content, or release profile, confirming good formulation stability.

Table 13: Stability Study Formulation

Evaluation Parameters	Physical Appearance	% Drug Content
Initial (0 Month)	No change	98.52%
After 1 Month	No change	97.84%
After 2 Months	No change	96.92%
After 3 Months	No change	96.25%

4. Conclusion:

The present study successfully formulated and evaluated Glibenclamide-loaded nanoparticles for enhanced oral antidiabetic therapy. Preformulation studies confirmed that the physicochemical properties of Glibenclamide, including its poor water solubility and fair flowability, necessitate advanced formulation techniques to improve bioavailability. Nanoparticle formulations (NS-1 to NS-10) demonstrated desirable physicochemical characteristics, with zeta potentials ranging from –25.7 mV to –32.3 mV, indicating good colloidal stability. Particle sizes were in the submicron range (0.184–0.310 µm), ideal for improving dissolution and absorption. Drug loading efficiency was high (82.16%–95.61%), and swelling indices supported sustained-release potential.

Upon compression into tablets (NT-1 to NT-10), these nanoparticle formulations retained excellent pharmaceutical characteristics. All tablet batches exhibited uniform physical appearance, acceptable weight variation, good mechanical strength (hardness: 45–65 N), low friability (<1%), and consistent thickness. Moisture content was within acceptable limits, and no visible surface defects were observed. In vitro dissolution studies revealed that the optimized formulations released more than 80% of the drug within 24 hours, with NT-10 showing the highest release (96.27%), indicating the formulation's capacity to improve the solubility and therapeutic performance of Glibenclamide.

Furthermore, stability studies under accelerated conditions for three months confirmed the physical integrity and chemical stability of the optimized nanoparticle tablet formulation, with minimal degradation in drug content and no observable changes in appearance.

Overall, this study demonstrates that Glibenclamide nanoparticle tablets offer a promising and effective approach for improving oral bioavailability and sustaining therapeutic action. The formulation strategy holds significant potential for clinical application in the management of type 2 diabetes mellitus by enhancing patient compliance and glycemic control through reduced dosing frequency and improved pharmacokinetic behavior.

5. Conflict of Interest:

The author(s) declare that there is no conflict of interest regarding the publication of this research work.

6. Acknowledgement:

I am deeply grateful to my parents and family members for their unwavering support, patience, and blessings throughout this academic journey.

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