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Research

Development and Characterization of Albumin-Based Nanoparticles for Sustained Release of Repaglinide

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ABSTRACT

The study focuses on the development and characterization of repaglinide-loaded albumin nanoparticles for sustained drug release, aimed at improving the management of Type 2 diabetes. The nanoparticles were synthesized using a solvent evaporation method, resulting in uniform particle size (150 ± 5 nm) with a low polydispersity index (PDI) of 0.23, and a negative zeta potential of -20 ± 1 mV, ensuring colloidal stability. The drug loading capacity and encapsulation efficiency were 4.5 ± 0.2% and 75 ± 3%, respectively. In vitro release studies demonstrated a controlled drug release profile, with 80 ± 8% of repaglinide released over 48 hours, suggesting potential for reducing dosing frequency and enhancing patient compliance. Kinetic analysis revealed that the release followed a Fickian diffusion mechanism (R^2 = 0.982). The nanoparticles showed good stability over 30 days, with only slight increases in particle size and PDI. Additionally, cytotoxicity studies confirmed the biocompatibility of the nanoparticles. Comparative analysis with other drug delivery systems showed that albumin nanoparticles offer superior controlled release and drug encapsulation efficiency, making them a promising alternative for repaglinide delivery in diabetes management. Further clinical validation is required for real-world applications.

KEYWORDS: Albumin nanoparticles, sustained release, repaglinide, drug delivery system, biocompatibility, controlled release, pharmacokinetics, bioavailability.

1. INTRODUCTION:

The management of diabetes mellitus, particularly type 2 diabetes, often requires the use of oral hypoglycemic agents. Repaglinide, a non-sulfonylurea insulin secretagogue, is widely used in the treatment of type 2 diabetes due to its rapid onset of action and short duration of effect. However, the therapeutic potential of repaglinide is limited by its short half-life, necessitating frequent dosing to maintain its blood glucose-lowering effects. This frequent dosing not only affects patient compliance but can also lead to fluctuations in blood glucose levels, which can compromise treatment efficacy.(1) To address these challenges, the development of controlled drug delivery systems has gained significant attention. Nanoparticle-based drug delivery systems, particularly albumin nanoparticles, offer a promising solution for the

sustained release of drugs. Albumin, being a biocompatible and biodegradable protein, has been extensively explored as a carrier for various therapeutic agents. Its ability to encapsulate hydrophobic drugs, protect them from degradation, and release them in a controlled manner makes it an ideal candidate for drug delivery applications.(2) This research aims to develop albumin-based nanoparticles for the sustained release of repaglinide. By formulating repaglinide into nanoparticles, the goal is to enhance the drug's pharmacokinetics, reduce the frequency of administration, and improve patient compliance. The study further investigates the characterization of these nanoparticles, including their size, surface properties, drug-loading capacity, and in vitro release profiles. The ultimate aim is to evaluate the potential of albumin-based nanoparticles as an effective and sustainable drug delivery system for repaglinide, contributing to the improvement of diabetes management.

2. LITERATURE REVIEW

2.1 Background of Diabetes Mellitus:

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels resulting from either inadequate insulin production or poor insulin utilization by the body. It is a major global health concern, affecting millions of people worldwide. The two most common types of diabetes are Type 1 and Type 2. Type 1 diabetes occurs when the immune system mistakenly destroys the insulin-producing beta cells in the pancreas, leading to absolute insulin deficiency. In contrast, Type 2 diabetes is primarily caused by insulin resistance, where the body's cells become less responsive to insulin, leading to elevated blood sugar levels over time. As Type 2 diabetes progresses, the pancreas may also lose its ability to produce sufficient insulin. Uncontrolled diabetes can lead to various complications, including cardiovascular diseases, kidney failure, nerve damage, and poor wound healing. The management of diabetes typically involves lifestyle modifications, such as diet and exercise, along with medications to control blood sugar levels. Oral hypoglycemic agents, such as repaglinide, are commonly used in the treatment of Type 2 diabetes to help lower blood glucose levels by stimulating insulin release from the pancreas.(3)

2.2 Overview of Type 2 Diabetes and Its Treatment:

Type 2 diabetes (T2D) is a chronic condition that affects how the body processes glucose (sugar). Unlike Type 1 diabetes, where the body produces little or no insulin, in T2D, the body either becomes resistant to insulin or does not produce enough insulin to maintain normal blood sugar levels. Over time, the pancreas can become less effective at producing insulin, contributing to the development of high blood glucose levels. The primary risk factors for T2D include obesity, physical inactivity, unhealthy diet, genetic predisposition, and advancing age.(4)

The treatment of T2D focuses on controlling blood sugar levels to prevent complications such as heart disease, kidney damage, and nerve disorders. Lifestyle changes, such as adopting a healthy diet, increasing physical activity, and losing weight, are critical components of managing the disease. In addition to lifestyle modifications, various oral medications are used to control blood sugar. Common treatments include metformin, sulfonylureas, and insulin secretagogues like repaglinide. These medications help lower blood glucose either by improving the body's sensitivity to insulin or by stimulating the pancreas to release more insulin. However, despite the availability of these therapies, managing blood sugar levels remains challenging for many patients due to fluctuating insulin production and the need for frequent dosing, highlighting the importance of novel drug delivery strategies like sustained-release formulations to improve treatment outcomes and patient compliance.(5)

2.3 Role of Repaglinide in Diabetes Management:

Repaglinide is an oral antidiabetic medication that belongs to the class of drugs known as meglitinides. It is commonly prescribed for the management of Type 2 diabetes, especially in patients whose blood glucose levels are not well-controlled with diet and exercise alone. Repaglinide works by stimulating the pancreas to release more insulin in response to meals, thereby helping to lower postprandial blood glucose levels. Unlike sulfonylureas, which have a prolonged action, repaglinide acts rapidly and has a short duration of action, making it effective for controlling blood sugar spikes after meals.(6)

One of the key advantages of repaglinide is its flexibility in dosing, as it is taken just before meals. This allows patients to adjust the dose based on their meal size, making it a convenient option for individuals with variable eating schedules.

Repaglinide is often used in combination with other antidiabetic medications to improve overall blood glucose control. However, its short half-life can lead to frequent dosing, which may impact patient adherence to the treatment regimen.

While effective, repaglinide's therapeutic potential can be limited by its quick metabolism and the need for multiple doses throughout the day. This highlights the need for innovative drug delivery systems, such as sustained-release formulations, which could improve the pharmacokinetics of repaglinide and provide more consistent blood sugar control with less frequent dosing.(7)

2.4 Need for Sustained Release Formulations:

Sustained release (SR) formulations are designed to release a drug at a controlled rate over an extended period, ensuring more consistent therapeutic effects while reducing the frequency of dosing. In the case of diabetes management, medications like repaglinide, which have a short half-life and require frequent dosing, may benefit significantly from SR formulations. The primary need for such formulations lies in their ability to maintain stable blood glucose levels over time, improving overall therapeutic outcomes and reducing the risk of hypoglycemia or hyperglycemia associated with fluctuating drug concentrations.(8)

Patients with Type 2 diabetes often experience challenges with adherence to treatment regimens due to the need for multiple daily doses, which can lead to missed doses and suboptimal blood sugar control. SR formulations can help mitigate this issue by reducing the dosing frequency, thereby improving patient compliance. Additionally, these formulations can offer improved pharmacokinetics, ensuring that the drug is released gradually and continuously, leading to better control of postprandial glucose levels. This controlled release also minimizes peak-trough fluctuations, which are common with immediate-release formulations, leading to more stable blood glucose levels throughout the day.

Ultimately, SR formulations not only enhance the efficacy of the drug but also improve patient convenience and quality of life. They represent a promising approach in optimizing the treatment of chronic conditions like diabetes, where long-term medication adherence and consistent control are critical.

2.5 Controlled Drug Delivery Systems: An Overview

Controlled drug delivery systems (CDDS) are designed to release therapeutic agents at a predetermined rate, ensuring that the drug maintains optimal therapeutic levels in the body for a prolonged period. These systems are developed to address the limitations of conventional drug delivery methods, such as frequent dosing and high variability in drug concentrations. CDDS can be categorized into various types, including oral, transdermal, and injectable systems. The key advantage of these systems is their ability to improve the pharmacokinetics of drugs, reduce side effects, and enhance patient compliance by decreasing the frequency of administration.(9)

In recent years, controlled drug delivery has gained significant attention due to its potential to target specific sites within the body, ensuring localized action of the drug and minimizing systemic exposure. This has proven especially useful for treating chronic conditions such as diabetes, cancer, and cardiovascular diseases. The development of controlled drug delivery systems involves the use of various materials, such as biodegradable polymers, liposomes, and nanoparticles, which offer the advantage of controlled release profiles, enhanced stability, and improved bioavailability.(10)

2.6 Nanoparticle-Based Drug Delivery Systems

Nanoparticle-based drug delivery systems are a promising advancement in the field of controlled drug delivery. These systems utilize nanoparticles, typically ranging from 1 to 100 nanometers in size, as carriers for drugs. Nanoparticles can be made from a variety of materials, including lipids, polymers, and proteins, offering versatility in drug encapsulation and release profiles. The small size of nanoparticles enables them to penetrate tissues more easily, enhancing the bioavailability of drugs and improving their therapeutic efficacy.

The main advantage of nanoparticle-based drug delivery systems is their ability to provide controlled, sustained, or targeted release of drugs. Nanoparticles can be engineered to release the drug in response to specific environmental conditions, such as pH, temperature, or the presence of specific enzymes, allowing for more precise delivery to the site of action. This is particularly useful in applications where localized drug delivery is required, such as in cancer therapy or diabetes management.(11)

In addition to providing controlled release, nanoparticle systems offer enhanced stability and

protection for drugs, especially those that are sensitive to degradation, such as proteins or peptides. The ability to modify the surface of nanoparticles allows for targeted delivery, ensuring that drugs are delivered to the intended site with minimal side effects. As a result, nanoparticle-based drug delivery systems have the potential to revolutionize treatment strategies for a wide range of diseases, offering better outcomes and improved patient compliance.

2.7 Albumin Nanoparticles: A Promising Drug Carrier

Albumin nanoparticles have emerged as a promising carrier for drug delivery systems due to their unique properties, such as biocompatibility, biodegradability, and low toxicity. Albumin, a naturally occurring protein in the human body, is widely used in drug delivery applications because it can safely interact with body tissues without triggering adverse immune responses. These nanoparticles are typically formed by self-assembly or through techniques such as solvent evaporation, coacervation, or nanoprecipitation, making them suitable for encapsulating a variety of hydrophobic and hydrophilic drugs.

One of the key advantages of albumin nanoparticles is their ability to enhance the solubility and stability of drugs that are otherwise poorly soluble in water. This characteristic is particularly beneficial for drugs like repaglinide, which have limited water solubility and can benefit from improved bioavailability when encapsulated in albumin nanoparticles. The albumin matrix protects the drug from premature degradation and enables controlled release over an extended period, which helps maintain therapeutic drug levels and reduces the frequency of dosing.

Furthermore, albumin nanoparticles can be easily modified to enhance their drug-loading capacity, surface properties, and release profiles. The surface of albumin nanoparticles can be functionalized with ligands or antibodies to enable targeted delivery to specific tissues or cells, thereby minimizing systemic side effects and improving the drug's therapeutic efficacy. Additionally, albumin's natural ability to bind to receptors on cell membranes facilitates the cellular uptake of the nanoparticles, enhancing drug absorption at the desired site of action.(12)

Overall, albumin nanoparticles represent a highly versatile and effective drug carrier system for various pharmaceutical applications. Their ability to encapsulate a wide range of therapeutic agents, combined with their controlled release properties and potential for targeted delivery, makes them an ideal candidate for developing advanced drug delivery systems, particularly in the management of chronic conditions such as diabetes.

2.8 Development of Repaglinide-Loaded Albumin Nanoparticles

The development of repaglinide-loaded albumin nanoparticles involves the formulation of a controlled drug delivery system that can effectively encapsulate the hydrophobic drug repaglinide while ensuring sustained release for improved therapeutic outcomes. The process typically begins with the selection of a suitable method for nanoparticle formation, such as solvent evaporation, coacervation, or nanoprecipitation, all of which allow for the incorporation of repaglinide into the albumin matrix. These methods help to create nanoparticles with a desired size and drug-loading efficiency while maintaining the stability and activity of the encapsulated drug.(14)

The primary objective of developing repaglinide-loaded albumin nanoparticles is to achieve a controlled release profile that enhances the pharmacokinetics of repaglinide. By encapsulating the drug in nanoparticles, it is possible to slow down the drug's release rate, thereby maintaining therapeutic drug levels over an extended period. This can reduce the frequency of dosing, improving patient compliance and ensuring more consistent blood glucose control. The development process also involves optimizing key factors such as the drug-to-carrier ratio, nanoparticle size, and surface charge to ensure effective drug delivery and controlled release.

Moreover, the formulation of repaglinide-loaded albumin nanoparticles must ensure biocompatibility and stability. The nanoparticles should not induce adverse immune responses or cause toxicity, as the aim is to improve the therapeutic effect without compromising patient safety. The development process also includes scaling up the formulation for potential clinical applications and conducting stability studies to ensure that the nanoparticles retain their drug-loaded capacity over time.(15)

3. MATERIALS AND METHODS

3.1 Materials

- **Albumin** (Bovine Serum Albumin, BSA) was obtained from Sigma-Aldrich (USA).

- **Repaglinide** was purchased from ChemBrite Pharmaceuticals (India).
- **Solvents**: Acetone, ethanol, and deionized water were used for nanoparticle synthesis and purification.
- **Reagents**: Polyvinyl alcohol (PVA) was used as a stabilizer. Phosphate-buffered saline (PBS) (pH 7.4) was used for in vitro release studies.
- **Other Materials**: Nitrogen gas for drying, glassware, and analytical instruments as required.

3.2 Synthesis of Repaglinide-Loaded Albumin Nanoparticles

Repaglinide-loaded albumin nanoparticles were prepared by a solvent evaporation method. Briefly:

1. **Preparation of Albumin Solution**: 10 mg of BSA was dissolved in 10 mL of deionized water, and the pH was adjusted to 7.4 using 0.1 M NaOH.
2. **Drug Loading**: Repaglinide (5 mg) was dissolved in a mixture of acetone and ethanol (1:1 v/v). The drug solution was added dropwise to the albumin solution under constant stirring at room temperature. The mixture was then sonicated for 5 minutes to ensure uniform dispersion.
3. **Nanoparticle Formation**: The organic solvents were evaporated using a rotary evaporator under reduced pressure, resulting in the formation of nanoparticles. The suspension was then centrifuged at 10,000 rpm for 30 minutes to remove unencapsulated drug.
4. **Washing**: The pellet was washed several times with deionized water to remove any residual solvents and free drug.
5. **Nanoparticle Collection**: The final nanoparticles were resuspended in PBS (pH 7.4) and stored at 4°C for further characterization.

3.3 Characterization of Nanoparticles

- **Particle Size and Zeta Potential**: The average particle size, polydispersity index (PDI), and zeta potential of the nanoparticles were measured using a Zetasizer Nano ZS (Malvern Instruments, UK).
- **Surface Morphology**: The surface morphology of the nanoparticles was observed using Scanning Electron Microscopy (SEM) (JEOL, JSM-7100F).
- **Drug Loading and Encapsulation Efficiency**: The drug loading capacity (DLC) and encapsulation efficiency (EE) were determined by measuring the amount of repaglinide in the supernatant after centrifugation using UV-Vis spectrophotometry (λ = 247 nm). DLC and EE were calculated using the following formulas:

$$\mathrm{DLC}(\%) = \left(\frac{\text{Weight of loaded drug}}{\text{Weight of nanoparticles}}\right) \times 100$$

$$\mathrm{EE}(\%) = \left(\frac{\text{Weight of encapsulated drug}}{\text{Total weight of drug used}}\right) \times 100$$

3.4 In Vitro Drug Release Studies

The in vitro release study of repaglinide-loaded albumin nanoparticles was performed using a dialysis membrane method. Briefly:

1. **Dialysis Setup**: An aliquot of nanoparticle suspension (1 mL) was placed in a dialysis bag (molecular weight cutoff of 10 kDa) and immersed in 50 mL of PBS at pH 7.4. The setup was stirred continuously at 37°C to mimic physiological conditions.
2. **Sample Collection**: At predetermined time intervals (1, 2, 4, 6, 8, 12, 24, and 48 hours), 1 mL of release medium was collected and replaced with an equal volume of fresh PBS.
3. **Analysis**: The collected samples were analyzed for repaglinide concentration using UV-Vis spectrophotometry. The cumulative drug release was plotted against time to determine the release profile.

3.5 Stability Studies

The physical stability of the nanoparticles was evaluated by monitoring changes in particle size, PDI, and zeta potential after storage at 4°C for 30 days. In addition, the drug release profile was re-evaluated at different time points to assess any significant change in release behavior over time.

3.6 Biocompatibility and Cytotoxicity Studies

The cytotoxicity of repaglinide-loaded albumin nanoparticles was evaluated using the MTT assay on human fibroblast cells (L929). Cells were cultured in RPMI 1640 medium with 10% FBS, and treated with varying concentrations of nanoparticle formulations. The cell viability was assessed by measuring the absorbance at 570 nm using a microplate reader.

4. ANALYSIS AND RESULTS

4.1 Nanoparticle Characteristics

Table 1: Characterization of Repaglinide-Loaded Albumin Nanoparticles

Parameter	Value	Units
Particle Size	150 ± 5	nm
Polydispersity Index (PDI)	0.23	-
Zeta Potential	-20 ± 1	mV
Drug Loading Capacity (DLC)	4.5 ± 0.2	%
Encapsulation Efficiency (EE)	75 ± 3	%

The characterization of repaglinide-loaded albumin nanoparticles is presented in Table 1. The nanoparticles exhibited a mean particle size of 150 ± 5 nm, which falls within the ideal size range for nanocarrier systems, allowing for efficient cellular uptake and prolonged systemic circulation. The polydispersity index (PDI) was measured at 0.23, indicating a relatively uniform and monodisperse distribution of particle sizes, which is essential for consistent drug delivery behavior. The zeta potential was found to be -20 ± 1 mV, signifying moderate surface charge that provides electrostatic repulsion between particles and helps maintain colloidal stability by minimizing aggregation. The drug loading capacity (DLC) of the nanoparticles was 4.5 ± 0.2%, demonstrating that the formulation can incorporate a reasonable amount of repaglinide per unit mass of nanoparticle. Furthermore, the encapsulation efficiency (EE) was 75 ± 3%, indicating that the formulation process was effective in incorporating the drug into the nanoparticulate matrix with minimal loss.

4.2 In Vitro Drug Release Profile

Table 2: In Vitro Drug Release Profile of Repaglinide-Loaded Albumin Nanoparticles

Time Point	Cumulative Drug Release (%)
1 hour	12 ± 2
2 hours	20 ± 3
4 hours	30 ± 4
6 hours	45 ± 5
8 hours	55 ± 6
12 hours	65 ± 6
24 hours	75 ± 7
48 hours	80 ± 8

Table 2 illustrates the in vitro drug release profile of the repaglinide-loaded albumin nanoparticles over a 48-hour period. The release began with a modest burst, where approximately 12 ± 2% of the drug was released within the first hour, followed by a gradual and sustained release over time. At the 2-hour mark, cumulative drug release reached 20 ± 3%, and by 4 hours, it had risen to 30 ± 4%. The release continued steadily with 45 ± 5% at 6 hours and 55 ± 6% at 8 hours, indicating a controlled release mechanism that prevents a sudden spike in drug levels. By 12 hours, 65 ± 6% of the drug had been released, reaching 75 ± 7% at 24 hours and eventually 80 ± 8% by the 48-hour point. These results suggest that the nanoparticles are capable of sustaining drug release over an extended period, which is beneficial for reducing dosing frequency and maintaining therapeutic levels of repaglinide in systemic circulation.

4.3 Drug Release Kinetics

Table 3: Kinetic Models Fit for Drug Release Data

Model	R^2 Value	Release Mechanism
Zero-Order	0.960	Constant drug release rate
First-Order	0.912	Exponential decay
Higuchi	0.943	Diffusion-controlled release
Korsmeyer-Peppas	0.982	Anomalous diffusion (Fickian)

Table 3 compares the fit of different kinetic models applied to the in vitro release data of repaglinide from albumin nanoparticles. The Korsmeyer-Peppas model showed the best correlation with an R^2 value

of 0.982, indicating that the drug release follows a diffusion-controlled mechanism, specifically Fickian diffusion. This model suggests that drug release is governed by both diffusion through the matrix and possible swelling or erosion of the nanoparticle structure. The zero-order model also showed a relatively high R^2 value of 0.960, implying that the drug is released at a constant rate to a certain extent. The Higuchi model, which also describes diffusion-based release from a matrix system, presented an R^2 of 0.943, supporting the hypothesis of controlled diffusion. The first-order model, which assumes a concentration-dependent release, had the lowest R^2 at 0.912. Overall, these results support the effectiveness of albumin nanoparticles in offering a controlled, predictable release pattern suitable for sustained drug delivery.

4.4 Stability of Nanoparticles Over Time

Table 4: Stability of Repaglinide-Loaded Albumin Nanoparticles (Stored at 4°C)

Time Point	Particle Size (nm)	PDI	Zeta Potential (mV)
Day 0	150 ± 5	0.23	-20 ± 1
Day 7	152 ± 6	0.24	-21 ± 1
Day 14	153 ± 7	0.25	-21 ± 1
Day 30	155 ± 8	0.26	-22 ± 1

Stability data, as shown in Table 4, reveals how the physical properties of repaglinide-loaded albumin nanoparticles evolve over a 30-day storage period at 4°C. Initially, the particle size was measured at 150 ± 5 nm. After 7 days, it slightly increased to 152 ± 6 nm, and further increased to 153 ± 7 nm and 155 ± 8 nm on Days 14 and 30 respectively. This slight increase in size could be attributed to mild aggregation or structural relaxation of the particles during storage. The PDI values also showed a gradual increase from 0.23 to 0.26, suggesting a minor broadening in the size distribution but remaining within an acceptable range for nanoparticle formulations. Zeta potential remained stable over the period, moving from -20 ± 1 mV to -22 ± 1 mV by Day 30. This indicates that the surface charge remained sufficiently negative to maintain colloidal stability and prevent aggregation. Overall, the results confirm that the nanoparticles retained their integrity and stability during storage.

4.5 Cytotoxicity Assessment (MTT Assay)

Table 5: MTT Cytotoxicity Assay Results for Repaglinide-Loaded Albumin Nanoparticles

Concentration (µg/mL)	Cell Viability (%)
10	97 ± 4
25	94 ± 3
50	92 ± 5
75	88 ± 6
100	85 ± 4

As outlined in Table 5, the biocompatibility of the repaglinide-loaded albumin nanoparticles was assessed using an MTT cytotoxicity assay on cultured cells. At a low concentration of 10 µg/mL, cell viability was observed to be 97 ± 4%, indicating minimal cytotoxicity. As the concentration increased to 25 µg/mL, cell viability slightly decreased to 94 ± 3%, and at 50 µg/mL, it dropped to 92 ± 5%. Even at higher concentrations of 75 and 100 µg/mL, the cell viability remained at 88 ± 6% and 85 ± 4% respectively, which is still within acceptable limits. These results strongly suggest that the albumin nanoparticle formulation is well tolerated by cells and exhibits a high degree of safety, making it a suitable candidate for further in vivo and clinical testing.

4.6 Comparative Release Profile of Different Nanoparticle Systems

Table 6: Comparison of Release Profiles of Repaglinide from Different Nanoparticle Formulations

Formulation	Initial Burst (%)	Release at 24 hours (%)	Release at 48 hours (%)
Albumin Nanoparticles	20 ± 2	75 ± 5	80 ± 8
Liposome-Based Formulation	25 ± 3	70 ± 6	72 ± 7
Polymeric Nanoparticles	30 ± 4	68 ± 5	71 ± 6

Table 6 offers a comparative view of the release performance of different nanoparticle-based delivery systems for repaglinide, including albumin nanoparticles, liposome-based systems, and polymeric nanoparticles. The albumin-based formulation showed a lower initial burst (20 ± 2%) and a higher cumulative release at 24 and 48 hours (75 ± 5% and 80 ± 8%, respectively). Liposome-based systems had a slightly higher burst release of 25 ± 3% and lower total drug release over time, with 70 ± 6% at 24 hours and 72 ± 7% at 48 hours. Polymeric nanoparticles demonstrated the highest initial burst (30 ± 4%) but lagged in sustained release with only 68 ± 5% and 71 ± 6% release at 24 and 48 hours. These comparisons highlight the superiority of albumin nanoparticles in maintaining a controlled and extended release profile, reducing potential fluctuations in plasma drug levels and improving overall therapeutic efficacy.

4.7 Comparison of Drug Loading and Encapsulation Efficiency

Table 7: Drug Loading and Encapsulation Efficiency for Various Drug Delivery Systems

Drug Delivery System	Drug Loading Capacity (DLC) (%)	Encapsulation Efficiency (EE) (%)
Albumin Nanoparticles	4.5 ± 0.2	75 ± 3
Liposomes	3.8 ± 0.3	72 ± 4
Polymeric Nanoparticles	5.2 ± 0.1	80 ± 2
Solid Lipid Nanoparticles	4.1 ± 0.2	70 ± 5

Table 7 presents a comparative assessment of various drug delivery systems in terms of their drug loading capacity and encapsulation efficiency. The polymeric nanoparticles demonstrated the highest drug loading capacity at 5.2 ± 0.1% and an encapsulation efficiency of 80 ± 2%, which is impressive but expected given their dense polymer matrix. Albumin nanoparticles closely followed with a DLC of 4.5 ± 0.2% and EE of 75 ± 3%, which balances high encapsulation with natural biocompatibility. Liposomes and solid lipid nanoparticles had lower DLC and EE values, ranging from 3.8 ± 0.3% to 4.1 ± 0.2% in loading, and 70–72% in encapsulation. These findings reinforce albumin nanoparticles as a strong contender for repaglinide delivery due to their excellent balance between loading efficiency and safety.

4.8 Visual and Physical Stability Characteristics

Table 8: Physical Characteristics of Repaglinide-Loaded Albumin Nanoparticles Over Time

Time Point	Appearance	Particle Size (nm)	PDI	Zeta Potential (mV)
Day 0	Transparent white	150 ± 5	0.23	-20 ± 1
Day 7	Slight turbidity	152 ± 6	0.24	-21 ± 1
Day 14	Slight turbidity	153 ± 7	0.25	-21 ± 1
Day 30	Mild turbidity	155 ± 8	0.26	-22 ± 1

Table 8 extends the stability data by also capturing changes in visual appearance along with size and charge characteristics. Initially, the nanoparticle suspension appeared **transparent white**, indicating good dispersion and minimal aggregation. By Day 7 and Day 14, **slight turbidity** was noted, though particle size and zeta potential remained stable. By Day 30, the suspension exhibited **mild turbidity**, with particle size reaching 155 ± 8 nm and zeta potential at -22 ± 1 mV. These minor changes suggest that while some physical aging of the suspension occurred, the overall formulation remained physically and chemically stable, and suitable for continued use in pharmaceutical applications.

4.9 Korsmeyer-Peppas Model-Based Release Comparison

Table 9: Release Kinetics Comparison of Different Nanoparticle Formulations

Formulation	Korsmeyer-Peppas Release Exponent (n)	R^2 Value
Albumin Nanoparticles	0.57 ± 0.04	0.982
Liposome-Based Formulation	0.65 ± 0.06	0.945
Polymeric Nanoparticles	0.72 ± 0.05	0.950
Solid Lipid Nanoparticles	0.80 ± 0.07	0.940

Table 9 provides a comparative analysis of the release kinetics using the Korsmeyer-Peppas model, where the release exponent (n) helps identify the type of diffusion controlling the drug release. Albumin nanoparticles had an n value of 0.57 ± 0.04 with a strong R^2 value of 0.982, confirming **Fickian diffusion** as the dominant release mechanism. In contrast, liposome-based formulations had a higher n value of 0.65 ± 0.06, indicating a slight deviation towards non-Fickian or anomalous transport. Polymeric and solid lipid nanoparticles demonstrated even higher n values (0.72 and 0.80), suggesting more complex release mechanisms potentially involving both matrix relaxation and diffusion. Among all, albumin nanoparticles demonstrated the most desirable kinetic profile for sustained drug delivery.

5. CONCLUSION

This study demonstrates the successful development of albumin-based nanoparticles for the sustained release of repaglinide, aimed at improving the management of Type 2 diabetes. The synthesized nanoparticles showed desirable characteristics, including a controlled drug release profile, good drug loading capacity, and enhanced stability. In vitro release studies confirmed a sustained release of repaglinide, which could potentially reduce dosing frequency and improve patient compliance. Additionally, the biocompatibility and low toxicity of the nanoparticles highlight their suitability for clinical use. The albumin-based nanoparticle system developed in this study holds significant promise as a more efficient and patient-friendly alternative to conventional repaglinide dosage forms. Further research, including clinical trials, is necessary to optimize the formulation and assess its effectiveness and safety in real-world applications for the treatment of diabetes.

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