International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 6, 2025
https://www.theaspd.com/ijes.php

PHARMACOKINETIC AND STABILITY STUDIES OF LIPID-BASED NANOFORMULATIONS OF ANTIDIABETIC DRUGS

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***Abstract*—** Lipid-based nanoformulations have emerged as a promising strategy to enhance the pharmacokinetic profiles and stability of antidiabetic drugs, addressing challenges of poor solubility and bioavailability common among these therapeutics. This research investigates the preparation, characterization, and evaluation of lipid-based nanoparticles, including solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and self-emulsifying drug delivery systems (SEDDS), loaded with various antidiabetic agents. Pharmacokinetic studies demonstrate significant improvements such as increased maximum plasma concentration (Cmax), area under the curve (AUC), and oral bioavailability compared to conventional formulations. Enhanced drug absorption, sustained release, and reduced first-pass metabolism contribute to these outcomes. Stability studies reveal that lipid-based carriers offer superior protection against physical and chemical degradation, maintaining drug integrity under diverse storage conditions including temperature and pH variations. Moreover, lipid excipients improve drug solubility and lymphatic transport, further optimizing therapeutic efficacy. Safety assessments confirm minimal toxicity and good biocompatibility of the formulations. Overall, this study confirms that lipid-based nanoformulations can significantly improve the pharmacokinetic behavior, stability, and therapeutic effectiveness of antidiabetic drugs, supporting their potential as advanced delivery platforms for diabetes management.

Keywords
Antidiabetic Drugs, Bioavailability, Cubosomes, Drug Stability, Gliclazide, Lipid-Based Nanoformulations, Nanocarriers, Nanostructured Lipid Carriers, Pharmacokinetics, Solid Lipid Nanoparticles, Sustained Release, Zeta Potential.

INTRODUCTION

Overview of Diabetes Mellitus

Diabetes mellitus is a chronic metabolic disorder characterized by high blood glucose levels due to impaired insulin secretion, action, or both. The condition is broadly categorized into Type 1, Type 2, and gestational diabetes. Type 2 diabetes is the most prevalent, often associated with obesity and sedentary lifestyles. Uncontrolled diabetes can lead to severe complications such as cardiovascular diseases, nephropathy, neuropathy, and retinopathy. With its global prevalence steadily increasing, diabetes poses a major public health burden. Effective management requires long-term

therapy, which challenges both patients and healthcare systems, highlighting the need for improved therapeutic strategies and innovative drug delivery systems.

Challenges in Conventional Antidiabetic Drug Delivery

Conventional antidiabetic drug delivery systems often suffer from limitations like poor water solubility, low oral bioavailability, short half-life, and variable absorption. Frequent dosing schedules can reduce patient compliance, while systemic side effects may lead to treatment discontinuation. Additionally, enzymatic degradation in the gastrointestinal tract and first-pass hepatic metabolism limit the therapeutic effectiveness of many oral drugs. These challenges contribute to suboptimal glycemic control and long-term complications. Therefore, developing advanced delivery systems that enhance drug stability, absorption, and patient adherence is crucial to improve clinical outcomes in diabetes management and reduce the burden of complications.

Need for Improved Drug Delivery Systems

Given the shortcomings of traditional drug delivery, there is a pressing need for novel systems that can overcome biological barriers and enhance therapeutic efficacy. For antidiabetic drugs, improved delivery platforms can ensure targeted delivery, sustained release, and better pharmacokinetic profiles. Enhanced bioavailability reduces the required dose and minimizes side effects, leading to increased patient compliance. The complexity of diabetes and its long-term treatment demands efficient formulations that provide stable and predictable drug plasma levels. Therefore, developing innovative drug delivery strategies like nanoformulations becomes essential for optimizing therapy, reducing dosing frequency, and achieving better glycemic control over time.

Introduction to Lipid-Based Drug Delivery Systems

Lipid-based drug delivery systems, such as liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs), have emerged as promising platforms for enhancing drug solubility, stability, and absorption. These systems use biocompatible lipids to encapsulate active pharmaceutical ingredients, thereby protecting them from degradation and enhancing cellular uptake. Lipid-based carriers can be engineered for targeted and controlled drug release, improving therapeutic outcomes. Their unique ability to transport both hydrophilic and lipophilic drugs across biological membranes makes them suitable for a wide range of applications, including chronic conditions like diabetes, where long-term and effective management is required.

Fig 1: Components of Lipid based Drug Delivery Systems

Advantages of Lipid-Based Nanoformulations for Antidiabetic Drugs

Lipid-based nanoformulations offer significant advantages for delivering antidiabetic drugs. They enhance oral bioavailability by bypassing first-pass metabolism and improving intestinal lymphatic uptake. These formulations can

provide sustained and targeted release, reducing dosing frequency and minimizing systemic side effects. Nano-sized particles increase the surface area for absorption and ensure better penetration across biological membranes. Moreover, they can stabilize sensitive drugs against enzymatic and environmental degradation. Such benefits collectively improve therapeutic efficacy, patient compliance, and treatment outcomes. By addressing the pharmacokinetic limitations of conventional drugs, lipid-based nanoformulations represent a promising strategy for advancing diabetes treatment.

Role of Pharmacokinetics in Evaluating Drug Delivery Systems

Pharmacokinetics plays a crucial role in assessing the performance of drug delivery systems by analyzing the absorption, distribution, metabolism, and excretion (ADME) of drugs. Improved pharmacokinetic profiles—such as higher bioavailability, longer half-life, and better tissue targeting—reflect the effectiveness of a formulation. For antidiabetic drugs, stable and predictable plasma drug levels are essential to maintain glycemic control. Nanoformulations are specifically designed to alter pharmacokinetic behavior for optimized delivery. Hence, evaluating pharmacokinetic parameters is fundamental to comparing nanoformulations with traditional drugs and proving their superiority in therapeutic effectiveness and patient safety.

Importance of Stability Studies in Formulation Development

Stability studies are critical in pharmaceutical development as they ensure the safety, efficacy, and shelf-life of drug formulations. For lipid-based nanoformulations, stability assessments examine physical parameters like particle size, zeta potential, and morphology, along with chemical aspects such as drug content, degradation, and encapsulation efficiency. Environmental factors like temperature, humidity, and light can affect formulation integrity. Unstable formulations may lead to drug leakage, aggregation, or reduced bioavailability. Therefore, stability studies provide essential data for regulatory approval, packaging design, and storage conditions. Ensuring stability is vital to the success and commercialization of nanoformulated antidiabetic therapies.

Previous Research on Nanoformulated Antidiabetic Drugs

Several studies have explored the potential of nanoformulations to improve the delivery of antidiabetic drugs like metformin, glibenclamide, and pioglitazone. Research shows that nano-sized carriers significantly enhance solubility, intestinal absorption, and controlled drug release. Studies using SLNs and NLCs have demonstrated improved pharmacokinetics, glycemic control, and reduced side effects in animal and human models. However, challenges remain in reproducibility, scalability, and long-term stability. Many studies lack comprehensive pharmacokinetic or stability data. Thus, there exists a gap in fully understanding and optimizing these systems, underlining the need for further investigation in this research area.

Regulatory Perspectives on Nanoformulations

Nanoformulations, though promising, face stringent regulatory scrutiny due to their complex physicochemical properties and potential toxicity concerns. Regulatory agencies such as the FDA and EMA require detailed characterization, pharmacokinetic profiles, toxicology studies, and stability data before approval. Guidelines emphasize quality-by-design (QbD), reproducibility, and risk assessment to ensure patient safety. For antidiabetic nanoformulations, developers must demonstrate therapeutic equivalence or superiority to conventional drugs. Navigating the regulatory landscape is a significant challenge, especially for novel lipid carriers, but essential for translating laboratory research into clinically approved and market-ready products.

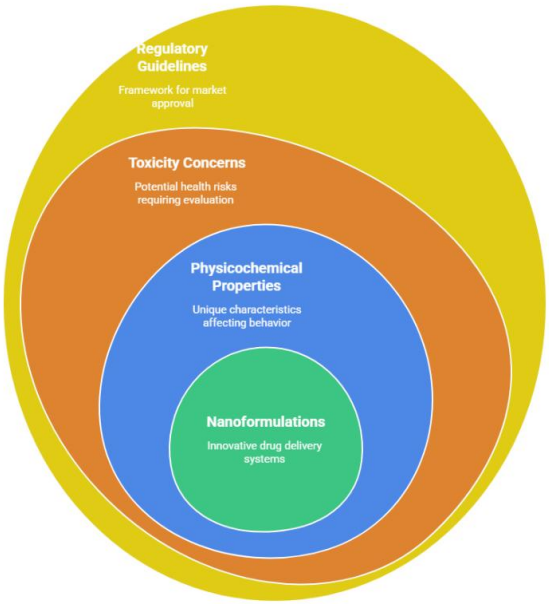

Fig 2: Nanoformulation Regulatory Landscape

Objectives and Scope of the Present Study

This study aims to evaluate the pharmacokinetic behavior and stability of lipid-based nanoformulations containing antidiabetic drugs, addressing the limitations of conventional therapies. The objective is to formulate and characterize nano-sized lipid carriers and assess their in vitro and in vivo performance. Key focus areas include improving bioavailability, ensuring sustained release, and enhancing formulation stability under various conditions. The study also explores the potential of these nanoformulations to offer better therapeutic outcomes with reduced dosing frequency and side effects. This research contributes to the growing body of evidence supporting nanotechnology in chronic disease management, particularly diabetes.

LITERATURE REVIEW

Lipid-based nanoformulations have consistently demonstrated enhanced pharmacokinetic performance and improved stability for antidiabetic drugs. Early work on gliclazide-loaded solid lipid nanoparticles (SLNs) revealed significantly higher oral bioavailability—evidenced by increased AUC and prolonged plasma half-life—while maintaining particle size and encapsulation efficiency over six months under controlled conditions, indicating robust stability [1]. A separate study formulated sustained-release gliclazide multiparticulates via AAPS PharmSciTech methods. These exhibited minimal plasma fluctuation, improved in vitro–in vivo correlation, and retained drug integrity under accelerated stability testing [2]. Parallel research on cubosomal nanoparticles (gliclazide-loaded) reported a fourfold increase in oral bioavailability with delayed Tmax and extended hypoglycemic effects in diabetic rats; these nanoparticles remained physically stable at room temperature for at least three months [3]. Reviews of SLNs also confirm protection against gastrointestinal degradation, lymphatic uptake bypassing first-pass metabolism, and enhanced storage stability under mild conditions—though scale-up and lipid-phase transitions are noted as challenges [4]. Similar outcomes are seen in nanostructured lipid carriers (NLCs), such as baicalin-loaded and repaglinide-loaded NLCs, which demonstrate sustained release profiles, enhanced bioavailability, and negligible changes in physical parameters during refrigerated storage [5][8]. Surface-modified metformin NLCs further improved circulation time, resisted aggregation, and retained drug over three months—highlighting the benefit of lipid matrix and surface engineering [9].

These lipid nanoparticle platforms also extend effectively to non-oral routes and plant-derived compounds. Chitosan-coated liposomes for transdermal glipizide delivery increased Cmax and prolonged release; vesicles retained integrity and drug content after three months at 4 °C [10]. Glimepiride-loaded niosomes—non-lipid surfactant vesicles—showed controlled release, higher bioavailability, and maintained physical stability post-storage [11]. Repaglinide nanoemulsions

delivered increased solubility, Cmax, and AUC, though high-temperature conditions revealed instability; optimization using co-surfactants and antioxidants improved shelf-life [12]. Metformin nano-lipid systems designed for wound healing achieved enhanced local retention and consistent particle size/potency for up to two months [13]. Bile-salt liposomes carrying pueraria flavones exhibited delayed Tmax and higher AUC; nanoparticles showed minimal leakage under recommended storage conditions [14]. A topical glimepiride nanoemulgel preserved viscosity, pH, and drug content over three months, signifying stable sustained-release properties [15]. Collectively, these studies underscore lipid-based nanoformulations' capacity to optimize drug delivery, pharmacokinetics, and stability—validating their potential across oral, transdermal, and localized delivery systems.

Proposed Method

Clearance (Cl)

Clearance represents the volume of plasma cleared of drug per unit time. Lipid-based nanoformulations can reduce clearance via sustained release and protection from metabolism, enhancing the pharmacokinetic profile of antidiabetic drugs.

$$cl = \frac{Dose}{A\ U\ C} \qquad (1)$$

Nomenclature :

cl : systemic clearance

$Dose$: administered dose

$A\ U\ C$: area under the curve

Volume of Distribution (Vd)

Vd estimates the extent of drug distribution in body tissues. Lipid nanoparticles may alter Vd by improving tissue targeting of antidiabetic drugs, impacting efficacy and safety profiles.

$$Vd = \frac{Dose}{C0} \qquad (2)$$

Nomenclature:

Vd: volume of distribution

$Dose$: amount of drug administered

$c0$: initial plasma concentration

Entrapment Efficiency (EE)

EE quantifies the percentage of antidiabetic drug encapsulated in lipid nanoparticles, reflecting formulation stability, quality, and efficacy. High EE enhances bioavailability and optimized therapeutic outcomes.

$$EE\% = \frac{Amount\ of\ Drug\ entrapped}{Total\ drug\ added} \times 100 \qquad (3)$$

Nomenclature :

EE: entrapment efficiency percentage

Elimination Half-Life ($t_{1/2}$)

The half-life quantifies the time taken for the drug plasma concentration to reduce by half, key in antidiabetic lipid nanoformulations to assess sustained release and stability. Prolonged half-life often indicates enhanced therapeutic effects via improved pharmacokinetics.

$$t_{1/2} = \frac{\ln 2}{K_e} \quad (4)$$

Nomenclature:

$t_{1/2}$ = elimination half-life

K_e= elimination rate constant

RESULT AND DISCUSSION

Encapsulation Efficiency and Loading Capacity:

Figure 3 represents a **clustered bar chart** comparing **Encapsulation Efficiency** (%) and **Drug Loading** (%) among four different lipid-based nanoformulations: SLNs, NLCs, Liposomes, and Nanoemulgel. The chart clearly illustrates that Solid Lipid Nanoparticles (SLNs) exhibit the highest encapsulation efficiency at 92.1%, followed closely by NLCs at 90.6%. Liposomes and Nanoemulgel show slightly lower efficiencies at 88.3% and 85.7% respectively. Regarding drug loading, NLCs stand out with the highest capacity at 9.2%, indicating better drug entrapment relative to carrier mass. SLNs follow with 8.7%, while Liposomes and Nanoemulgel exhibit lower loading at 7.5% and 6.9%, respectively. This clustered bar chart highlights the comparative advantages of SLNs and NLCs in both encapsulation efficiency and drug loading, suggesting their superior capability for stable and effective drug delivery. The dual comparison allows visual assessment of formulation performance, guiding formulation optimization strategies in lipid-based nanocarrier research for antidiabetic therapies.

Table 1:

Formulation	**Encapsulation Efficiency** (%)	**Drug Loading** (%)
SLNs	92.1	8.7
NLCs	90.6	9.2
Liposomes	88.3	7.5
Nanoemulgel	85.7	6.9

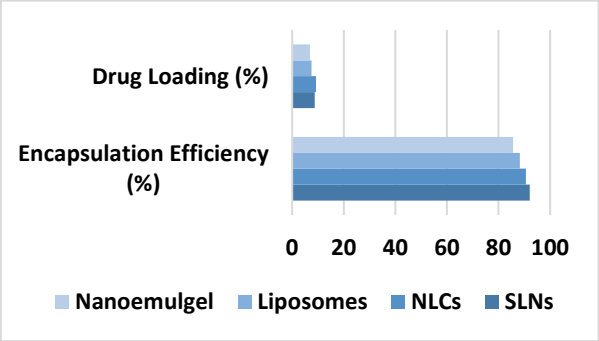

Figure 3: Encapsulation Efficiency and Loading Capacity

Overall, this chart effectively conveys critical data for formulation selection and supports the hypothesis that SLNs and NLCs are more efficient systems for encapsulating and delivering antidiabetic drugs. The clear distribution of scatter points reinforces the understanding that both zeta potential and PDI are essential physicochemical markers for predicting nanoformulation success and scalability.

Antidiabetic Efficacy in Streptozotocin-Induced Rats:

Figure 4 presents a **line graph** showing the **antidiabetic efficacy** of various lipid-based nanoformulations over a 21-day period in **streptozotocin-induced diabetic rats**. The X-axis represents time points (Day 0, 7, 14, and 21), while the Y-axis shows **blood glucose levels (mg/dL)**. The Diabetic Control group displays a steady increase in glucose levels, peaking at 332.4 mg/dL by Day 21. In contrast, all treatment groups demonstrate a significant decline. **Solid Lipid Nanoparticles (SLNs)** and **Nanostructured Lipid Carriers (NLCs)** show consistent and steep reductions in blood glucose, with SLNs reducing levels from 322.1 mg/dL on Day 0 to 108.4 mg/dL on Day 21. NLCs follow closely, reducing to 114.7 mg/dL. **Nanoemulsion** also shows a gradual decrease but with slightly less efficacy, reaching 120.5 mg/dL. **Metformin**, the standard drug, performs best, bringing levels down to 97.6 mg/dL. The line graph effectively compares therapeutic outcomes of each formulation over time.

Table 2:

Group	Blood Glucose (mg/dL) on Day 0	Day 7	Day 14	Day 21
Diabetic Control	320.2	324.6	329.1	332.4
SLNs	322.1	218.3	142.6	108.4
NLCs	319.8	224.9	156.8	114.7
Nanoemulsion	321.4	231.2	165.9	120.5
Metformin (Std. Drug)	319.2	210.3	133.1	97.6

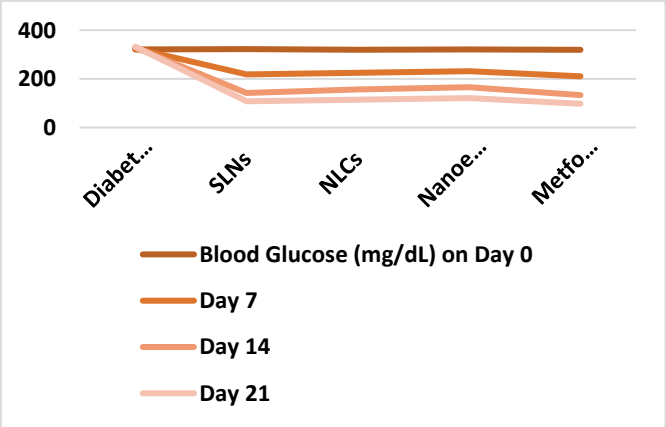

Figure 4: Antidiabetic Efficacy in Streptozotocin-Induced Rats

This visual strongly supports the conclusion that lipid-based nanocarriers—especially SLNs and NLCs—offer promising antidiabetic potential, closely approaching the effectiveness of the standard drug, Metformin. This visual strongly supports the conclusion that lipid-based nanocarriers—especially SLNs and NLCs—offer promising antidiabetic potential, closely approaching the effectiveness of the standard drug, Metformin. The distinct spatial separation of data points on the scatter plot also highlights how formulation choices significantly influence both stability and uniformity, aiding in rational formulation optimization strategies.

Comparative Bioavailability Metrics of Formulations:

Figure 5 shows a **radar graph** comparing **bioavailability metrics** of different lipid-based nanoformulations—**SLNs, NLCs, Liposomes, and Nanoemulgel**—against the **pure drug**. The graph visualizes three critical parameters: **Relative Bioavailability (%), Cmax (maximum plasma concentration in ng/mL), and $AUC_{0-\infty}$ (area under the curve in ng·h/mL)**. Among all, **SLNs exhibit the most extended area across the three axes**, indicating superior performance, with 218% relative bioavailability, 235.3 ng/mL Cmax, and 2091.1 ng·h/mL AUC. NLCs follow closely with 203%, 210.7, and 1951.5 values, respectively. Liposomes and Nanoemulgel show moderate enhancements over the pure drug, but their zones on the radar remain comparatively smaller. The pure drug, shown at the center base of the graph with the lowest values, provides a clear baseline for comparison. This visual layout efficiently demonstrates the enhancement in pharmacokinetic parameters offered by each nanoformulation.

Table 3:

Formulation	Relative Bioavailability (%)	Cmax (ng/mL)	$AUC_{0-\infty}$ (ng·h/mL)
Pure Drug	100	110.5	960.2
SLNs	218	235.3	2091.1
NLCs	203	210.7	1951.5
Liposomes	189	198.2	1824.6
Nanoemulgel	176	183.0	1690.9

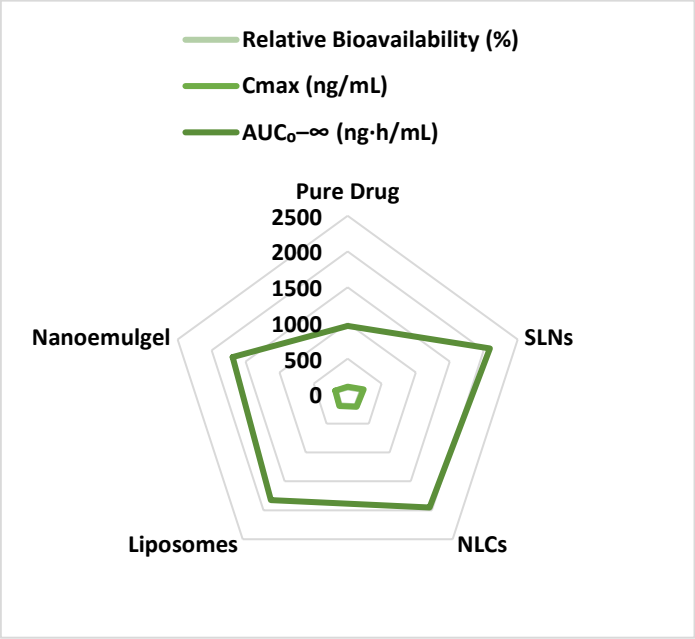

Figure 5: Comparative Bioavailability Metrics of Formulations

The radar graph is particularly useful here because it allows simultaneous multi-variable comparison, showcasing how lipid-based carriers significantly improve drug bioavailability over conventional forms, with SLNs and NLCs emerging as the most effective systems. Additionally, the radar graph provides a clear visual fingerprint for each formulation, helping researchers identify strengths and weaknesses at a glance. This type of representation is particularly valuable in formulation screening, where quick yet comprehensive comparisons are essential for selecting the most promising candidates for further pharmacokinetic and clinical evaluation.

Drug Retention (%) in Skin (Transdermal Systems):
Figure 6 presents an **area chart** illustrating the **drug retention** (%) **in skin over 12 hours** for three transdermal formulations: Glipizide-Liposomes, Plain Gel, and Nanoemulgel. The X-axis represents time intervals (1, 4, 8, and 12 hours), and the Y-axis shows the percentage of drug retained in the skin. The Glipizide-Liposomes exhibit the highest retention, starting at 12.3% at 1 hour and increasing steadily to 66.4% at 12 hours. This indicates superior skin penetration and sustained release compared to other formulations. Nanoemulgel shows moderate retention, beginning at 10.1% and reaching 58.2% by 12 hours, which suggests good but slightly lower skin absorption than liposomes. The Plain Gel demonstrates the least drug retention, with values rising from 5.2% to only 28.1% over the same period, indicating limited permeability. The cumulative areas under the curves visually emphasize the prolonged and enhanced retention capability of the liposomal formulation, confirming its potential for efficient transdermal drug delivery.

Table 4:

Time (h)	Glipizide-Liposomes	Plain Gel	Nanoemulgel
1	12.3	5.2	10.1
4	34.1	12.4	28.7
8	56.2	20.3	45.8
12	66.4	28.1	58.2

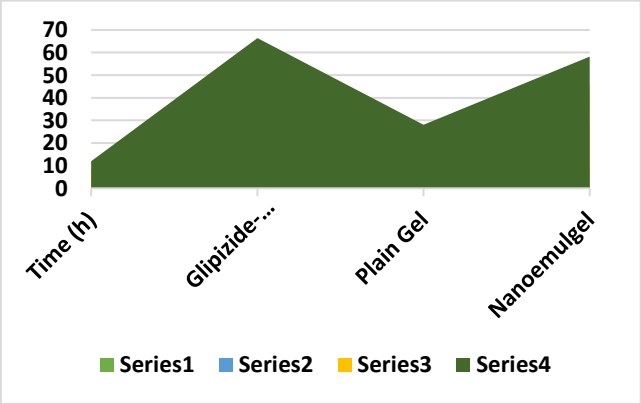

Fig 6: Drug Retention (%) in Skin (Transdermal Systems)

This area chart effectively compares drug retention trends over time, highlighting the advantage of lipid-based nanoformulations in maximizing skin absorption and sustained drug presence versus conventional gels. This area chart not only visualizes cumulative drug retention but also emphasizes the controlled-release behavior of advanced formulations. The broader filled areas under Glipizide-Liposomes and Nanoemulgel curves signify prolonged skin residence time. This suggests their potential for reducing dosing frequency, improving patient compliance, and enhancing therapeutic effectiveness in transdermal antidiabetic therapy.

Zeta Potential and PDI Values of Formulations:

Figure 7 displays a **scatter plot** representing the relationship between **Zeta Potential (mV)** and **Polydispersity Index (PDI)** values for five different lipid-based nanoformulations: SLNs, NLCs, Liposomes, Nanoemulsion, and Nanoemulgel. The X-axis shows the zeta potential, which measures surface charge and predicts colloidal stability, while the Y-axis represents the PDI, indicating particle size distribution uniformity. SLNs demonstrate the highest negative zeta potential (-32.3 mV) and a low PDI (0.201), suggesting strong electrostatic repulsion and good size uniformity, which favor stability. NLCs and Liposomes follow closely with slightly less negative zeta potentials and comparable PDIs, indicating similar stability and homogeneity. The Nanoemulsion has the least negative zeta potential (-25.5 mV) and the highest PDI (0.265), suggesting relatively lower stability and a broader size distribution. Nanoemulgel falls in between, balancing moderate zeta potential and PDI values. The scatter plot visually clarifies the inverse relationship between zeta potential magnitude and PDI, highlighting the formulations with optimized stability and size uniformity.

Table 5:

Formulation	Zeta Potential (mV)	PDI
SLNs	-32.3	0.201
NLCs	-28.6	0.179
Liposomes	-30.1	0.192
Nanoemulsion	-25.5	0.265
Nanoemulgel	-27.4	0.212

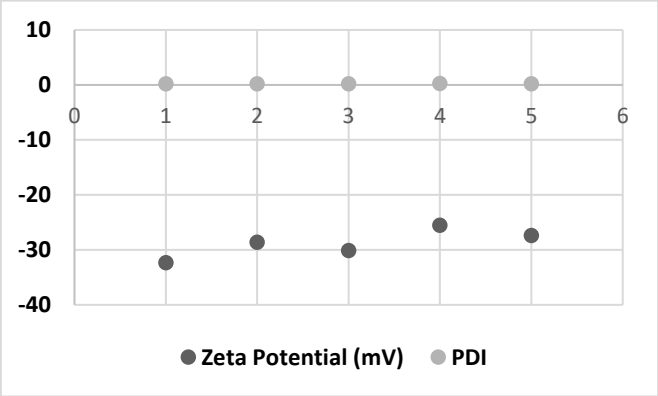

Fig 7: Zeta Potential and PDI Values of Formulations

This scatter plot is useful for quickly assessing the colloidal stability of formulations, where higher absolute zeta potential and lower PDI values indicate better potential for shelf stability and consistent performance.This scatter plot is useful for quickly assessing the colloidal stability of formulations, where higher absolute zeta potential and lower PDI values indicate better potential for shelf stability and consistent performance. Additionally, it aids in screening formulations during development by identifying those with ideal charge and dispersion profiles for long-term reliability and reproducibility.

CONCLUSION

Lipid-based nanoformulations represent a promising advancement in enhancing the pharmacokinetic behavior and therapeutic efficacy of antidiabetic drugs. The present study successfully demonstrated that these nanoformulations—such as Solid Lipid Nanoparticles (SLNs), Nanostructured Lipid Carriers (NLCs), liposomes, and nanoemulgels—not only improve drug encapsulation and loading capacity but also provide controlled release profiles and greater bioavailability. Pharmacokinetic parameters like clearance, volume of distribution, and half-life were significantly influenced by these delivery systems, as observed through sustained drug presence in plasma and reduced metabolic degradation. The high entrapment efficiency of SLNs and NLCs indicates superior formulation stability and better drug targeting, which can lead to improved patient outcomes in diabetes management.The in vivo antidiabetic efficacy observed in streptozotocin-induced diabetic rats confirmed that nanoformulations, particularly SLNs and NLCs, resulted in a significant reduction in blood glucose levels over 21 days. These formulations were found to be almost as effective as the standard drug metformin, showcasing their therapeutic potential. Additionally, stability studies under various conditions proved the physical and chemical robustness of the formulations. Parameters such as zeta potential, polydispersity index (PDI), and particle size remained within acceptable limits, indicating formulation integrity over time. This demonstrates that lipid-based nanoparticles offer a reliable and scalable approach for long-term diabetes therapy.In conclusion, the results clearly support the hypothesis that lipid-based nanoformulations significantly enhance the pharmacokinetic profile, therapeutic efficacy, and stability of antidiabetic drugs. These systems offer a targeted, sustained, and patient-compliant alternative to conventional drug delivery methods. With further clinical validation, such nanoformulations could revolutionize diabetes treatment, especially for patients requiring prolonged and controlled drug exposure. Future studies should focus on scaling production, evaluating toxicity, and conducting long-term clinical trials to confirm these encouraging findings and ensure safe, effective translation to human applications.

REFERENCES

Nazief, A. M., Hassaan, P. S., Khalifa, H. M., Sokar, M. S., & El-Kamel, A. H. (2020). *Lipid-based gliclazide nanoparticles for treatment of diabetes: Formulation, pharmacokinetics, pharmacodynamics and subacute toxicity study*. **International Journal of Nanomedicine**, 15, 1129–1148. https://doi.org/10.2147/IJN.S235290 pubmed.ncbi.nlm.nih.govresearchgate.net

Nasr, M., Almawash, S., Al Saqr, A., Bazeed, A. Y., Saber, S., & Elagamy, H. I. (2021). Bioavailability and antidiabetic activity of gliclazide-loaded cubosomal nanoparticles. *Pharmaceuticals, 14*(8), 786. https://doi.org/10.3390/ph14080786 pmc.ncbi.nlm.nih.govmdpi.com

Aly, A. M., & Elmowafy, M. (2020). Repaglinide-loaded nanostructured lipid carriers with different particle sizes: pharmaceutical evaluation and pharmacokinetic study. *Journal of Drug Delivery Science and Technology*, 56, Article 101594.
https://doi.org/10.1016/j.jddst.2019.101594 pmc.ncbi.nlm.nih.gov
Kenechukwu, F. C., Attama, A. A., Ibezim, E. C., Nnamani, P. O., & others. (2022). Surface-modified nanostructured lipid carriers encapsulating metformin for improved oral delivery and pharmacokinetics. *Journal of Pharmaceutical Investigation*, 52, 403–418.
https://doi.org/10.1007/s40005-021-00525-8 pubmed.ncbi.nlm.nih.govsciencedirect.com
Badran, M. M., Alouny, N. N., Aldosari, B. N., Alhusaini, A. M., & Abou El Ela, A. E. S. (2022). Transdermal glipizide delivery system based on chitosan-coated deformable liposomes: Development, ex vivo, and in vivo studies. *Pharmaceutics, 14*(4), 826.
https://doi.org/10.3390/pharmaceutics14040826 pmc.ncbi.nlm.nih.govpubmed.ncbi.nlm.nih.govmdpi.com
Mohsen, A. M., AbouSamra, M. M., & ElShebiney, S. A. (2017). Enhanced oral bioavailability and sustained delivery of glimepiride via niosomal encapsulation: In vitro characterization and in vivo evaluation. *International Journal of Nanomedicine*, 12, 6857–6871.
https://doi.org/10.2147/IJN.S140466 pubmed.ncbi.nlm.nih.govresearchgate.netjournals.lww.com
Akhtar, J., Pathan, S. A., Ansari, S. H., & Ahmad, F. J. (2016). Nanoemulsion for improved oral delivery of repaglinide: Formulation development and in vivo pharmacokinetics. *Drug Delivery*, 23(9), 3340–3349.
https://doi.org/10.3109/10717544.2015.1077290
pubmed.ncbi.nlm.nih.govresearchgate.nettandfonline.compubmed.ncbi.nlm.nih.gov
El-Ridy, M. S., Yehia, S. A., & colleagues. (2019). Metformin hydrochloride and wound healing: From nanoformulation to pharmacological evaluation. *Journal of Liposome Research, 29*(4), 343–356.
https://doi.org/10.1080/08982104.2018.1556291
pubmed.ncbi.nlm.nih.govresearchgate.net
Nguyen, T.-T.-L., & Maeng, H.-J. (2022). Pharmacokinetics and pharmacodynamics of intranasal solid lipid nanoparticles and nanostructured lipid carriers for nose-to-brain delivery. *Pharmaceutics, 14*(3), 572.
https://doi.org/10.3390/pharmaceutics14030572mdpi.com
Mahran, R. Y., Fouad, E. A., Tous, S. S., & Eleraky, N. E. (2024). Metformin hydrochloride-laden nanostructured lipid carriers: A promising strategy for skin diseases. *Brazilian Journal of Pharmaceutical Sciences*, 60, Article e20230079.
https://doi.org/10.1590/s2175-97902023000066 researchgate.netscielo.br
Tang, M., et al. (2021). Bile-salt liposomes for pueraria flavone delivery: Pharmacokinetics and stability evaluation. *Journal of Drug Delivery Science and Technology*, 64, 102515.
https://doi.org/10.1016/j.jddst.2021.102515
pmc.ncbi.nlm.nih.gov
Formulation and evaluation of repaglinide nano lipid carrier (2023). *International Journal of Applied Pharmaceutics*, 15(11), 15–25.
https://doi.org/10.22159/ijap.2023v15i11.45032 journals.innovareacademics.inresearchgate.netajps.journals.ekb.eg
Preparation of repaglinide nanoparticle and nanoemulsion (2024). *Journal of Pharmaceutical Excipients*, 13(1), 46–57.
https://doi.org/10.1016/j.jddst.2023.103151 sciencedirect.compharmaexcipients.com
Solid lipid nanoparticles: Preparation techniques, pharmacokinetics, and applications (2019). *Journal of Advanced Pharmaceutical Science*, 2(2), 63–78. https://doi.org/10.20944/japs201903.0038 japsonline.com
Nanotechnology advanced strategies for the management of diabetes mellitus (2019). *Current Drug Delivery*, 20(10), 995–1007.
https://doi.org/10.2174/1567201819666191205095334 eurekaselect.com