Role of Nanoparticles in Improving Drug Delivery Efficiency

Kyaw Zaw Win[1], Sergey Gupalo[2], Wana Hla Shwe[3], Phone Myint Htoo[4], Yuan Seng Wu[5], Tahmina Afrose Keya[6], Manglesh Waran Udayah[7], Rohini Karunakaran[8], Than Than Aye[9], Sutha Devaraj[10] and Nazmul MHM[11]*

[1]*Faculty of Medicine, Quest International University, Ipoh, Malaysia*
[2]*Saint James School of Medicine, Cane Hall Road, Arnos Vale, Saint Vincent and the Grenadines*
[3]*Faculty of Medicine and Health Sciences, UCSI University, Springhill, Negeri Sembilan, Malaysia*
[4]*International Medical School, Management and Science University, Shah Alam, Selangor, Malaysia*
[5]*Sir Jeffery Cheah Sunway Medical School and Sunway Microbiome Centre, Faculty of Medical and Life Sciences, Sunway University, Sunway City, Malaysia*
[6]*Faculty of Medicine, AIMST University, Bedong, Kedah, Malaysia*
[7]*School of Medicine, Perdana University, Damansara Heights, Kuala Lumpur, Malaysia*
[8]*Faculty of Medicine, Nursing and Health Sciences, SEGi University, Sibu Clinical Campus, Sibu, Sarawak, Malaysia*
[11]**poorpiku@yahoo.com*

Received: 16th Dec, 2025; Revised: 8th Feb 2026; Accepted: 24th Feb, 2026; Available Online: 30th March, 2026

ABSTRACT
Nanoparticle-based drug delivery has gained importance as an advanced approach to improve therapeutic efficiency by enhancing drug stability, transport, and targeted release, while conventional systems often face limitations such as low bioavailability and non-specific distribution. Recent studies have demonstrated that nanoparticles can significantly improve cellular uptake, control release behavior, and enhance accumulation at the target site through optimized size and surface properties, yet a clear understanding of how these parameters influence overall delivery efficiency remains limited. This study addresses this gap by developing a simulation-based multiscale framework to analyze the role of nanoparticle size and surface charge in transport, cellular uptake, and controlled drug release across biological barriers. The article presents computational models, release kinetics analysis, and comparative accumulation maps to evaluate performance differences between conventional and nanoparticle-based systems. The results show that nanoparticle-assisted delivery provides sustained release and higher localized drug concentration, leading to improved bioavailability and reduced off-target effects. These findings highlight the importance of nanoparticle design in enhancing drug delivery efficiency and provide practical insights for applications in targeted therapy, gene delivery, and precision medicine.
Keywords: *Nanoparticles, Drug Delivery, Cellular Uptake, Controlled Release, Therapeutic Efficiency*
How to cite this article: Win KZ, Gupalo S, Shwe WH, Htoo PM, Wu YS, Keya TA, Udayah MW, Karunakaran R, Aye TT, Devaraj S, Nazmul MHM., Role of Nanoparticles in Improving Drug Delivery Efficiency. Int J Drug Deliv Technol. 2026;16(24s): 484-489. DOI: 10.25258/ijddt.16.24s.53
Source of support: Nil.
Conflict of interest: None

1. INTRODUCTION

Nanoparticle-based drug delivery has emerged as an important area in pharmaceutical research because many conventional drug formulations still suffer from poor stability, low target-site accumulation, and unwanted distribution in healthy tissues. By packaging therapeutic compounds within nanoscale carriers, it becomes possible to protect sensitive payloads during circulation and improve delivery toward diseased cells and organs [1]. This shift is especially important for modern treatment systems in which the success of therapy depends not only on the drug itself, but also on how efficiently it crosses biological barriers and reaches the required site of action. For this reason, nanoparticle-enabled transport is now widely studied as a direct route to improving therapeutic performance.

The recent literature shows that nanoparticles can improve delivery efficiency through multiple mechanisms rather than through a single universal effect. Lipid nanoparticle systems have been used for in vivo gene-editing and messenger RNA delivery, showing that nanoscale carriers can support precise biological transport for advanced therapeutic payloads [2]. Related work has also shown that engineered lipid nanoparticles can produce measurable therapeutic outcomes after targeted in vivo delivery, which strengthens the case for nanoparticle-mediated control over biodistribution and intracellular access [3]. These findings indicate that nanoparticle formulations are increasingly being designed not only to carry drugs, but also to actively control where and how the therapeutic cargo is released.

**Author for Correspondence: poorpiku@yahoo.com*

At the same time, studies based on polymeric and targeted nanomedicine platforms have shown that surface modification, ligand attachment, and microenvironment-responsive design can enhance selective accumulation and improve treatment response in difficult disease settings [4]. Organ-specific and receptor-mediated systems have further demonstrated that nanoparticle coating and interface engineering can increase cellular uptake and reduce non-productive distribution losses during transport [5]. However, much of the existing work remains application-specific, and many reports focus strongly on treatment outcomes while giving less attention to the broader transport logic that explains why one nanoparticle system improves delivery efficiency more effectively than another. This leaves a clear need for a more focused discussion centered on delivery efficiency itself.

The present study narrows this broad field to one core problem: how nanoparticles improve the efficiency of drug transport across biological barriers from administration to target-site accumulation. This problem is important because therapeutic loss can occur at several stages, including degradation in circulation, weak tissue penetration, limited cellular internalization, and premature release before the drug reaches the intended site. A protein-based selective nanocarrier study has shown that well-designed nanosystems can achieve strong tumor localization with minimal non-target distribution, which highlights the direct connection between nanoparticle architecture and transport efficiency [6]. Understanding this connection is essential for designing delivery systems that are not only biologically active but also operationally efficient.

In response to this need, this article examines the role of nanoparticles from a transport-efficiency perspective rather than from a single disease or formulation viewpoint. Figure 1 presents the simulation-based schematic of nanoparticle-mediated drug transport across biological barriers and conceptually illustrates the sequence of circulation, barrier interaction, penetration, uptake, and localized release that defines delivery efficiency. Based on this framework, the article identifies the major mechanisms through which nanoparticles improve drug delivery, organizes the discussion around transport performance, and prepares a clear foundation for the methodological and analytical sections that follow. These contributions help position the study around a practical and scientifically important question in advanced drug delivery.

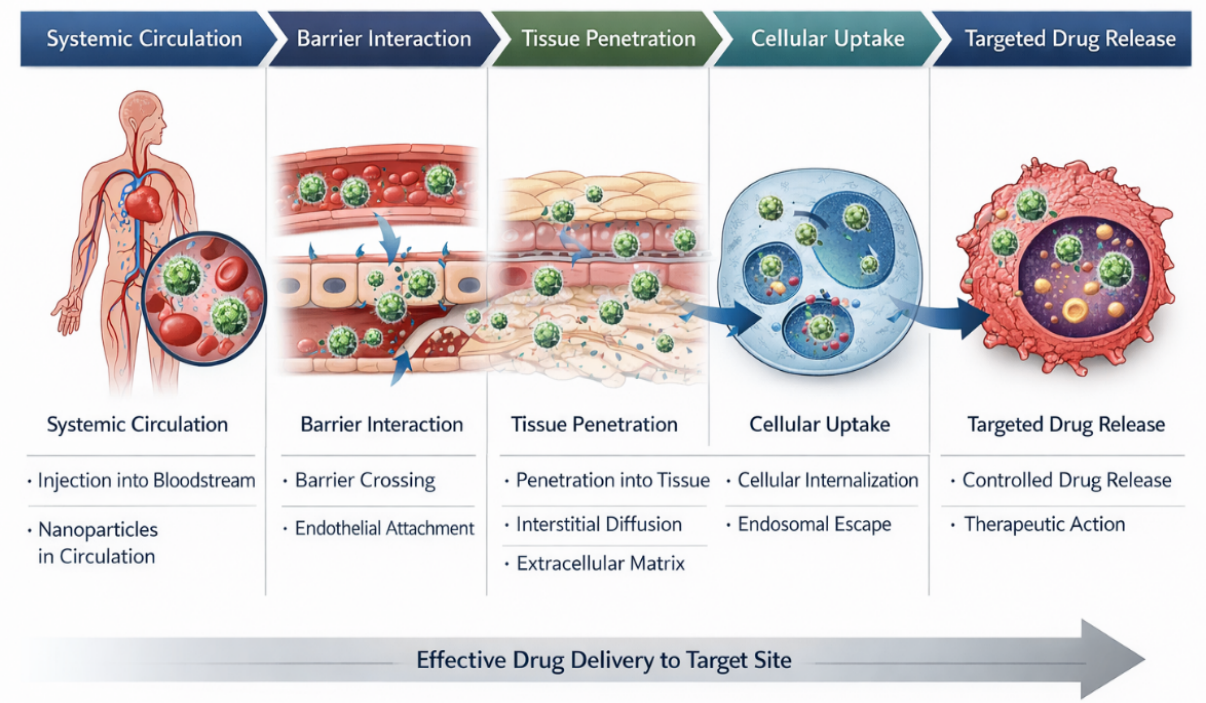

Figure 1. Simulation-Based Schematic of Nanoparticle-Mediated Drug Transport Across Biological Barriers

2. METHODOLOGY

This study follows a structured, simulation-oriented methodology to understand how nanoparticle properties influence drug delivery efficiency, particularly focusing on size and surface charge. Instead of relying on a single experimental setup, the approach integrates computational modeling with evidence from recent nanoparticle formulation studies to build a generalized framework of transport and uptake behavior. This allows the study to capture the multiscale nature of drug delivery, where interactions occur from systemic circulation down to the cellular level [7]. The methodology is designed to remain adaptable so that it can represent different nanoparticle systems without being limited to a single formulation or disease condition. This flexibility makes the framework suitable for comparative analysis across multiple delivery scenarios.

The first step in the methodology involves defining nanoparticle design parameters based on recent formulation research. Parameters such as particle size distribution, surface charge (zeta potential), and surface functionalization are selected because they directly influence cellular uptake and biodistribution. Studies on targeted polymeric nanoparticles have shown that controlled surface modification can significantly enhance selective uptake in diseased cells, which supports the inclusion of these variables in the model [7]. These parameters are treated as independent variables in the simulation framework. Additional constraints such as stability in circulation and resistance to aggregation are also considered to ensure realistic representation of nanoparticle behavior.

The second step focuses on constructing a multiscale transport model that represents nanoparticle movement across biological environments. This includes circulation dynamics, interaction with endothelial barriers, diffusion through extracellular matrices, and eventual cellular internalization.

Recent work on quality-by-design nanoparticle synthesis highlights that transport efficiency depends on how well formulation variables are aligned with biological conditions, which justifies the need for a system-level modeling approach [8]. The model therefore captures both physical transport and biological interaction stages. It also incorporates time-dependent behavior to reflect how nanoparticles evolve during their journey from administration to target localization.

To simulate cellular uptake, the methodology incorporates receptor-mediated endocytosis and passive uptake mechanisms. Surface charge is modeled as a key factor influencing membrane interaction, where positively charged nanoparticles are assumed to show higher affinity toward negatively charged cell membranes. Experimental findings from functionalized nanoparticle systems demonstrate that uptake efficiency increases with optimized surface interactions, especially in targeted delivery systems [9]. This relationship is integrated into the uptake module of the model. In addition, variability in cell membrane properties is considered to reflect differences across tissue types and disease environments.

The release behavior of nanoparticles is modeled using a controlled drug release framework that considers environmental triggers such as pH and enzymatic conditions. pH-responsive nanoparticle systems have been shown to improve drug release specifically at the target site, which reduces premature drug leakage during transport [10]. Based on this, the model includes a condition-dependent release function that activates once nanoparticles reach intracellular or target microenvironments. This approach allows the simulation to distinguish between stable transport phases and active release phases. As a result, the model can evaluate both delivery efficiency and release precision simultaneously.

Figure 2 presents the software-generated multiscale model used in this study, showing how nanoparticle size and surface charge influence different stages of the delivery process, from circulation stability to cellular uptake efficiency. The figure visually represents the relationship between design parameters and transport outcomes, allowing clear interpretation of how variations in nanoparticle properties affect overall delivery performance. This figure acts as a central framework that connects all stages of the methodology into a unified model. It also helps in validating the conceptual assumptions by linking them directly to observable transport patterns in the simulation.

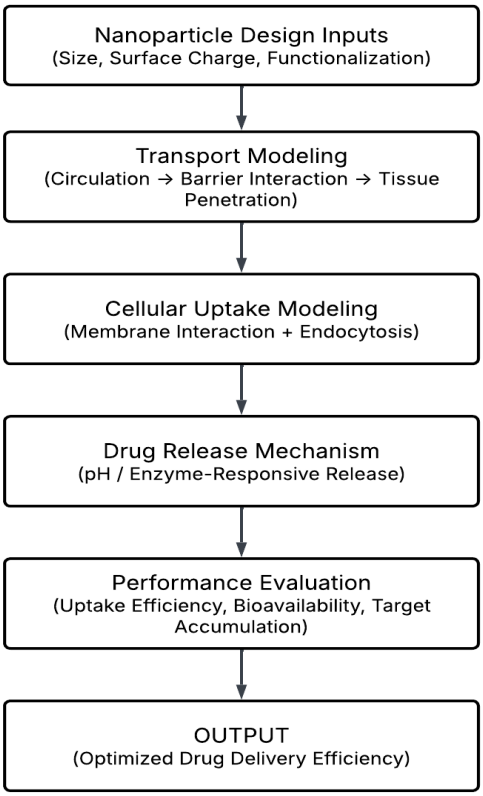

Figure 2. Software-Generated Multiscale Model of Nanoparticle Size and Surface Charge Effects on Cellular Uptake Efficiency

To support the simulation findings, a comparative evaluation is included in Table 1, which summarizes key performance metrics between conventional drug delivery systems and nanoparticle-based systems. The table includes parameters such as bioavailability, targeting efficiency, cellular uptake rate, and controlled release capability. Studies on nanohybrid and advanced delivery systems show that nanoparticle-based approaches consistently outperform conventional systems in these metrics, particularly in improving bioavailability and reducing off-target effects [11]. This comparison helps validate the assumptions used in the simulation model. It also provides a quantitative basis for evaluating improvements achieved through nanoparticle engineering.

Table 1. Comparative Performance Metrics of Conventional and Nanoparticle-Based Drug Delivery Systems

Metric	Conventional	Nanoparticle-Based
Bioavailability	Low	High
Targeting Efficiency	Non-specific	Targeted
Cellular Uptake	Limited	Enhanced
Release Control	Uncontrolled	Controlled
Circulation Time	Short	Extended
Toxicity	Higher	Reduced

Finally, the methodology integrates all modeled components into a unified evaluation framework that measures delivery efficiency as a combined outcome of transport, uptake, and release processes. By linking nanoparticle design parameters with measurable delivery outcomes, the study creates a systematic way to analyze how formulation changes impact therapeutic efficiency. This integrated approach ensures that the results presented in the next section are not isolated observations but are derived from a consistent and well-defined modeling structure. It also enables reproducibility and future extension of the model to include additional biological factors.

3. RESULTS AND DISCUSSION

The simulation results clearly show that nanoparticle-based delivery improves drug transport and release behavior compared to conventional systems. Figure 3 presents the computational release kinetics profile of free drug and nanoparticle-encapsulated drug under physiological conditions. The free drug shows a rapid release pattern, where a large fraction of the drug becomes available in a short time and then declines quickly due to degradation and clearance. In contrast, the nanoparticle-encapsulated drug demonstrates a controlled and sustained release profile, where the drug is released gradually over time. This difference confirms that nanoparticle systems help in maintaining effective drug concentration for a longer duration.

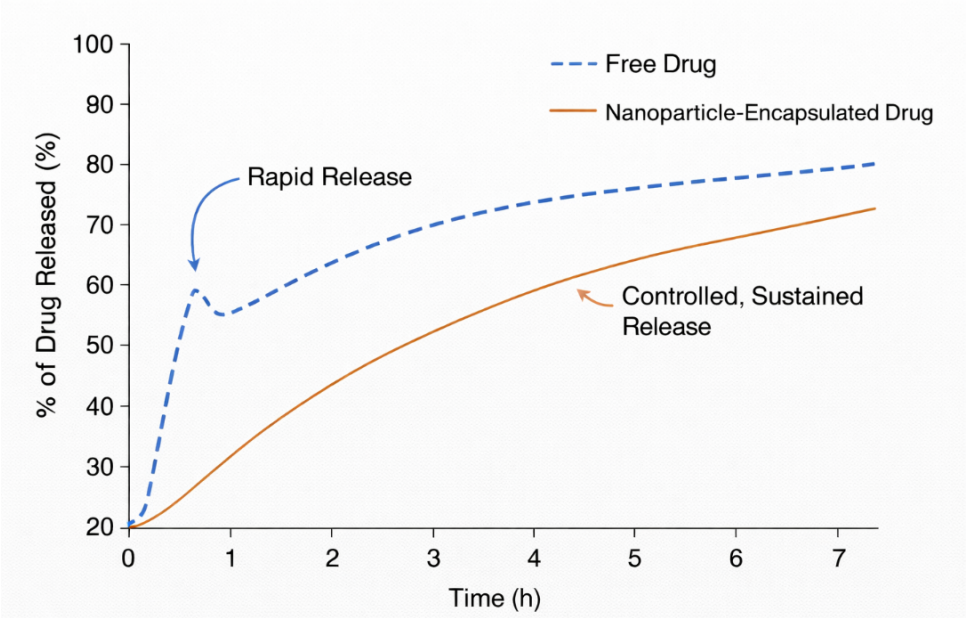

Figure 3. Computational Release Kinetics Profile of Free Drug and Nanoparticle-Encapsulated Drug Under Physiological Conditions

The controlled release behavior observed in Figure 3 directly affects therapeutic efficiency. A rapid release from conventional systems often leads to an initial spike in drug concentration followed by a sharp decrease, which can reduce treatment effectiveness and increase side effects. In comparison, nanoparticle-based systems provide a more stable release pattern, allowing continuous availability of the drug at the target site. This controlled behavior reduces the need for repeated dosing and improves overall treatment consistency. The results therefore indicate that release kinetics is a key factor in improving delivery efficiency.

Figure 4 shows the simulation-derived comparative therapeutic accumulation map for conventional and nanoparticle-assisted drug delivery. The conventional system displays a scattered and low-intensity accumulation pattern, indicating poor targeting and significant drug loss during transport. On the other hand, the nanoparticle-based system shows a highly concentrated and localized accumulation in the target region. This demonstrates that nanoparticles improve the ability of drugs to reach and remain in the desired tissue.

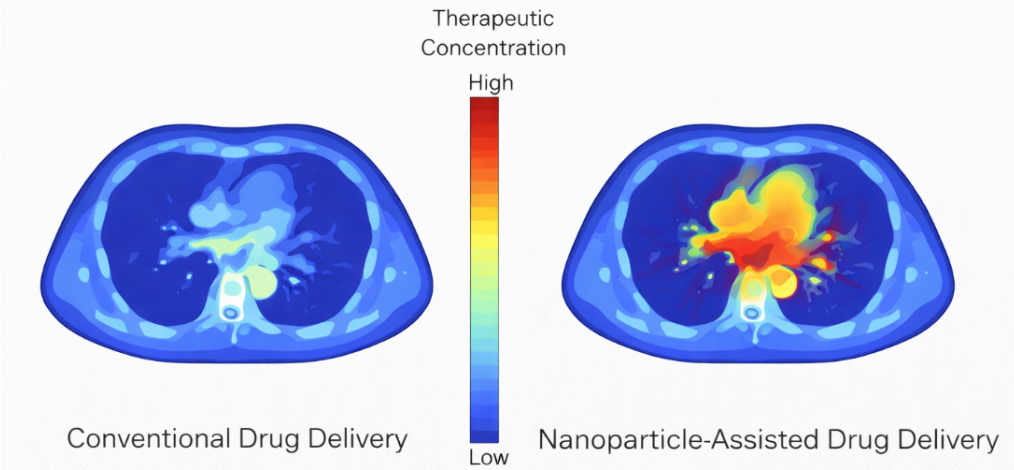

Figure 4. Simulation-Derived Comparative Therapeutic Accumulation Map of Conventional and Nanoparticle-Assisted Drug Delivery

The improved accumulation seen in Figure 4 can be explained by the combined effects of enhanced transport, better barrier penetration, and increased cellular uptake. Nanoparticles are able to cross biological barriers more efficiently and interact with target cells more effectively due to their optimized size and surface properties. This leads to higher retention of the drug in the target region and reduces off-target distribution. As a result, the overall therapeutic impact is significantly improved compared to conventional delivery methods.

When the results from both figures are considered together, a clear relationship emerges between controlled release and targeted accumulation. The sustained release profile ensures that the drug remains available during and

after accumulation at the target site, which strengthens the therapeutic effect. At the same time, improved localization reduces drug wastage and minimizes side effects. These findings confirm that nanoparticle-based delivery systems provide a more efficient and reliable approach for drug delivery, making them highly suitable for advanced therapeutic applications.

4. CONCLUSION

This study shows that nanoparticle-based drug delivery can significantly improve how drugs move through the body and reach the target site. The results clearly indicate that nanoparticles help in protecting the drug during transport, improving its stability, and enabling controlled release. Compared to conventional systems, nanoparticle-based delivery provides a more consistent and sustained release profile, which helps in maintaining effective drug levels for a longer time. This sustained behavior directly supports better therapeutic outcomes and reduces fluctuations in drug concentration.

The findings also demonstrate that nanoparticles improve drug accumulation at the target site. The simulation results show that conventional delivery leads to scattered and low drug concentration, while nanoparticle-assisted delivery results in more localized and higher concentration in the desired region. This improvement is mainly due to better barrier penetration, enhanced cellular uptake, and reduced drug loss during transport. As a result, nanoparticle systems can reduce side effects and improve overall treatment efficiency, making them more suitable for targeted therapies.

Overall, this study confirms that nanoparticle design plays a key role in improving drug delivery performance. By optimizing properties such as size and surface charge, it is possible to enhance transport, uptake, and release behavior. The approach presented in this work provides a clear framework for understanding and improving drug delivery systems. These insights can be useful for developing more effective and reliable therapies in future biomedical applications and advanced precision medicine strategies.

REFERENCES

1. Hunter, T. L., Bao, Y., Zhang, Y., Matsuda, D., Riener, R., Wang, A., ... & Aghajanian, H. (2025). In vivo CAR T cell generation to treat cancer and autoimmune disease. *Science*, *388*(6753), 1311-1317.
2. Musunuru, K., Grandinette, S. A., Wang, X., Hudson, T. R., Briseno, K., Berry, A. M., ... & Ahrens-Nicklas, R. C. (2025). Patient-specific in vivo gene editing to treat a rare genetic disease. *New England Journal of Medicine*, *392*(22), 2235-2243.
3. Garcia, D. A., Pierre, A. F., Quirino, L., Acharya, G., Vasudevan, A., Pei, Y., ... & Diaz-Trelles, R. (2025). Lipid nanoparticle delivery of TALEN mRNA targeting LPA causes gene disruption and plasma lipoprotein (a) reduction in transgenic mice. *Molecular Therapy*, *33*(1), 90-103.
4. Li, Z., Liu, P., Chen, W., Liu, X., Tong, F., Sun, J., ... & Qin, Y. (2023). Hypoxia-cleavable and specific targeted nanomedicine delivers epigenetic drugs for enhanced treatment of breast cancer and bone metastasis. *Journal of Nanobiotechnology*, *21*(1), 221.
5. Wang, Q., Han, S., Zhu, Y., Wang, G., & Chen, D. (2023). Poly-γ-glutamic acid coating polymeric nanoparticles enhance renal drug distribution and cellular uptake for diabetic nephropathy therapy. *Journal of Drug Targeting*, *31*(1), 89-99.
6. Rioja-Blanco, E., Arroyo-Solera, I., Alamo, P., Casanova, I., Gallardo, A., Unzueta, U., ... & Leon, X. (2022). Self-assembling protein nanocarrier for selective delivery of cytotoxic polypeptides to CXCR4+ head and neck squamous cell carcinoma tumors. *Acta Pharmaceutica Sinica B*, *12*(5), 2578-2591.
7. Ramalho, M. J., Nóbrega, C., Andrade, S., Lima, J., Loureiro, J. A., & Pereira, M. C. (2025). Targeted fluoxetine delivery using folic acid-modified plga nanoparticles for selective uptake by glioblastoma cells. *Pharmaceutics*, *17*(9), 1116.
8. Tekade, M., & Sharma, M. C. (2025). Quality-by-design (QbD) assisted synthesis of nanoparticle for efficient loading, stabilization, and intracellular delivery of bioactive for the treatment of arthritis. *Indian Journal of Microbiology*, *65*(1), 477-504.
9. Thi Phuong Thao, N., Nguyen, N. Y., Co, V. B., Thanh, L. H. V., Nguyen, M. Q., Pan-On, S., & Pham, D. T. (2024). Formulations of poly (vinyl alcohol) functionalized silk fibroin nanoparticles for the oral delivery of zwitterionic ciprofloxacin. *Plos one*, *19*(8), e0306140.
10. Pham, D. T., Nguyen, D. X. T., Nguyen, N. Y., Nguyen, T. T. L., Nguyen, T. Q., Tu, A. V. T., ... & Thuy, B. T. P. (2024). Development of pH-responsive Eudragit S100-functionalized silk fibroin nanoparticles as a prospective drug delivery system. *PLoS One*, *19*(5), e0303177.
11. Ashar, F., Mohammed, A. A. S., & Selvamuthukumar, S. (2024). Enhancement of oral bioavailability of ibrutinib using a liposil nanohybrid delivery system. *PLoS One*, *19*(9), e0310492.