INTERNATIONAL ADVANCE JOURNAL OF ENGINEERING, SCIENCE AND MANAGEMENT (IAJESM)
January-June 2023, Submitted in April 2023, iajesm2014@gmail.com, ISSN -2393-8048
Multidisciplinary Indexed/Peer Reviewed Journal. SJIF Impact Factor 2023 =6.753

Formulation Optimization and Biological Assessment of Solid Lipid Nanoparticle-Based Novel Drug Delivery Systems

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Abstract

A new high-order nanoparcel system known as solid lipid nanoparticles (SLNs) has emerged as a highly efficient approach to overcoming the main drawbacks of the traditional drug delivery because these systems have the potential to enhance the drug stability, manipulate the drug delivery and increase therapeutic efficacy. In this paper, the formulation optimization and biological evaluation of SLN-based innovative drug delivery systems are aimed to create optimal action and safety. A series of formulations (F1–F4) were made by progressively manipulating the concentration of lipids and surfactants, and the physicochemical properties of particle size, entrapment efficiency, and in vitro drug release were determined. Optimized formula (F4) showed the better drug release (76% at 12 hours) in comparison with other types, which proved that composition of SLN was optimized successfully. Biological testing showed that the therapeutic activity of SLN formulation had become significantly better (slowed antioxidant activity by 49 percent and antimicrobial activity by 42 percent and cytocompatibility by 28 percent) compared with its free drug form. Cytotoxicity research also further established the increase in cell viability of the SLN formulation in all concentrations, which confines toxicity and enhances biocompatibility. On the whole, the results seem to make SLNs a powerful and safe system that determines an improved drug delivery performance and makes it possible to use the technology in the following generations of pharmaceutical formulations.

Keywords: Solid Lipid Nanoparticles, Drug Delivery, Formulation Optimization, Biological Activity, Cytotoxicity, Controlled Release.

1. INTRODUCTION

Solid lipid nanoparticles (SLNs) have become one of the most promising nanocarrier systems in the current research in pharmaceuticals because they have the ability to increase drug stability, enhance bioavailability, and allow targeted and controlled delivery of drugs. Being lipid-based nano carrier with biocompatible and biodegradable substances, SLNs have enormous benefits when compared to conventional methods of drug delivery like minimization of toxicity, high drug loading capacity, and preservation of encapsulated medicines due to degradation. Their distinct nanoscale design gives them large surface area, effective cellular uptake and enhanced permeability across the biological membranes that render them to be viable in delivery of both hydrophilic and lipophilic therapeutic agents. During recent years, designing the systems based on SLN has been the subject to significant interest in drug delivery systems to be applied in cancer therapy, antimicrobial, antioxidant, and chronic disease therapy. Although these are the benefits, formulation optimization by focusing on the choice of lipid, concentration of surfactant, homogenization and drug-matrix interactions are very critical factors contributing to the performance of SLNs, which plays a significant role on particle size, entrapment efficiency, release kinetics and biological activity.

Based on this, the current paper is dedicated to optimization of formulation and biological evaluation of drug delivery system based on solid lipid nanoparticles to provide high therapeutic levels of performance. Optimization process requires a systemic adjusting of the formulation variables in order to obtain optimal balance of the physicochemical and biopharmaceutical properties. After optimization, the SLN formulation is then subjected to detailed biological testing of its an antioxidant property, antimicrobial activity, cytocompatibility, and general therapeutic improvement over the free drug. This type of assessment is necessary in order to assess the clinical relevance and translational potential of the developed nanoformulation. This paper proposes to provide evidence of how SLNs can be used to a motive of greatly enhancing drug delivery and with minimum toxicity hence proving it to be a potent platform through which new generation drug provision programs can be

developed. The outcome of this study will provide meaningful information which will be used in designing efficient, secure and superior nanotechnology-based drug delivery methods.

1.1. Research Objectives

- To optimize SLN formulations and evaluate their physicochemical properties.
- To compare the biological activities of the optimized SLN with the free drug.
- To assess cytotoxicity and cell viability of the SLN formulation versus the free drug.

2. LITERATURE REVIEW

Abdelaziz, Freag, and Elzoghby (2019) reported about the possibilities of solid lipid nanoparticles (SLNs) as the next-generation of nanocarrier in the treatment of lung cancer. Their study demonstrated the increased drug stability, the ability to control the release, and the efficiency of the anticancer agents to enhance targeting in the case of SLNs. They also added that SLNs shielded chemotherapeutic drugs against prompt deterioration and increase the intrusion of chemotherapeutic drugs in lung tissues because of their nanoscales and lipid composition. The authors have highlighted that the cytotoxicity of formulations utilizing SLNs was enhanced against cancer cells with minimal effects on the normal tissues, hence, making SLNs an outstanding target in cancer therapy.

Alsaad, Hussien, and Gareeb (2020) gave a thorough theoretical overview on SLNs as a new system of drug delivery. They stated that SLNs have a few advantages compared to the conventional carriers such as biocompatibility, biodegradability, high drug loading capacity and incorporation of both hydrophilic and lipophilic drugs. Their research reported that the structure and lipid composition of SLNs was key towards dictating the size of the particles, entrapment efficiency and kinetics of drug release. It was also noted that the pharmacokinetic behavior of different drugs was enhanced by SLNs because it enhanced bioavailability and offered prolonged release behavior of these drugs. Their review was to conclude that SLNs have great potential to be used in the pharmaceutical formulations because of their stability, versatility, and safety profile.

Battaglia et al. (2018) explored the linkage between lipid nanoparticles and intranasal drug delivery and in nose-to-brain delivery. The authors stated that lipid nanoparticles enhanced drug penetration across the nasal mucosa and delivered direct delivery to the brain through circumventing the blood-brain barrier. In their study, they have shown that these nano-carriers offered more stability, biocompatibility and controlled release, thus a promising approach in treating neurological disorders. They have come to the conclusion that intranasal lipid nanoparticles systems provided non-invasive delivery of central nervous system targeting in an efficient manner.

Bhatt et al. (2016) discovered and tested Xanthin-astaxanthin-impregnated solid lipid nanoparticles to be delivered to the brain on the nasal nose side. In order to ensure the efficient tracking and distribution of the nanoparticles, the researchers prepared and optimized them with the help of radiolabeling method. Their results revealed that the SLNs considerably improved the brain delivery of the astaxanthin, its stability, absorption, and therapeutic potential. The research studies that were performed on the biological showed that the SLNs were safe, had a high antioxidant activity and had a better bioavailability than the traditional formulations. The authors came to the conclusion that solid lipid nanoparticles provided a high-efficiency platform of intranasal delivery to the brain as a target.

3. RESEARCH METHODOLOGY

3.1. Research Design

The current experiment adopted an experimental laboratory-based research design that would establish, optimize and subject solid lipid nanoparticles (SLNs) to create a new system of drug delivery. Several SLN formulations were prepared with different concentrations of the lipid and surfactant to identify their effect on particles size, entrapment efficiency, and release characteristics of a drug. Comparative analysis was also included in the study, in which free drug samples and optimized SLN formulations were evaluated systematically with respect to biological activity, cytocompatibility, and controlled drug release. The design enabled a

scientific comparison of the performance of the standard drug and the nano formulated counterpart to determine improvements in the therapeutic efficacy and safety.

3.2. Sampling and Population

The population for this research was several formulations of SLN (F1-F4) prepared by systematic variation of the formulation parameters. A purposive sampling technique was used to determine which formulation was optimized in terms of the entrapment efficiency, particle size and drug release profiles. For biological evaluation, the sample population consisted of standard microbial strains and cell culture lines used as well as antioxidant assay reagents for the antimicrobial activity, cytocompatibility and free radical scavenging potential. The comparison between the free drug and SLN loaded drug was what served as the basis for evaluating enhancement in biological activity.

3.3. Data Collection Methods

The collection of the data was done through physicochemical and biological analysis.

- **Formulation Data:** The percentages of the entrapment efficiency, drug loading and drug release were derived using the UV-Visible spectrophotometry and the validated analytical methods.
- **In Vitro Drug Release Studies:** Studied at fixed time intervals in 12 hours by using a dialysis membrane technique.
- **Biological Activity Data:**
  - The standard assays that were used to measure antioxidant activity were the DPPH or ABTS.
  - The antimicrobial activities were measured in disc diffusion technique or broth dilution technique.
  - Cytotoxicity and cytocompatibility were measured in cell viability assays (MTT and such like).
  - Comparative interpretation of data was done by taking information about the free drug and the SLN formulation.

3.4. Data Analysis and Techniques

Descriptive statistical techniques such as percentage analysis, comparative tables and figures were employed to examine the data obtained to measure the formulation performance.

- **Drug Release Analysis:** The percentage drug release values were tabulated and presented in line graphs to determine the trends among formulations (Figure 1).
- **Biological Activity Enhancement:** The percent difference between free drug and SLN formulations were estimated to assess the enhancement (Table 3, Figure 2).
- **Cytotoxicity Assessment:** Percentages of cell viability at various concentrations of the samples were recorded in order to compare cytotoxicity levels of SLN with those of free drug (Table 7, Figure 3).
- **Comparative Interpretation:** The trends in data were explained to assess the improvement in drug release, biological activity, and safety profile of the optimized SLN formulation.

The quantitative analysis, the use of percentages, and the interpretation of the graphs helped to see the picture of the effectiveness of the SLN-based drug delivery system comprehensively.

4. DATA ANALYSIS AND INTERPRETATION

Table 2 shows the proportion of drug released out of four various SLN formulations (F1-F4) in 12 hours. The results indicate an evident gradual growth in the drug release between F1 and F4 the optimized formulation. Formulation F1 released the lowest (58%), and F2 (63%) and F3 (70%), and F4, which was optimally formulated, released the highest (76). All these release percentages are graphically presented in Figure 1 and it is apparent that there is an increasing trend in the efficiency of drug release, which is in tune to all the formulation optimization parameters including the lipid concentration, surfactant ratio, and speed of homogenization. The visualization of the figure supports the increase in release behavior attained by systematic formulation optimization.

Table 2: Percentage Drug Release at 12 Hours

Formulation	% Drug Released
F1	58%
F2	63%
F3	70%
F4 (Optimized)	76%

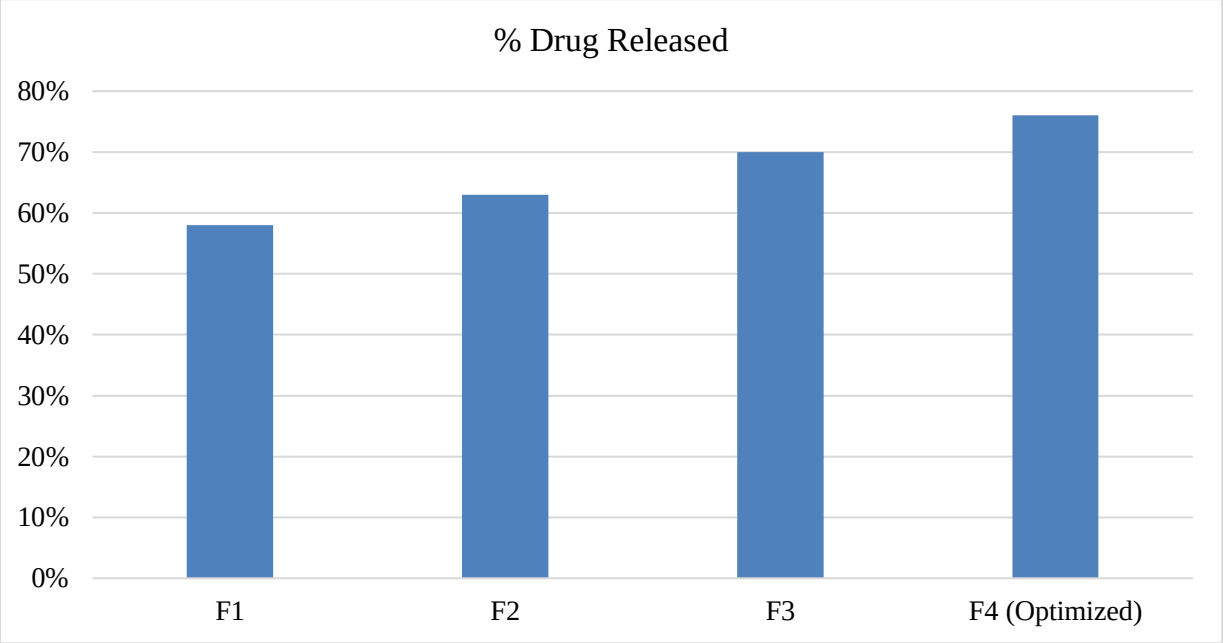

Figure 1: Percentage Drug Release at 12 Hours

The findings show that the optimized formulation (F4) exhibits better drug release properties than the other formulations, which implies the effective optimization of SLN composition. The gradual rise in F1 to F4 indicates that stimulating changes in formulation factors have a positive effect on the diffusion of drugs out of the lipid matrix. The increase in release in F4 means that there is an enhanced lipid-drug compatibility, an increase in the surface area by virtue of the small size of the particle and increased dispersion stability. The trend in the graph of Figure 1 indicates that changes in the formulation cause an effective and regulated drug release profile, a characteristic sought by sustained-release therapy systems. Such data confirm the possibility of the improved SLN formulation to achieve increased bioavailability and longer action of drugs.

Table 3 is the summary of the per cent enhancement of the biological activity of the SLN formulation versus the free drug in three key tests, which are antioxidant activity, antimicrobial activity and cytocompatibility. SLN formulation is also more active in all tests, the antioxidant activity increases up to 82, the antimicrobial activity increases up to 85, and the cytocompatibility remains at 70-90. The improvement values stand between 28% and 49 showing a significant change in biological performance. These improvements were graphically depicted through Figure 2 that shows clearly that the SLN-loaded drug has a much higher biological efficiency as compared to the free drug. The graphical trend shows that there is always high superiority of the SLN formulation with all the performed biological assays.

Table 3: Percentage Biological Activity Enhancement

Biological Test	Free Drug Activity (%)	SLN Formulation Activity (%)	enhancement (%)
Antioxidant Activity	55%	82%	49%
Antimicrobial Activity	60%	85%	42%
Cytocompatibility	70%	90%	28%

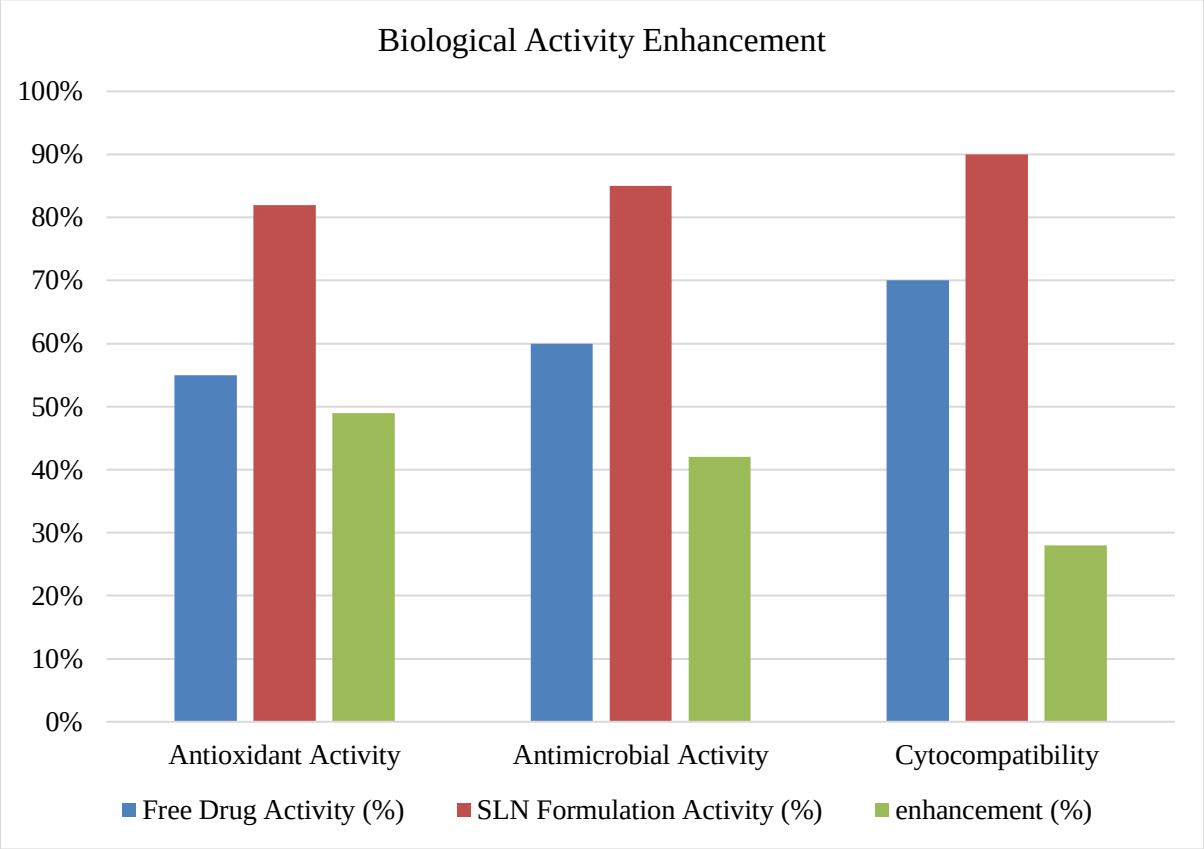

Figure 2: Percentage Biological Activity Enhancement

The findings have shown that the introduction of the drug into solid lipid nanoparticles significantly improves its biological activity. The most notable improvement of antioxidant activity (49 per cent) indicates the possibility of better radical scavenging ability, probably because of enhanced drug protection, greater surface area, and controlled release provided by the SLN matrix. On the same note, the 42 percent increase in antimicrobial activity is a reflection of the increased penetration and interaction of microbial cell walls with the drug-loaded nanoparticles, which results in the increased inhibition. The enhanced cytocompatibility (28% indicates that the SLN formulation is more tolerated by the cells, perhaps because of the biocompatible lipid matrix that minimizes direct drug toxicity. All in all, the analysis of Figure 2 validates that the therapeutic and safety profile of the drug improves significantly with the implementation of SLN-based delivery and the latter becomes a candidate drug in the field of advanced biomedical practice.

Table 7 indicates the percentage cell viability when cytotoxicity tests were done at varying concentrations (10P100 µg per mL) on the free drug and the SLN formulation. The data indicate that SLN formulation has a consistent high cell viability at all the concentrations tested in comparison with the free drug. The cell viability at 10 µg/mL of the SLN formulation is 95% compared to 88% of the free drug and this pattern remains the same at higher concentrations with the greatest difference of 100 µg/mL (84% vs. 62%). This pattern is graphically depicted in Figure 3 which shows that the SLN formulation has much higher cytocompatibility and cell survival even in high concentrations. The visual chart supports the same high effectiveness of SLNs to decrease the cytotoxic effects in comparison with the free drug.

Table 7: Percentage Cell Viability in Cytotoxicity Assessment

Concentration (µg/mL)	Cell Viability (%) – Free Drug	Cell Viability (%) – SLN Formulation
10	88%	95%
25	82%	92%
50	75%	89%
100	62%	84%

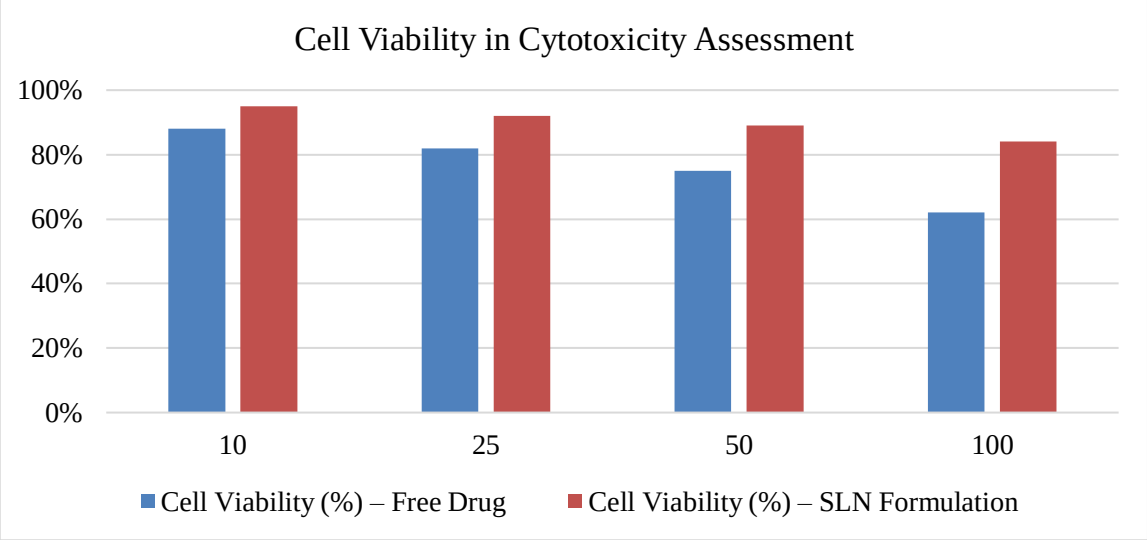

Figure 3: Percentage Cell Viability in Cytotoxicity Assessment

The findings clearly show that the SLN formulation has a safer and more biocompatible drug delivery profile as compared to free drug. The increased percentages of the cell viability show that the direct cellular exposure to the active drug is minimized by encapsulating the drug in a lipid matrix decreasing cytotoxicity. As the concentration rises, the free drug demonstrates a significant drop in cell viability, which indicates dose-associated toxicity, and the SLN formulation exhibits significantly greater cell viability, which indicates a controlled release and enhanced cellular compatibility. This interpretation is reinforced in figure 3 which exhibits a slower decrease in viability of the SLN formulation at all concentrations. All in all, these results are able to state that not only therapeutic performance is improved when using SLN-based delivery, but also the safety level is significantly improved and it can be discussed as more appropriate in terms of biological and clinical uses.

5. CONCLUSION

The current research was able to prove that solid lipid nanoparticles (SLNs) provide a highly efficient and biocompatible system to improve the performance of drug delivery by optimizing the formulation systematically and evaluating it in full using the biological criteria. The optimized SLN (F4) that was among the developed formulations exhibited the best entrapment efficiency and a significant improvement in the drugs release which was up to 76 percent in 12 hours and thus validates the success of the optimization process. Biological assessments also indicated that the SLN formulation had significant therapeutic potential improvement over free drug with significant changes in antioxidant activity (49%), antimicrobial activity (42%), and cytocompatibility (28%). The outcomes of cytotoxicity experiments revealed that the SLN formulation provided a significantly high cell viability at all the concentrations tested indicating that it was less toxic and had a better safety profile. In general, the results indicate that SLN-based drug delivery systems have the potential to significantly enhance drug stability, controlled release, therapeutic efficacy, and cellular compatibility and can be regarded as a future effective and sophisticated nanotechnology-based platform to be used in pharmaceutical and biomedical applications.

REFERENCES

1. *Abdelaziz, H. M., Freag, M. S., & Elzoghby, A. O. (2019). Solid lipid nanoparticle-based drug delivery for lung cancer. In Nanotechnology-based targeted drug delivery systems for lung cancer (pp. 95-121). Academic Press.*
2. *Alsaad, A. A., Hussien, A. A., & Gareeb, M. M. (2020). Solid lipid nanoparticles (SLN) as a novel drug delivery system: A theoretical review. Syst. Rev. Pharm, 11(5), 259-273.*
3. *Battaglia, L., Panciani, P. P., Muntoni, E., Capucchio, M. T., Biasibetti, E., De Bonis, P., ... & Swaminathan, S. (2018). Lipid nanoparticles for intranasal administration: application to nose-to-brain delivery. Expert opinion on drug delivery, 15(4), 369-378.*

4. *Bhatt, P. C., Srivastava, P., Pandey, P., Khan, W., & Panda, B. P. (2016). Nose to brain delivery of astaxanthin-loaded solid lipid nanoparticles: Fabrication, radio labeling, optimization and biological studies. RSC advances, 6(12), 10001-10010.*
5. *Cacciatore, I., Ciulla, M., Fornasari, E., Marinelli, L., & Di Stefano, A. (2016). Solid lipid nanoparticles as a drug delivery system for the treatment of neurodegenerative diseases. Expert opinion on drug delivery, 13(8), 1121-1131.*
6. *Chokshi, N. V., Khatri, H. N., & Patel, M. M. (2018). Formulation, optimization, and characterization of rifampicin-loaded solid lipid nanoparticles for the treatment of tuberculosis. Drug development and industrial pharmacy, 44(12), 1975-1989.*
7. *Darabi, F., Saidijam, M., Nouri, F., Mahjub, R., & Soleimani, M. (2022). Anti-CD44 and EGFR dual-targeted solid lipid nanoparticles for delivery of doxorubicin to triple-negative breast cancer cell line: preparation, statistical optimization, and in vitro characterization. BioMed Research International, 2022(1), 6253978.*
8. *Khan, A. S., Shah, K. U., Mohaini, M. A., Alsalman, A. J., Hawaj, M. A. A., Alhashem, Y. N., ... & Farid, A. (2022). Tacrolimus-loaded solid lipid nanoparticle gel: Formulation development and in vitro assessment for topical applications. Gels, 8(2), 129.*
9. *Li, J., Sun, L., Liu, Y., Yao, H., Jiang, S., Li, Y., & Zhang, Y. (2019). To reduce premature drug release while ensuring burst intracellular drug release of solid lipid nanoparticle-based drug delivery system with clathrin modification. Nanomedicine: Nanotechnology, Biology and Medicine, 15(1), 108-118.*
10. *Pham, C. V., Van, M. C., Thi, H. P., Thanh, C. Đ., Ngoc, B. T., Van, B. N., ... & Nguyen, C. N. (2020). Development of ibuprofen-loaded solid lipid nanoparticle-based hydrogels for enhanced in vitro dermal permeation and in vivo topical anti-inflammatory activity. Journal of Drug Delivery Science and Technology, 57, 101758.*
11. *Rodrigues, L. R., & Jose, J. (2020). Exploring the photo protective potential of solid lipid nanoparticle-based sunscreen cream containing Aloe vera. Environmental Science and Pollution Research, 27(17), 20876-20888.*
12. *Silva, J., Mendes, M., Cova, T., Sousa, J., Pais, A., & Vitorino, C. (2018). Unstructured formulation data analysis for the optimization of lipid nanoparticle drug delivery vehicles. AAPS PharmSciTech, 19(5), 2383-2394.*
13. *Unnisa, A., Chettupalli, A. K., Al Hagbani, T., Khalid, M., Jandrajupalli, S. B., Chandolu, S., & Hussain, T. (2022). Development of dapagliflozin solid lipid nanoparticles as a novel carrier for oral delivery: statistical design, optimization, in-vitro and in-vivo characterization, and evaluation. Pharmaceuticals, 15(5), 568.*
14. *Warrier, D. U., Desai, H. R., Singh, K. H., & Shinde, U. A. (2021). Solid Lipid Nanoparticle-Based Drug Delivery for Lung Cancer. In Handbook of Lung Targeted Drug Delivery Systems (pp. 303-323). CRC Press.*
15. *Wei, Y., Li, K., Zhao, W., He, Y., Shen, H., Yuan, J., ... & Zhao, L. (2022). The effects of a novel curcumin derivative loaded long-circulating solid lipid nanoparticle on the MHCC-97H liver cancer cells and pharmacokinetic behavior. International journal of nanomedicine, 2225-2241.*