International Journal of Pharmaceutics and Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Original Research Article

DESIGN AND CHARACTERIZATION OF PACLITAXEL LOADED NANOPARTICLES WITH PIPERINE

Surbhi Kurmi*, Mr. Yashwant Singh Jat, Dr. Sunil K. Jain, Dr. Harshita Jain
Adina Institute of Pharmaceutical Science, Sagar (M.P.)

***Correspondence Info:**
Surbhi Kurmi
Adina Institute of Pharmaceutical Science, Sagar (M.P.)
Email: surbhikurmi578@gmail.com

***Article History:**

Received: 28/01/2024
Revised: 15/02/2024
Accepted: 04/03/2024

ABSTRACT

Cancer treatment efficacy is often hampered by the limited solubility and systemic toxicity of chemotherapeutic agents, such as paclitaxel. Nanoparticle-based drug delivery systems have emerged as a promising strategy to overcome these challenges. This study focuses on the design and characterization of paclitaxel-loaded nanoparticles with the bioenhancer piperine, aiming to enhance the therapeutic potential of paclitaxel. The incorporation of piperine into paclitaxel-loaded nanoparticles aims to harness its bioenhancing effects, potentially improving the pharmacokinetics and therapeutic outcomes of paclitaxel. Piperine, derived from black pepper, has shown synergistic effects with paclitaxel in various cancer cell lines, making it an attractive candidate for combination therapy. In vitro drug release provide insights into the robustness of the formulation for clinical translation. This research endeavors to bridge the gap between conventional chemotherapy limitations and innovative nanotechnological solutions. By elucidating the intricate interplay between paclitaxel, piperine, and polymeric nanoparticles, this study seeks to contribute valuable insights that may pave the way for improved cancer treatment strategies with enhanced efficacy and reduced systemic toxicity.

Key words: Paclitaxel, Nanoparticles, Piperine, Formulation, Evaluation

INTRODUCTION

Cancer remains a formidable global health challenge, necessitating continuous exploration of innovative therapeutic strategies. Among the various chemotherapeutic agents, paclitaxel has demonstrated significant efficacy in treating various malignancies (Chintamaneni *et al.,* 2024). However, its clinical application is hindered by inherent limitations, such as poor water solubility and systemic toxicity. Nanoparticle-based drug delivery systems have emerged as promising solutions to address these challenges, offering improved drug solubility, bioavailability, and targeted delivery (Thakuria *et al.,* 2021). In the realm of nanotechnology, the design and characterization of paclitaxel-loaded nanoparticles have gained prominence. Nanoparticles, typically in the range of 1-100 nanometers, exhibit unique physicochemical properties that can be tailored for efficient drug delivery (Mohapatra *et al.,* 2018). Various materials, including polymers, lipids, and proteins, have been explored for formulating paclitaxel-loaded nanoparticles. The choice of material influences the stability, drug release kinetics, and biocompatibility of the nanoparticles (Ping *et al.,* 2013).

Polymeric nanoparticles, such as those composed of poly(ε-caprolactone) (PCL) and d-α-tocopheryl polyethylene glycol 1000 succinate (TPGS), have shown promise in encapsulating paclitaxel (Wang *et al.,* 2014). These formulations not only enhance the solubility of paclitaxel but also provide sustained release profiles, contributing to prolonged therapeutic effects. The encapsulation efficiency and loading capacity of paclitaxel in these nanoparticles are critical parameters that impact the overall efficacy of the drug delivery system.

Incorporating piperine, a bioactive alkaloid derived from black pepper, into paclitaxel-loaded nanoparticles introduces a novel dimension to cancer therapy (Kaur *et al.,* 2021). Piperine has been recognized for its bioenhancement properties, primarily attributed to its ability to inhibit drug metabolism and enhance absorption. Combining paclitaxel with piperine holds the potential to improve the pharmacokinetics and therapeutic outcomes of paclitaxel (Tripathi *et al.,* 2022).

The synergistic effects of paclitaxel and piperine have been demonstrated in various studies. Piperine has been shown to potentiate the efficacy of paclitaxel in cancer cells, possibly through modulating drug metabolism pathways or exerting anti-cancer effects itself. The co-delivery of paclitaxel and piperine in nanoparticles aims to harness this synergism, enhancing the overall therapeutic impact (Iswarya *et al.,* 2006).

Several natural compounds have shown the potential to enhance the therapeutic effects of anticancer drugs. Piperine, a bioactive alkaloid isolated from black pepper (Piper nigrum), has demonstrated remarkable bioenhancement properties by inhibiting drug metabolism and improving absorption. In this context, the co-delivery of paclitaxel and piperine using nanoparticles presents a novel strategy to improve the pharmacokinetics and therapeutic outcomes of paclitaxel.

MATERIALS & METHODS

Nanoparticle Formation: Emulsion Solvent Evaporation Method

In the preparation of paclitaxel-loaded nanoparticles, the emulsion solvent evaporation method was employed. The polymer used, poly(lactic-co-glycolic acid) (PLGA), was dissolved in dichloromethane (DCM). Paclitaxel was then added to the polymer solution, and the resulting mixture was sonicated or vortexed to achieve homogeneity. Subsequently, the polymer-drug solution was added dropwise into an aqueous phase containing a surfactant, such as polyvinyl alcohol (PVA). The resulting oil-in-water (o/w) emulsion was sonicated or homogenized, and the organic solvent was evaporated under reduced pressure or with stirring, resulting in the formation of solid nanoparticles (Desgouilles *et al.,* 2003).

Table 1: Formulation of paclitaxel-loaded nanoparticles

Ingredients	F1	F2	F3	F4
Drug paclitaxel (mg)	20	20	20	20
Piperine (mg)	10	20	30	40
Polymer PLGA (mg)	100	150	150	100
Surfactant PVA (%)	1.25	1.25	1.25	1.25
Solvent (DCM)	Q.S.	Q.S.	Q.S.	Q.S.

Characterization of Nanoparticles

Nanoparticles are characterized using various techniques:

Electron Microscopy

Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) provide high-resolution images of nanoparticles, allowing for detailed examination of internal structure (TEM) and surface morphology and topography (SEM) (Buhr *et al.,* 2009).

Size Determination by Optical Microscopy

Optical microscopy involves preparing the sample for clear visualization. The microscope is calibrated, and measurements are made on the eyepiece reticle or using digital measuring tools in the microscope software (Wang *et al.,* 2018).

Evaluation of Physicochemical properties and drug release kinetics

Physicochemical properties and drug release kinetics were evaluated using the following methods:

Apparent Bulk Density: Determined by transferring an accurately weighed powder sample to a grounded cylinder and calculating the density using the formula: Density = Mass/Volume.

Tapped Density: Weighed powder samples were subjected to a fixed number of taps (500 times) using a tap density apparatus. Density was calculated using the formula: Density = Mass/Tapped Volume.

Carr's Index: The percentage compressibility of granules was computed using Carr's index formula: Carr's Index = (Tapped Density – Bulk Density) / Tapped Density x 100.

Hausner's Ratio: This ratio indicates powder flow properties and is measured by the ratio of tapped density to bulk density.

Drug Loading and Encapsulation Efficiency: Determined by centrifugation followed by UV spectroscopy at 235 nm. Encapsulation efficacy was assessed using the Equation provided.

In-vitro Drug Release Study: Conducted using the dialysis bag diffusion process in phosphate buffer, pH 7.4, with the cumulative percentage drug release sustained over 24 hours. Initial burst release was observed, attributed to weakly bound drug on the nanoparticle surface (Adibkia *et al.,* 2011).

RESULTS AND DISCUSSION

The provided data offers a comprehensive insight into the characteristics and performance of paclitaxel nanoparticles across different formulations. Among these formulations, F3 emerges as particularly promising. Its small particle size of 123.22 nm indicates efficient size reduction during formulation, potentially enhancing cellular uptake and distribution. Furthermore, F3 demonstrates excellent bulk and tapped density values, indicating favorable flow properties crucial for manufacturing and administration processes. Carr's index and Haunser's ratio further affirm its suitability for dosage form processing, highlighting good flowability and compressibility. Importantly, F3 exhibits the highest entrapment efficiency (86.12%) and loading capacity (0.93 mg/ml), ensuring optimal drug encapsulation and potential for improved therapeutic efficacy.

In the in-vitro drug release study, F3 displays sustained release kinetics over 24 hours, releasing 95.47% of the drug within this

timeframe. This sustained release profile is desirable for paclitaxel, offering the potential to maintain therapeutic drug levels, reduce dosing frequency, and minimize side effects. Overall, these findings suggest that F3 holds promise as an optimized formulation for paclitaxel delivery, though further in-vivo studies are warranted to validate its efficacy and safety in clinical settings.

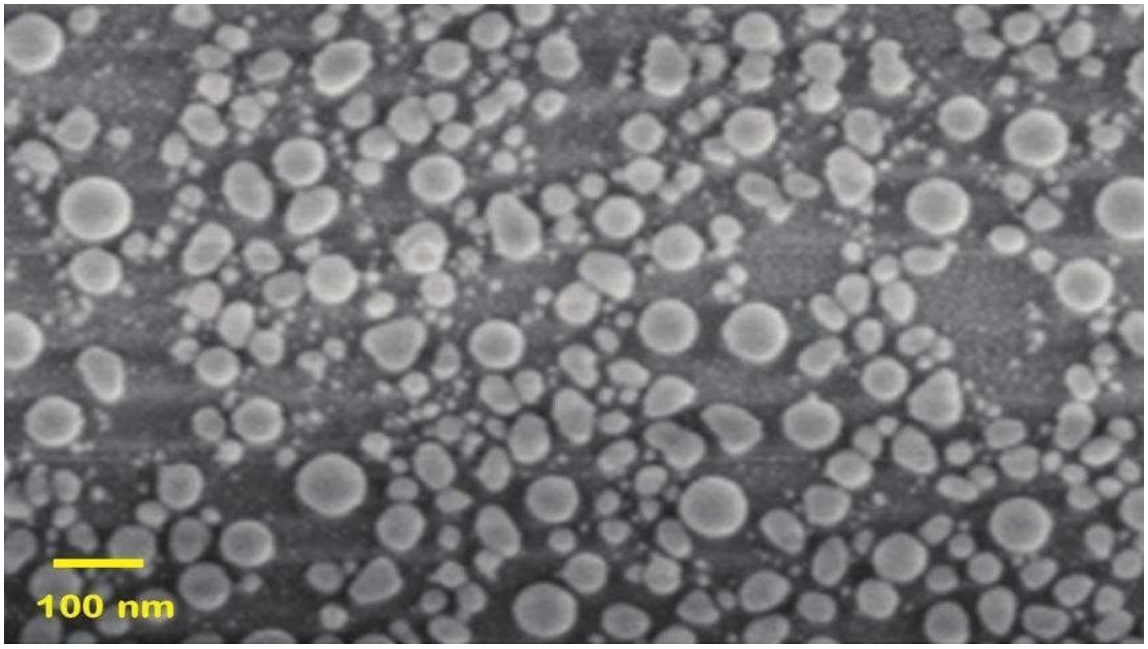

Figure 1: Paclitaxel nanoparticles in electron microscopy

Table 2: Results of Particle size of the various formulations

F. Code	F1	F2	F3	F4
Particle Size (nm)	197.00	180.00	123.22	190.00

Table 3: Evaluation of paclitaxel nanoparticles of optimized formulation F3

S. No.	Parameters	Results
1	Bulk density	0.584±0.01 (gm/ml)
2	Tapped density	0.563±0.04 (gm/ml)
3	Carr's index	3.69±0.40
4	Haunser's ratio	1.038±0.02

Table 4: % Entrapment efficiency and Loading capacity

Formulation	%EE	LC (mg/ml)
F1	57.21	0.55
F2	64.58	0.63
F3	86.12	0.93
F4	78.91	0.89

Table 5: *In vitro* drug release study of Formulation

Time (h)	F1	F2	F3	F4
1	0	0	0	0
2	2.00	4.50	7.00	5.15
4	3.56	5.80	9.23	7.55
6	5.25	7.58	11.25	10.22
12	26.00	28.00	33.00	30.00
24	79.00	81.00	95.47	85.00

CONCLUSION

The study has successfully evaluated various formulations of paclitaxel nanoparticles, with a focus on optimizing their characteristics for enhanced drug delivery. Among the formulations examined, F3 stands out as the most promising candidate due to its small particle size, favorable flow properties, high entrapment efficiency, substantial loading capacity, and sustained drug release profile. These attributes collectively suggest that F3 has the potential to improve therapeutic outcomes by ensuring efficient drug delivery, minimizing drug wastage, and reducing dosing frequency. However, while the in-vitro results are encouraging, further research, including in-vivo pharmacokinetic and pharmacodynamic studies, is essential to confirm the efficacy and safety of F3 in clinical applications. Overall, this work provides valuable insights into the development of optimized paclitaxel nanoparticle formulations, offering promising prospects for more effective cancer therapy.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

REFERENCES

- Chintamaneni, P.K., Pindiprolu, S.K.S.S., Swain, S.S., Karri, V.V.S.R., Nesamony, J., Chelliah, S. & Bhaskaran, M. (2024) Conquering chemoresistance in pancreatic cancer: Exploring novel drug therapies and delivery approaches amidst

desmoplasia and hypoxia. *Cancer Letters*, 216782

- Thakuria, A., Kataria, B. & Gupta, D. (2021) Nanoparticle-based methodologies for targeted drug delivery—An insight. *Journal of Nanoparticle Research*, 23, 87
- Mohapatra, S. *et al.,* editors (2018). *Characterization and Biology of Nanomaterials for Drug Delivery: Nanoscience and Nanotechnology in Drug Delivery*. Elsevier: Amsterdam.
- Ma, P. & Mumper, R.J. (2013) Paclitaxel nano-delivery systems: A comprehensive review. *Journal of Nanomedicine and Nanotechnology*, 4, 1000164
- Wang, Z., Zeng, X., Ma, Y., Liu, J., Tang, X., Gao, Y., Liu, K., Zhang, J., Ming, P., Huang, L. & Mei, L. (2014) Antitumor efficiency of D-α-tocopheryl polyethylene glycol 1000 succinate-b-poly(ε-caprolactone-ran-lactide) nanoparticle-based delivery of docetaxel in mice bearing cervical cancer. *Journal of Biomedical Nanotechnology*, 10, 1509–1519
- Kaur, J., Singh, R.R., Khan, E., Kumar, A. & Joshi, A. (2021) Piperine-loaded PLGA nanoparticles as cancer drug carriers. *ACS Applied Nano Materials*, 4, 14197–14207
- Tripathi, A.K., Ray, A.K. & Mishra, S.K. (2022) Molecular and pharmacological aspects of piperine as a potential molecule for disease prevention and management: Evidence from clinical trials. *Beni-Suef University Journal of Basic and Applied Sciences*, 11, 16
- HemaIswarya, S. & Doble, M. (2006) Potential synergism of natural products in the treatment of cancer. *Phytotherapy Research*, 20, 239–249
- Desgouilles, S., Vauthier, C., Bazile, D., Vacus, J., Grossiord, J., Veillard, M. & Couvreur, P. (2003) The design of nanoparticles obtained by solvent evaporation: A comprehensive study. *Langmuir*, 19, 9504–9510
- Buhr, E., Senftleben, N., Klein, T., Bergmann, D., Gnieser, D., Frase, C.G. & Bosse, H. (2009) Characterization of nanoparticles by scanning electron microscopy in transmission mode. *Measurement Science and Technology*, 20, 084025 [DOI: 10.1088/0957-0233/20/8/084025].
- Wang, W. (2018) Imaging the chemical activity of single nanoparticles with optical microscopy. *Chemical Society Reviews*, 47, 2485–2508
- Adibkia, K., Hamedeyazdan, S. & Javadzadeh, Y. (2011) Drug release kinetics and physicochemical characteristics of floating drug delivery systems. *Expert Opinion on Drug Delivery*, 8, 891–903