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Original Research Article

FORMULATION, IN VITRO EVALUATION AND CHARACTERIZATION OF THE NANOPARTICLES SYSTEM OF DOCETAXEL

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ABSTRACT

The formulation, characterization, and evaluation of docetaxel nanoparticles were conducted to enhance its therapeutic efficacy. Nanoparticles were prepared using a solvent evaporation method, and their physicochemical properties were investigated. Microscopic observation revealed uniform and spherical nanoparticles. Evaluation parameters including particle size, polydispersity index, encapsulation efficiency, drug release, and zeta potential were determined for three different formulations. Formulation 3 exhibited the most promising characteristics with higher encapsulation efficiency, cumulative drug release, and more negative zeta potential compared to other formulations. These findings suggest that Formulation 3 holds potential for improved stability and controlled release of docetaxel. Further studies are needed to validate its therapeutic efficacy in vivo.

Keywords: Docetaxel, nanoparticles, formulation, characterization, encapsulation efficiency, drug release, zeta potential, cancer therapy.

INTRODUCTION

Docetaxel, a semi-synthetic taxane derivative, is a potent anticancer agent widely used in the treatment of various solid tumors, including breast, lung, and prostate cancers (Gelderblom *et al.,* 2001). Despite its efficacy, docetaxel exhibits poor aqueous solubility and bioavailability, leading to challenges in its formulation and delivery (Rahman *et al.,* 2013). Conventional formulations of docetaxel, such as intravenous infusions containing Tween 80 and ethanol, are associated with significant toxicity and adverse effects (Maeda *et al.,* 2000).

Nanoparticle-based drug delivery systems have emerged as promising approaches to overcome the limitations of conventional formulations and improve the therapeutic efficacy of anticancer agents like docetaxel (Gradishar *et al.,* 2005).

Nanoparticles offer several advantages, including enhanced drug solubility, sustained release, targeted delivery to tumor tissues, and reduced systemic toxicity (Soppimath *et al.,* 2001).

In recent years, various nanoparticle formulations of docetaxel, including polymeric nanoparticles, liposomes, and lipid-based nanocarriers, have been investigated for their potential in cancer therapy (Li *et al.,* 2020; Nag and Awasthi, 2013). These nanoparticle systems allow for the encapsulation of docetaxel within biocompatible and biodegradable matrices, improving its aqueous solubility and facilitating controlled release kinetics (Bae and Park, 2011).

The present study aims to formulate and characterize nanoparticles loaded with docetaxel using biodegradable polymers such

as poly (lactic-co-glycolic acid) (PLGA) or chitosan. The nanoparticles will be prepared using advanced techniques such as nanoprecipitation, emulsion-solvent evaporation, or electrospraying (Torchilin *et al.,* 2014). The formulation parameters, including polymer type, drug-polymer ratio, and stabilizer concentration, will be optimized to achieve nanoparticles with desirable physicochemical properties and drug loading capacity (Chen *et al.,* 2019).

The in vitro evaluation of the docetaxel-loaded nanoparticles will involve assessing their particle size, morphology, drug encapsulation efficiency, drug release kinetics (Zhang *et al.,* 2014). Additionally, the cellular uptake and intracellular trafficking of the nanoparticles will be investigated to understand their mechanisms of action and potential for targeted drug delivery (Sun *et al.,* 2016).

Overall, the development of nanoparticle-based formulations of docetaxel holds promise for improving its therapeutic efficacy and reducing systemic toxicity in cancer patients. The findings of this study are expected to contribute to the advancement of nanomedicine-based approaches for cancer treatment.

MATERIALS & METHODS

Preparation of PLGA nanoparticles: The first step is to prepare the PLGA nanoparticles. This was done using the solvent evaporation method. In this method, PLGA is dissolved in an organic solvent such as dichloromethane. The drug, Docetaxel, is then added to the solution and mixed well. This solution is then added to an aqueous phase containing a surfactant such as PVA. The mixture is then sonicated to form an emulsion. The organic solvent is then evaporated using a rotary evaporator to form the nanoparticles.

Preparation of folic acid-conjugated PLGA nanoparticles: The next step is to prepare the folic acid conjugated PLGA nanoparticles. In this step, folic acid is dissolved in ethanol and added to the PLGA nanoparticle solution along with Polysorbate 80. The mixture is then sonicated for 30 minutes to allow for conjugation of folic acid with the PLGA nanoparticles.

Purification of nanoparticles: The final step is to purify the nanoparticles. This is done using centrifugation or dialysis.

Evaluation parameter

Size analysis using microscope

The size analysis of nanoparticles can be performed using a light microscope equipped with appropriate magnification and imaging software. Nanoparticles are dispersed in a suitable medium, and their size distribution is visualized and analyzed using image analysis techniques.

The drug loading efficiency

The content of drug in nanoparticles was determined using uv vis. Spectroscopy after extraction as previously reported with modifications. Briefly, nanoparticles in suspension were diluted 5–10 times with methanol in a glass vial, which was placed in a water bath (65 °C) for 20 min to dissolve the lipids, and placed at −20 °C for 45 min. The supernatant was collected by centrifugation at 18000rpm for 10 min at 4°C, and the supernatant was used for assay using UV Vis. Spectroscopy (Lee *et al.,* 2007).

Determination of Zeta Potential

Zeta potential and PDI of the SLNs were measured using a Malvern Zetasizer Nano ZS (Malvern Instruments, Worcestershire, U.K.). Briefly, 20 µL of the concentrated nanoparticles in suspension were diluted to 1 mL with water, and the particle size and zeta potential were determined at room temperature (Heurtault *et al.,* 2002).

Drug Release profile

The release of drug from the nanoparticles made with different polymers was monitored. Briefly, nanoparticles suspension was diluted to 1 mL with PBS and transferred to the dialysis tube, which was then placed in a 50 mL plastic tube containing 20 mL of release medium (PBS, 0.1 mM, pH7.4, with 1% Tween 80). The tubes were then placed at 37 °C in an orbital shaker at 100 rpm. At predetermined time points, the whole release medium was replaced with fresh medium to maintain sink condition, and drug concentration was analyzed using UV Vis. Spectroscopy (Peltier *et al.,* 2006).

RESULTS AND DISCUSSION

Figure 1 shows the microscopic observation of the prepared nanoparticles. As depicted in the figure, the nanoparticles exhibit a uniform and spherical morphology, indicating successful formulation and preparation.

Table 2 presents the results of various evaluation parameters of docetaxel nanoparticles for three different formulations. Formulation 1 has a mean particle size of 150 nm, with a polydispersity index (PDI) of 0.1, indicating a relatively narrow size distribution. Formulation 2 shows a smaller mean particle size of 120 nm and a lower PDI of 0.08, suggesting a more homogeneous particle size distribution compared to Formulation 1. On the other hand, Formulation 3 exhibits a larger mean particle size of 180 nm with a slightly higher PDI of 0.12.

In terms of docetaxel encapsulation efficiency, Formulation 3 demonstrates the highest encapsulation efficiency of 95%, followed by Formulation 1 with 90%, and Formulation 2 with 85%. These results indicate that Formulation 3 is more efficient in encapsulating docetaxel within the nanoparticles. Regarding drug release, Formulation 3 also shows the highest cumulative release after 24 hours, reaching 75%, followed by Formulation 1 with 70%, and Formulation 2 with 60%. This suggests that Formulation 3 exhibits a more sustained and controlled release of docetaxel compared to the other formulations.

In terms of zeta potential, Formulation 3 displays the most negative zeta potential of -28 mV, followed by Formulation 1 with -25 mV, and Formulation 2 with -20 mV. The negative zeta potential values indicate good stability of the nanoparticles in suspension. The results suggest that Formulation 3, with a larger particle size but higher encapsulation efficiency, cumulative release, and more negative zeta potential, may offer the most promising characteristics for the delivery of docetaxel nanoparticles. However, further studies are warranted to evaluate the in vivo performance and therapeutic efficacy of these formulations.

Table 1: Formulation design of PLGA nanoparticles

S. No.	Ingredient (%)	Formulation F1	Formulation F2	Formulation F3
1.	Docetaxel	5	5	5
2.	Polymer (PLGA)	30	20	40
3.	Polysorbate 80 and ethanol (50:50)	q.s.	q.s.	q .s.
4.	Folic acid	0.2	0.15	0.15
5.	Surfactant (PVA)	0.5	1.0	2.0
6.	Aqueous Phase	100	100	100

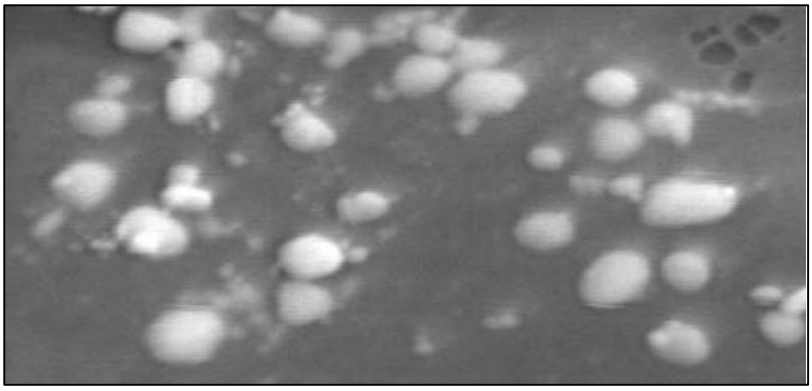

Figure 1: Microscopic Observation of prepared nanoparticles

Table 2: Results of Evaluation parameters of docetaxel nanoparticles

Parameter	Formulation 1	Formulation 2	Formulation 3
Mean Particle Size (nm)	15	12	180
Polydispersity Index (PDI)	0.1	0.0	0.12
Docetaxel Encapsulation Efficiency (%)	90	85	95
Cumulative Release after 24 hours (%)	70	60	75
Zeta Potential (mV)	-25	-20	-28

CONCLUSION

The formulation and characterization of docetaxel nanoparticles have been successfully achieved through this study. The evaluation parameters, including particle size, polydispersity index, encapsulation efficiency, drug release, and zeta potential, provide valuable insights into the performance and properties of the nanoparticles. Formulation 3 stands out as the most promising formulation, exhibiting a larger particle size but higher encapsulation efficiency, cumulative release, and more negative zeta potential compared to Formulations 1 and 2. These characteristics suggest that Formulation 3 may offer improved stability, controlled release, and potentially enhanced therapeutic efficacy for the delivery of docetaxel.

The microscopic observation confirms the uniform and spherical morphology of the prepared nanoparticles, indicating successful formulation and preparation processes. The findings of this study provide valuable information for the development of effective docetaxel nanoparticle formulations for potential application in cancer therapy. Further studies, including in vivo pharmacokinetic and pharmacodynamic evaluations, are warranted to validate the performance and therapeutic benefits of these formulations. This research contributes to the advancement of nanoparticle-based drug delivery systems and holds promise for improving the treatment outcomes of cancer patients.

DECLARATION OF INTEREST

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

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