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Fabrication, Characterization and in Vitro Evaluation of Polymeric Nanoparticles Loaded with Anticancer Drug

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A B S T R A C T

Anticancer drugs like Paclitaxel are effective in treating a variety of cancer forms. However, due to its poor solubility, paclitaxel is manufactured commercially using ethanol and Cremophor EL, or Taxol. Sadly, there are major negative effects linked to this Cremophor EL. Therefore, novel delivery methods are needed to increase anticancer efficacy and decrease adverse effects in order to remove the Cremophor EL-based vehicle. Preparing polymeric nanoparticles loaded with Paclitaxel, an anticancer medication, and assessing the experimental nanoparticle preparation were the primary goals of this work. The objective of the study was to create polymeric nanoparticles utilizing TPGS, PVA, and PLGA. The process of double-emulsion solvent evaporation was utilized to generate polymeric nanoparticles loaded with paclitaxel. It was discovered that the optimized formulation's mean particle size, polydispersity index, zeta potential, drug loading, drug entrapment efficiency, and drug release were all satisfactory. According to the kinetic analysis of the in vitro release, the medication releases according to the "Fickian diffusion" theory proposed by Korsmeyer Peppas. Therefore, it can be said that the formulation created in this study offers promise as an anticancer drug delivery method for long-term cancer therapeutic treatment.

Keywords:Paclitaxel, Anticancer, Polymeric nanoparticle, PLGA, Polyvinyl alcohol

INTRODUCTON

Because some medications are hazardous and some diseases are complex, there is an increasing need for novel drug delivery methods. A drug-delivery system (DDS) is a formulation or device that facilitates the introduction of active ingredients into the body to improve their safety and efficacy by controlling the drug's amount, time, and release at the site of action and allowing it to cross biologic membranes to reach the therapeutic target. This includes administering medications and applying and absorbing them into the human body more quickly through the use of vectors. In fact, different combinations of vectors and active ingredients may offer a broad range of customisation choices depending on certain conditions and patients. The techniques used to inject and administer active chemicals to their intended location are crucial for treating a disease [1-4]. Different applications of these approaches could lead to different results. The administration is usually systemic. Because of the drug's inherent toxicity or the severity of the illness, it may occasionally be necessary to administer the medication directly to the affected organ. Figure 1 shows the many anatomic routes of administration for pharmaceutical delivery that are now available. Every delivery route for a formulation has its share of difficulties. As was previously indicated, the possible toxicity of the active ingredients or the high dosage needed to induce pharmacological effect is a common disadvantage of the systemic administration routes. For instance, the oral mode of administration limits the use of drugs that are highly hydrophilic or pH-resistant to ensure the required absorption by the intestinal epithelium cells. Similarly, because injections are intrusive, there was an increased risk of infection [4-6].

As previously mentioned, in an effort to reduce the risks and disadvantages associated with conventional administration routes, drug delivery systems (DDSs) are becoming increasingly sophisticated. These DDSs focus on better controlled release, maintaining therapeutic efficacy, and targeting the active ingredient to the specific site of action, thereby avoiding systemic release of the active substance. Since nanotechnology could be able to solve some of the issues with the previously listed conventional distribution techniques, it is becoming more and more relevant in this area. Bioavailability is the term used to describe the amount of a bioactive substance that is absorbed by the body, enters the systemic circulation, and performs functions. In general, improving the solubility of nanoparticles (NPs) or their ability to traverse biological membranes might increase their absorption and bioavailability [7-9]. Drug release might potentially be controlled and maintained at therapeutic levels by modifying the composition of the nanoparticulate system. They could even include a lot of active chemicals, which would simplify the combined therapy. The improvement of biologic or immunotherapies has been facilitated by the development of nanotechnology, which has improved the delivery of drugs based on genes or proteins. Functionalization of NPs allows for the exact localization of action by minimising side effects and preventing excessive systemic concentrations. This feature, which combines accurate targeting with the movement and release of a contrast agent, has shown to be especially beneficial in the field of diagnosis [10-12].

Given the aforementioned characteristics of a nanoparticulate delivery structure, it is essential to conduct research on the use of various materials as precursors for nanocarriers in order to improve the efficacy of the system and provide better results. These precursors should satisfy certain characteristics, such as biocompatibility, biodegradability, and non-immunogenicity. When one or more types of constituents, known as monomers, unite covalently to form a linear or branched chain, macromolecules known as polymers are produced. These monomers can have any structure as long as they have two or more functional groups that

allow them to react with other monomers. Ideally, by selecting the right kind of monomer or monomers, a polymer can be made to have specific properties. Polymers are not only a special form of material that can possess all the attributes mentioned above, but they also exhibit a high degree of synthetic adaptability that allows the researcher to customise the material to the requirements or desired outcomes. Chemical derivatization can be used to directly apply polymeric tailoring to biopolymers in order to acquire desired properties. Another option is to create synthetic polymers from their corresponding monomers, which can lead to a wide range of forms and applications [13-17]. These are the reasons behind polymeric materials' increasing importance in nanotechnology in general and their use as NP precursors for DDSs.

Using surfactants may be something to take into account when making polymeric NPs. Surfactants are organic molecules that are amphiphilic and have the capacity to self-assemble in a solution. Most commonly used surfactants consist of an ionic functional group bonded to a hydrocarbon chain (hydrophobic section); these are referred to as cationic surfactants, such as tetramethylammonium hydroxide or benzalkonium chloride, or anionic surfactants, such sodium laurate or docusate. Non-ionic surfactants, such ethoxylated amines and alkyl and nonyl-phenol ethoxylates, can also be found; in these cases, the combination of hydrophobic and hydrophilic molecules results in an amphiphilic property. Low molecular weight polymers, in particular block copolymers (such Pluronic F127 or Pluronic P123), can also behave as surfactants [16]. Usually included in the formulation of nanocarriers, stabilizing agents help to stabilize the dispersion during nanoemulsion operations, which is a critical step in creating a well-structured nanosystem. Stabilizers have a number of advantages, such as enhancing NPs' affinity for lipidic structures and reducing surface tension. Some surfactants have also demonstrated a significant reduction in the mean NPs diameter in addition to their dual purpose as a cryoprotectant. Studies on surfactant surface-modified nanoparticle systems' pharmacokinetics and biodistribution have shown improved drug retention and accumulation in the target tissue, longer blood circulation times, lower nephrotoxicity and hepatotoxicity, as well as a decline in macrophage uptake and cardiovascular effects [16, 18-21]. Multidrug resistance (MDR), which is mediated by the human ATP-binding Cassette (ABC) transporter superfamily and includes P-glycoprotein (P-gp/ABCB1), multidrug resistance-associated protein 2 (MRP2/ABCC2), and breast cancer resistance protein (BCRP/ABCG2), has been identified as the main obstacle to the efficacy of multiple chemotherapeutic agents [19]. Both organic and inorganic NPs have been demonstrated to impede the MDR. Two examples of excipients that enhance the effects of organic NPs include surfactants and polymers [18-21].

According to the World Health Organisation, cancer is the second most common cause of death globally, with an estimated 9.6 million deaths in 2018. According to these statistics, one of the diseases with the greatest rates of morbidity and mortality in the modern world is cancer. One of the main objectives in the development of NPs as DDSs has come to be the creation of effective techniques for early diagnosis, treatment, and detection [18-21]. Detecting cancer in its early stages is especially difficult because typical imaging and detection techniques can only detect tumor masses that are at least one millimeter in size [22-25]. Because of this, a lot of researchers are trying to develop new, smaller composites that have the ability to identify malignant cells connected to cancer processes. This would make it easier for medical personnel to create treatment programmes and give patients advice. In an effort to enhance the imaging of malignant cells, polymeric nanoparticles (NPs) have emerged as a potential replacement for traditional contrast agents due to their capacity to alter the surface and regulate the solubility of the embedding agents. For both therapeutic and diagnostic purposes, the following recent studies—referred to as "theranostic agents"—have been consulted. This portion of the review is mostly

concerned with the results of imaging and diagnosis, and just a few aspects of treatment are covered.

As was previously said, cancer is currently one of the leading causes of death in wealthy countries. In fact, experts predict that within the next 20 years, the incidence of this disease would rise by 70% [22-25]. The conventional methods of treating cancer include radiation, chemotherapy, and surgery. Chemotherapy is used to treat most cancers, however it can be extremely destructive because it likes both healthy and diseased cells [22-25]. Nanomedicine—the use of materials at the nanometric scale in medicine—offers a more concentrated choice. The main objective of the medicine in oncology is to selectively deliver it to cancer cells in order to maximise its efficacy and minimise its toxicity. The potential application of nanomedicine may also result in combination medications that enhance prognosis and treatment effectiveness, as well as early cancer detection methods.

MATERIALS AND METHODS

Materials

Paclitaxel was received as a gift sample from Fresenius Kabi Oncology Ltd and serves as the active pharmaceutical ingredient in the preparation of polymeric nanoparticles. The nanoparticles employ PLGA (50:50), a biodegradable copolymer, as matrix material, which ensures controlled release and biocompatibility. Polyvinyl Alcohol (PVA) is utilized as a stabilizer in both the primary and secondary emulsions during the nanoparticle formulation process, helping to maintain the integrity and uniformity of the emulsions. Additionally, TPGS (D-α-tocopheryl polyethylene glycol 1000 succinate) is incorporated as an emulsifier and permeation enhancer. This component not only aids in the emulsification process but also enhances the bioavailability of paclitaxel, facilitating more effective delivery to target cells. These components are critical for optimizing the delivery and therapeutic efficacy of the nanoparticles in medical applications.

Drug-Excipients Interactions Study

FTIR and DSC study

A Fourier transform infrared (FTIR) spectroscope (Alpha, Bruker, Ettlingen, Germany) was used to obtain FTIR spectra of Paclitaxel, PLGA, PVA, their physical mixture (1:1), and the prepared lyophilized formulation with the drug over the range of wave number 4000 cm^{-1} to 400 cm^{-1} and IR spectra obtained were observed for any interaction. Differential scanning calorimetry of drug along with the excipients and the prepared lyophilized formulation with the drug was done using DSC (Perkin, DSC 4000). Approximately 2–10 mg of samples were kept in a sealed aluminium pan and were analysed at the rate of 10°C/min over a temperature range of 35°C to 445°C in nitrogen gas environment having flow rate of 20ml/min. The obtained thermogram was observed and interpreted.

Preparation of Polymeric Nanoparticles

The technique of double-emulsion solvent evaporation was employed to produce paclitaxel-loaded polymeric nanoparticles. Here is a concise overview of the method, illustrated with different formulations coded NPF1 to NPF6. Initially, paclitaxel was dissolved in a suitable organic solvent (e.g., dichloromethane or chloroform) along with PLGA. This solution forms the oil phase. The aqueous phase containing PVA (when used in primary emulsion as per specific formulations) was then added to this oil phase. The mixture was homogenized using high-speed homogenization or ultrasonication to form the primary W1/O emulsion. The primary emulsion was

further emulsified into an aqueous solution containing PVA or TPGS for secondary stabilization, according to the specific requirements of each formulation batch (NPF1-NPF6). This step ensures the encapsulation of the drug within the polymer matrix and forms the secondary W1/O/W2 emulsion. The secondary emulsion was then stirred continuously at room temperature or under reduced pressure to facilitate the evaporation of the organic solvent. This process leads to the formation of hardened nanoparticles. The resulting nanoparticles were collected by centrifugation, washed with distilled water to remove residual solvents and unencapsulated drugs, and lyophilized for storage. NPF1 and NPF4 contained higher amounts of PLGA and both primary and secondary PVA concentrations. NPF2 and NPF5 lacked primary PVA but included TPGS in the primary emulsion. NPF3 and NPF6 did not have PVA in either emulsion but utilized TPGS in differing concentrations in the primary and secondary phases. The variations in formulations primarily impact the nanoparticle's stability, drug release profile, and bioavailability. Each batch was designed to explore the effects of different stabilizers and their concentrations on the encapsulation efficiency and release kinetics of paclitaxel. The compositions of the different formulations are given in Table 1.

Table 1: Composition of trial batches of polymeric nanoparticles ([1] = Paclitaxel, [2] = PLGA, and [3] = Polyvinyl alcohol).

Codenamed Formulation	Drug [1] (mg)	Polymer [2] (50:50) (mg)	PVA (% w/v)		TPGS (%)	
			Primary	Secondary	Primary	Secondary
NPF1	15	120	3.5	2.5	---	---
NPF2	15	120	---	2.5	0.3	---
NPF3	15	120	---	---	1.0	0.05
NPF4	15	60	3.5	2.5	---	---
NPF5	15	60	---	2.5	0.3	---
NPF6	15	60	---	---	1,0	0.05

Characterization Polymeric Nanoparticles

Drug Loading and Entrapment Efficiency Determination:

To test the drug loading and entrapment efficiency, a centrifuge tube containing 2 mg of precisely weighed Paclitaxel-loaded nanoparticles was filled with 2 mL of acetonitrile. After that, it was agitated nonstop in an incubator shaker for three to four hours at 37℃. Centrifugation was used to separate the scattered phase from the continuous phase. The released medication was then measured spectrophotometrically at 227.4 nm after the supernatant was collected. These formulas were used to determine the proportion of drug loading and entrapment efficiency:

$$Theoretical\ Drug\ loading(\%) = \frac{\text{Amount of drug}}{\text{Amount of drug } + \text{ Amount of polymer}} x100$$

$$Actual\ Drug\ loading(\%) = \frac{\text{Drug Amount in nanoparticles}}{\text{Nanoparticles weight}} x100$$

$$Entrapment\ efficiency(\%) = \frac{\text{Drug loading} - \text{ Actual}}{\text{Drug loading} - \text{Theoretical}} x100$$

Evaluation of Particle Size and Zeta Potential (ZP) Measurement:

Dynamic light scattering (DLS) was utilized to assess the zeta potential, size distribution of the nanoparticles, and particle size utilizing a solid-state laser equipped with the Malvern NANO ZS90. Before the measurement, an appropriate amount of the dried nanoparticles from each formulation was suspended in double-distilled water and subjected to an acceptable degree of sonication. Next, the average hydrodynamic particle size, size distribution, polydispersity index, and zeta potential of the resulting homogeneous suspension were ascertained.

Thermogram Properties:

Using a DSC-4000 from Perkin in Tokyo, Japan, differential scanning calorimetry was used to study the phase behaviour of the particles loaded with and free of paclitaxel. A sealed aluminium pan containing 2–10 mg of the drug sample was used for the analysis, which was conducted at a rate of 10°C/min over a temperature range of 35°C to 445°C in a nitrogen gas atmosphere with a flow rate of 20 ml/min. After obtaining the thermogram, it was examined and evaluated.

Scanning Electron Microscopy (SEM):

A Hitachi SEM (S-3600N) was used for scanning electron microscopy to examine the shape and surface morphology of the nanoparticles. A suitable sample of nanoparticles was placed on metal stubs and broken with a razor blade using double-sided carbon tape adhesive. The samples were sputter-coated in gold in an argon atmosphere for secondary electron emissive SEM, and their morphology was analysed.

Transmission Electron Microscopy (TEM):

The morphology of the nanoparticles was examined using point-to-point resolution, 200 kv transmission electron microscopy (TEM) JEM CX 100. A combination of several modes and bright field imaging at magnification was utilised to disclose the size and shape of the polymeric nanoparticle. Negative staining is used to process the material. Following the sample's drying on a carbon-coated grid, 2% aqueous uranyl acetate solution is used to adversely stain it.

Drug Release Study in Vitro

The in vitro drug release from the nanoparticles was studied in phosphate buffer at a pH of 7. 4. Two milliliters of the necessary medium were added individually to each tube containing five milligrams of each formulation. The samples were shaken gently at 120 revolutions per minute while being maintained at 37°C in an incubator. Following the scheduled time intervals of 0 hours, 1 hour, 3 hours, 6 hours, 9 hours, 12 hours, 24 hours, 36 hours, and 48 hours, the tubes were centrifuged, and 0.5 milliliter of supernatant was collected. The sample tube

was filled with the same volume of fresh medium and incubated under the previously described conditions. Following collection, the samples were subjected to spectrophotometric analysis at 227.4 nm.

RESULTS AND DISCUSSIONS

Drug Excipient Interaction Studies: FTIR Spectroscopy & DSC Studies:

The DSC testing and the retention of the IR peaks show that the medicine and excipients used are compatible. To ascertain whether the drug and excipients are compatible, FTIR analysis was performed on pure drug, individual excipients, physical mixes of the excipients with drug, and polymeric nanoparticles loaded with Paclitaxel. FTIR spectra are shown in figures. The physical mixture of the drug, excipients, and Paclitaxel-loaded polymeric nanoparticles had all of the drug's significant peaks, according to the interpretation of IR spectra, indicating that there were no chemical interactions between the drug and excipients. The DSC thermograms generated for pure drug, lyophilized polymeric nanoparticles, and drug polymers mixed physically have been compared. On the DSC thermogram, paclitaxel displays a broad endotherm at 225.6ºC, whereas PLGA is seen at 53.52ºC. The drug is compatible with the polymer if a drug peak is seen in the DSC thermogram of the physical combination and the drug-loaded formulation.

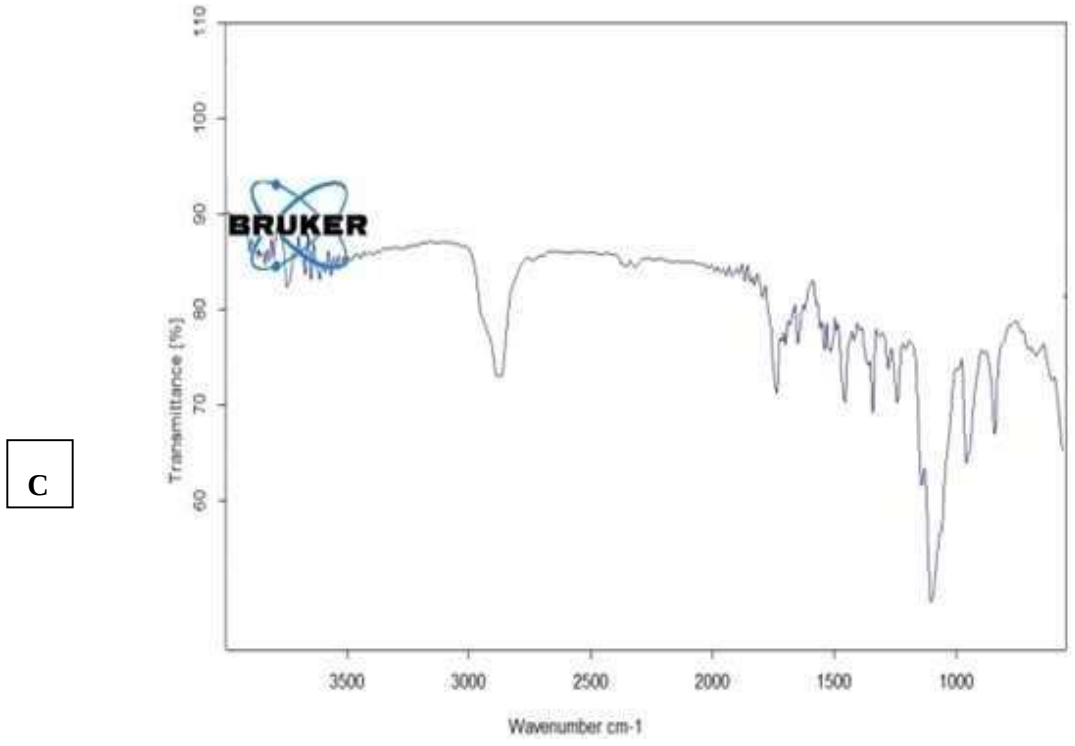


Figure 1. The drug's physical mixing with the excipients (Paclitaxel, PLGA, PVA, TPGS) and its Fourier transform infrared (FTIR) spectra.

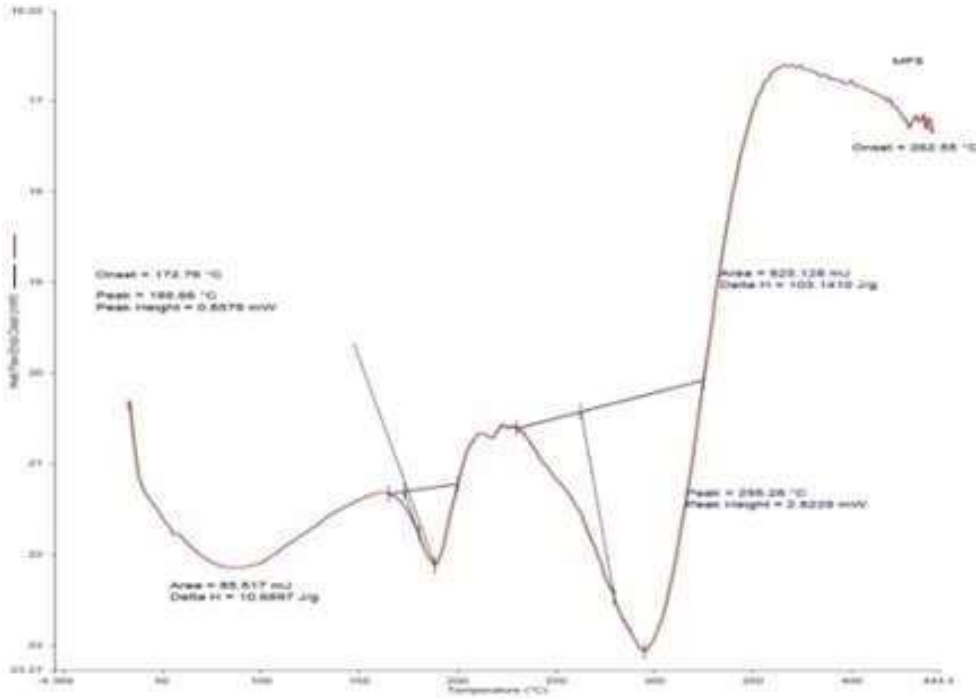


Figure 2. Differential scanning calorimetry thermograms of the pharmaceutical mixture in physical form having excipients containing PVA, PLGA, and paclitaxel.

Particle Size and Size Distribution Study:

The particle size distribution of the generated polymeric nanoparticles is shown in Table 2. Based on the particle size data, it was found that the drug polymer ratio and surfactant concentration significantly affected the mean particle size of nanoparticles. The average diameters of all drug-loaded formulations (NPF1 through NPF6) ranged from 318.8 nm to 587.7 nm. The polymer nano-dispersion is polydispersed in nature, as indicated by the average polydispersity index for the drug-loaded formulation, which ranged from 0.382 to 0. 762.

Zeta Potential Determination:

The surface charge of PLGA nanoparticles loaded with Paclitaxel was ascertained through the application of Zeta potential (ZP) analysis. The ZP provides information regarding long-term stability as well as characterization of the particle surface charge. The dissociation of the hydrogen ion from the carboxyl group of the PLGA chain may be the cause of the negative surface charge values observed for all formulations. The pharmacokinetic profile and biodistribution of nanoparticles are significantly influenced by their surface charge (ZP). Since negatively charged polysaccharide glycoseaminoglycans make up the majority of the glomerulus's basement membrane, positively charged particles are filtered more quickly than negatively charged ones. The experimental nanoparticles did not have the charge-dependent quick clearance issue through the kidney because their ZP was negative.

Estimating Drug Loading and Entrapment Efficiency:

Table 2 displays the calculated drug loading (%) and entrapment efficiency (%). All formulations had entrapment efficiency percentages ranging from 58.85±0.51% to 71.73±0.33%, and percentage drug loading

varied between 7.47±0.25% and 13.55±0.15%. Drug polymer ratio and varying stabiliser concentrations were found to have a considerable impact on both drug loading and entrapment efficiency based on the values of these parameters. When comparing nanoparticles generated using PVA as stabilizer to those prepared with TPGS as stabilizer, it was found that the 10:50 (drug: PLGA) ratio had higher drug loading and entrapment efficiency than the 10:100 ratio.

Table 2. Particle size (nm), Polydispersity index (PDI), Zeta potential (mV), Drug loading (%), Entrapment efficiency (%) and Polymeric nanoparticles

Formulation code	Particle size (nm)	Polydispersity index (PDI)	Zeta potential (mV)	Drug loading (%)	Entrapment efficiency (%)
				(Mean ± SD) *	
NPF1	587.7	0.632	-5.12	7.82±0.22	64.88±0.19
NPF2	521	0.492	-8.36	7.47±0.25	60.91±0.22
NPF3	388	0.467	-7.83	7.67±0.31	64.68±0.28
NPF4	321	0.572	-13.9	13.55±0.15	71.73±0.33
NPF5	444	0.383	-4.18	11.71±0.19	58.85±0.51
NPF6	318.8	0.762	-4.87	12.78±0.18	67.39±0.23

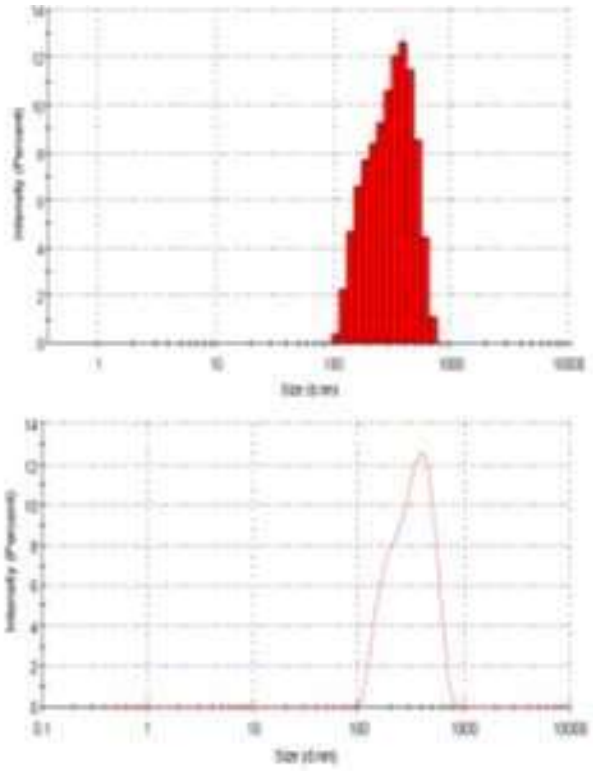


Figure 3. Particle size distribution data of the optimized formulation NPF4

SEM and TEM study

SEM and TEM scans revealed that the nanoparticles were spherical and had smooth surfaces (Fig. 5 to 6). The images demonstrated that all of the Paclitaxel-loaded particles were uniformly dispersed and had a submicron size. TEM pictures indicate that the medication was dispersed throughout the body of the nanoparticles in the form of particles.

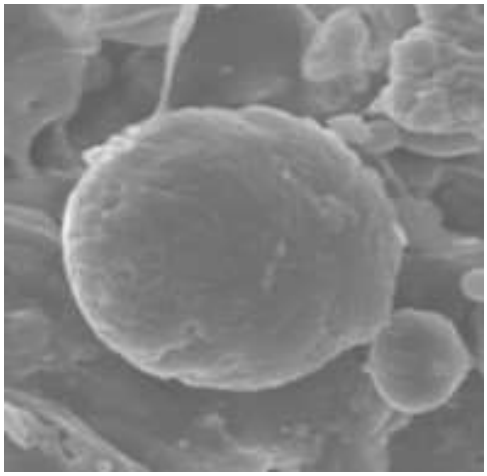


Figure 4. SEM pictures Polymeric nanoparticles loaded with Paclitaxel (NPF4)

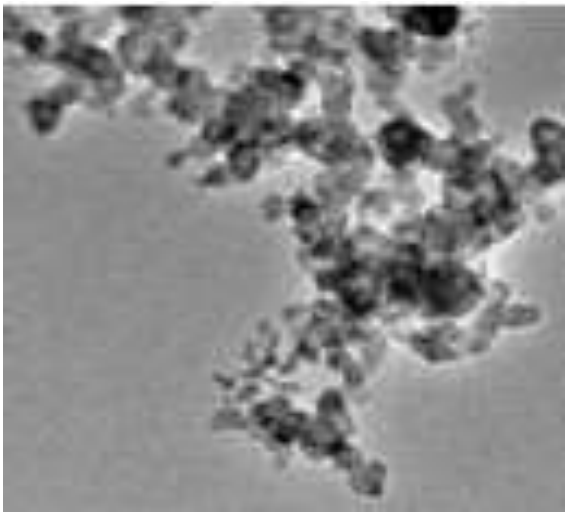


Figure 5. TEM pictures of polymeric nanoparticles loaded with paclitaxel (NPF4)

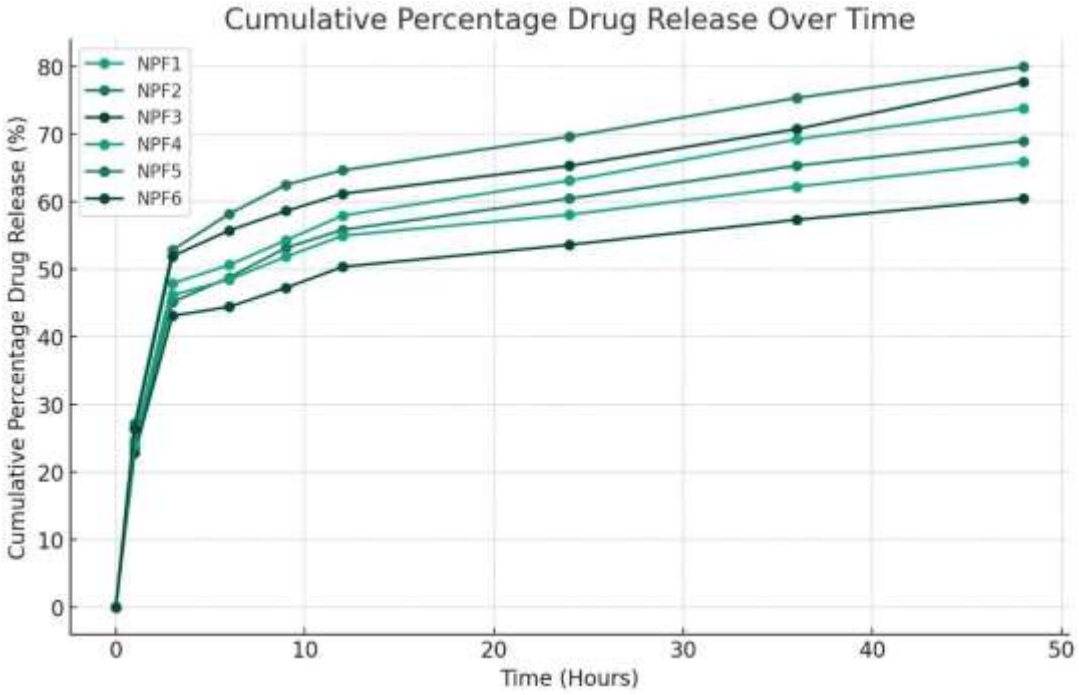
Drug Release from Polymeric Nanoparticles in Vitro

Release studies were conducted on the polymeric nanoparticles loaded with Paclitaxel in phosphate buffer (pH 7.4). The calculated cumulative percentage of medicines released is shown in Table 3. The findings of the 48-hour drug release study showed that the formulation (NPF4) demonstrated 77.12% of cumulative percentage

drug release, which is higher than other formulations.

Table 3. Data on drug release from polymeric nanoparticles in vitro

Time (hours)	NPF1	NPF2	NPF3	NPF4	NPF5	NPF6
0	0	0	0	0	0	0
1	24.78±0.10	23.77±0.13	22.85±0.07	27.15±0.08	24.13±0.15	26.44±0.09
3	47.91±0.07	45.16±0.92	43.12±0.08	52.86±0.13	46.17±0.10	51.94±0.07
6	50.65±0.11	48.80±0.15	44.45±0.10	58.21±0.08	48.50±0.11	55.76±0.11
9	54.30±0.10	53.18±0.13	47.27±0.13	62.50±0.10	51.87±0.08	58.63±0.08
12	57.96±0.13	55.85±0.07	50.37±0.09	64.64±0.11	54.98±0.07	61.18±0.13
24	63.13±0.08	60.47±0.14	53.63±0.11	69.64±0.06	58.09±0.09	65.32±0.11
36	69.22±0.09	65.33±0.06	57.33±0.08	75.35±0.15	62.24±0.13	70.74±0.07
48	73.78±0.11	68.98±0.11	60.44±0.07	79.99±0.11	65.87±0.10	77.75±0.10



*n=3

Figure 6. Cumulative percentage of drugs released plotted against time.

Pharmacokinetic Mathematical Modelling of in-Vitro Drug Release

The analysis of the in-vitro drug release data for six formulations (NPF1 through NPF6) using three different

kinetic models—zero-order, first-order, and Korsmeyer-Peppas—revealed distinct characteristics of drug release mechanisms. The zero-order model, which implies a constant release rate independent of concentration, showed moderate correlation across all formulations, with coefficients ranging from 0.706 to 0.756. This suggests a controlled release behavior that could be suitable for maintaining consistent drug levels in a system. Conversely, the first-order model, where the release rate is dependent on the drug concentration remaining in the carrier matrix, exhibited lower correlation coefficients (0.665 to 0.712). This indicates that for some formulations, the release mechanism might not strictly follow a concentration-dependent process, or there are other factors influencing the release kinetics that are not captured by this model. Remarkably, the Korsmeyer-Peppas model demonstrated excellent fit with correlation coefficients between 0.980 and 0.985 for all formulations. The values of the release exponent (n) ranged from 0.179 to 0.209, indicating non-Fickian diffusion (anomalous transport), where the drug release is controlled by more than one process (both diffusion and erosion of the matrix). This model's high adaptability and the resulting high correlation suggest its effectiveness in describing complex release behaviors typically seen in polymeric drug delivery systems, making it an essential tool for the formulation development process in pharmaceutical research.

Table 4. Data on drug release in vitro using several kinetic models.

Formulation	Zero Order k_0 [%/hour]	Zero Order R^2	First Order k_1 [1/hour]	First Order C_0 [%]	First Order R^2	Korsmeyer-Peppas k	Korsmeyer-Peppas n	Korsmeyer-Peppas R^2
NPF1	2.07	0.756	-0.017	36.71	0.712	0.00334	0.209	0.985
NPF2	1.96	0.739	-0.016	35.41	0.694	0.00324	0.202	0.984
NPF3	1.73	0.707	-0.015	32.50	0.665	0.00308	0.180	0.981
NPF4	1.88	0.709	-0.015	35.20	0.667	0.00332	0.183	0.980
NPF5	2.27	0.729	-0.016	41.36	0.685	0.00381	0.198	0.981
NPF6	2.16	0.731	-0.016	39.36	0.690	0.00366	0.194	0.980

SUMMARY AND CONCLUSION

Polymeric nanoparticle-based drug delivery techniques are one of the fastest-growing areas of nanotechnology. Numerous medications, including as biologic macromolecules, hydrophilic and hydrophobic tiny medicines, vaccinations, and chemicals to be taken orally or inhaled, can be delivered via nanoparticles. High stability, a large carrier capacity, and the capacity to integrate both hydrophilic and hydrophobic materials are further benefits of these particles. In this work, different stabiliser kinds and ratios, such as PVA, TPGS, and blends of PVA and TPGS, were employed to generate Paclitaxel-loaded polymeric nanoparticles utilising the double emulsion-solvent evaporation procedure. The synthesised formulations of polymeric nanoparticles loaded with

paclitaxel were evaluated for their physiochemical properties. Characterization showed that formulation (NPF4) was the best option. The optimised formulation's morphological characteristics were investigated through the use of transmission electron microscopy (TEM) and scanning electron microscopy (SEM). TEM and SEM images revealed the spherical shape of polymeric nanoparticles. The lyophilized paclitaxel-loaded polymeric nanoparticles in the optimised formulation NPF4 had a cumulative percentage drug release of 79.99±0.11% at the end of 48 hours, which is higher than previous formulations. Based on the in-vitro drug release kinetics studies, R2 values were shown to be more linear in the Korsmeyer-Peppas plot, followed by zero order kinetics. Drug release exponent (n value) from matrix type nanoparticle formulation was found to be less than 0.5 in the Korsmeyer-Peppas plot, indicating "Fickian diffusion" of the drug. In the end, it can be said that the study's objective was accomplished by developing a paclitaxel nanoparticulate drug delivery system with controlled release using PLGA. The method used in this work allowed for the rapid and reliable fabrication of a scaffold of nanoparticles with a homogeneous, spherical morphology. Thus, it can be concluded that the formulation created in this work may be viewed as a successful and promising anticancer drug delivery technique for the long-term management of cancer therapy.

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