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Docetaxel Surface Engineered Polymeric Nanoparticles for Improved Cancer Chemotherapy: Fabrication and Characterization

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Abstract: It is commonly known that docetaxel (DTX) is an effective treatment for cancer. It has to do with a solubility issue that can be fixed by adding polysorbate 80, and it is marketed commercially. To improve DRX's anticancer effectiveness and lessen adverse effects, alternative delivery methods or techniques must be used, as DTX with polysorbate 80 has substantial side effects, adverse reactions and extended pharmacological actions. Creating and producing docetaxel-loaded surface folate-decorated and pegylated PLGA (PPegF) nanoparticles and assessing them in vitro drug release, drug loading, polydispersity index, zeta potential, and particle size were the main objectives of this study. Using polyvinyl alcohol as a surfactant, the nanoparticles were created using the modified nanoprecipitation technique. The optimal formulation, PVAF4, was chosen based on the results of the in vitro drug release characteristics inquiry so that its surface shape could be examined using SEM and TEM. The PVAF4 formulation was also subjected to the MTT assay. According to an in vitro release kinetics investigation, the delivery mechanism followed the Korsmeyer-Peppas model, which postulated "Fiskian diffusion." Additionally, the PVAF4 nanoformulations outperformed the free medication in the MTT assay. The study used PVA as the only surfactant to clearly construct and characterise the folate coated pegylated PLGA nanoparticle.

Keywords: Docetaxel, Anticancer, Polyvinyl alcohol, Nanoparticle. Surfactant, Folate receptor.

INTRODUCTION:

One of the most dangerous illnesses known to man, cancer is characterised by unchecked, fast cell division that results in aberrant cells known as cancer cells. According to the World Health Organisation (WHO), 10 million cancer-related deaths are anticipated to occur within a year, and there are an estimated 18.1 million cancer cases worldwide [1]. The three most common malignancies in the world are prostate cancer (1.41 million fatalities), 2.21 million deaths from lung cancer and 2.26 million deaths from breast cancer [2]. Nitrogen mustard and anti-folate medications were initially utilised in cancer chemotherapy in the 1940s. These days, several anticancer medications, such as taxanes, protein kinase inhibitors, alkylating agents, antimetabolites, etc., are utilised to treat different types of cancer [3]. Docetaxel (DTX), cabazitaxel, and paclitaxel are three medications that belong to the taxanes class, which is one of the most significant categories of anticancer medications [4, 5]. To separate DTX, the non-cytotoxic precursor of 10-deacetyl baccatin III, *Taxus baccata* needles are utilised[6]. DTX is the second example of a drug with a unique taxane ring [7]. The John Hopkins group published an article in 1989 in Ann. Intern. Med. regarding the use of taxol as a treatment for advanced ovarian cancer. DTX was approved by the US Food and Drug Administration (USFDA) in 1996 to treat refractory ovarian cancer. In 1993, Bristol-Myers Squibb Co. began selling taxol. In 1994, the USFDA authorised the use of taxol to treat

metastatic breast cancer. For the use of taxotere in the treatment of lung and breast cancers, the Manufacture Approval Authorisation(MAA) and New Drug Application (NDA) were filed concurrently. DTX has been the most commonly utilised medication for treating cancer globally [8]. DTX's commercial form, Taxotere®, was first authorised to treat anthracycline-resistant metastatic breast cancer. However, it was eventually approved to treat a wide range of cancers, including advanced cancer, platinum-refractory large-cell lung cancer, stomach cancer, ovarian cancer, and head and neck cancers [9]. Currently, Sanofi-Aventis, located in Bridgewater, New Jersey, USA, produces Taxotere®, the only commercially accessible form of DTX. It has 1040 mg/mL Tween 80 and 40 mg/kg DTX. The dosage range for the DTX is 60–100 mg/m2. Every three weeks, it is injected, usually over the course of an hour [10]. DTX affects different phases of cell growth through a variety of ways. The principal mechanism responsible for the anticancer activity of DTX is the hyperstabilization of microtubules [7]. DTX binds to the tubulin in the microtubules, which is the β-subunit protein. This tubulin that is coupled to DTX helps to stabilize microtubules, which prevents their depolymerization. The mechanism of DTX was described by Zhang et al. as the stabilisation of microtubule bundles causing perturbations in the dynamic balance between polymerization and depolymerization. This phenomenon results in cell death by halting the cell cycle during the mitotic G2 phase [9].Although DTX has shown promising therapeutic potential in treating a range of cancers, problems with solubility and adverse effects are common. Numerous minor to severe adverse effects, including alopecia, simple, temporary neutropenia, nausea, vomiting, diarrhoea, and mucositis, have been reported by patients using DTX. Mild arthralgia, myalgia, lethargy, hypotension, vasodilation, nephrotoxicity, neurotoxicity, the onset of febrile neutropenia, skin toxicity, hypersensitivity reactions, and fluid retention are among the infrequent adverse effects of DTX [3]. Because of its important physicochemical properties, such as its poor membrane permeability (1 cm/s × 10−6) and low aqueous solubility (0.025 μg/mL), DTX is categorised as a BCS class IV drug. These properties play a major role in determining the drug's pharmacodynamic characteristics and, ultimately, its therapeutic efficacy [6]. DTX is 98% protein-bound, as evidenced by its majority attachment to albumin and α−1 acidic glycoproteins [10]. DTX is characterized by poor commercial production, reduced patient compliance and a shorter biological half-life.

The previously noted disadvantage of DTX's traditional formulation highlights the necessity of a nano delivery method that can mitigate or address the drug's physicochemical issues. The nano delivery method has the potential to enhance the therapeutic potency and efficacy of DTX m[4]. Numerous options exist for a nano delivery system to enhance a drug's therapeutic efficacy, including changing the solubility of the drug using nanostructured lipid carriers or microemulsion nanocrystals. According to published research, DTX can avoid reticuloendothelial system (RES) uptake when it is synthesized as nanoparticles. By allowing for both active and passive targeting at the precise point of delivery, this can greatly increase the effectiveness of treatment. Different sizes, regulated drug release, tumor-specific targeting, enhanced permeability and retention (EPR) impact, and greater drug solubilisation are some of the advantages that these innovative systems have over traditional drug delivery methods. Through surface modification, the nanocarrier circumvents the reticuloendothelial system (RES) and prolongs in vivo circulation [11-14].

To deliver docetaxel to the targeted tissue, the current study set out to create and manufacture docetaxel nanoparticles using triblock conjugated polymer as a polymer [12]. This was accomplished by employing PVA as a stabilizer during the modified nanoprecipitation Method to produce nanoparticles. The folate-decorated nanoparticles were intended to specifically target cancer cells that expressed the folate receptor. Drug loading, encapsulation efficacy, surface charge, polydispersity index, particle size, and in vitro drug release characteristics were the parameters used to evaluate the properties of the nanoparticles. Furthermore, MCF7 cell lines were used for in vitro cytotoxicity assays.

MATERIAL AND METHODS:

The Docetaxel sample came from Fresenius Kabi Oncology Limited as a gift. We bought polymers PLGA 50:50 and PLGA 75:25 from Sigma Aldrich. The Mumbai-based Himedia Laboratory Pvt. Ltd. was the supplier of the cold-water soluble poly vinyl alcohol. Chemicals and reagents of analytical reagent grade made up the remaining components used in the experiment.

Drug Excipients Compatibility study:

The compatibility of docetaxel with other important excipients used in the manufacturing of nanoparticles was investigated using FTIR (Alpha, Bruker) and DSC (DSC 4000, Perkin). After that, FTIR spectra and DSC thermograms were examined for potential interactions.

Formulation of Docetaxel loaded PLGA nanoparticles:

Using the previously described modified nanoprecipitation method, a novel technique for producing docetaxel-loaded PPegF nanoparticles has been developed (12, 13). To fabricate polymeric nanoparticles using a modified nanoprecipitation technique with solvent evaporation, a triblock copolymer composed of PLGA, PEG and Folate is used. First, 100 mg of the copolymer and the desired amount of a hydrophobic drug are dissolved in 10 mL of acetone, ensuring complete dissolution by stirring for 30 minutes. PVA is dissolved in 50 mL of distilled water to create a 1% (w/v) PVA solution, which is then heated to 60°C while stirring to completely dissolve the PVA and cooled to room temperature. Then, using a syringe pump, the organic phase containing the medication and copolymer is gradually added to the aqueous PVA solution at a rate of 1 mL/min while being continuously stirred magnetically at 500 rpm. In this step, the organic solvent diffuses into the aqueous phase, causing the polymer to precipitate and form nanoparticles. A stable nanoparticle suspension is obtained by transferring the resultant suspension to a rotary evaporator and gradually removing the organic solvent at 40°C under decreased pressure until all of the acetone has evaporated. To pellet the nanoparticles and gather and clean them, the suspension is centrifuged for 20 minutes at 15,000 rpm. After discarding the supernatant, the particle is resuspended in distilled water. This washing step is repeated three times to remove any residual PVA and unencapsulated drug. Finally, the washed nanoparticle suspension is freeze-dried to obtain a dry powder by first freezing the suspension at -80°C and then lyophilizing it for 48 hours. The coding name for this initial formulation was PVAF1. Similar to PVAF1, PVAF2, PVAF3, PVAF4, PVAF5 and PVAF6 were also created with PVA at different concentrations mentioned in the formulation composition table.

ion composition table.

Table 1: Composition of Docetaxel loaded PPegF nanoparticles.

Formulation	PPegF (mg)	Docetaxel (mg)	Organic Solvent (mL)	Polyvinyl alcohol (%w/v) Stabilizer cum Surfactant	Aqueous Phase Volume (mL)
PVAF1	10	10	10	0.5	20
PVAF2	10	10	10	1.0	40
PVAF3	10	10	15	1.5	60
PVAF4	10	10	15	2.0	80
PVAF5	10	10	20	2.5	100
PVAF6	10	10	20	3.0	120

Docetaxel-loaded PPegF nanoparticle characterization:

Drug Loading and Entrapment Efficiency:

Following assessments of the drug loading and entrapment efficiency, a centrifuge tube containing 2 mL of acetonitrile and 2 mg of docetaxel-loaded nanoparticles was continuously shaken in an incubator shaker set at 37°C for three to five hours until it cooled to room temperature. Centrifugation was used to separate the continuous phase from the dispersed phase, and a spectrophotometric measurement at 231 nm on the

supernatant collected after the reaction was finished was used to determine how much medication was released [15, 16].The percentages of drug loading and entrapment efficiency were computed using the following formulas:

$$Actual\ Drug\ loading(\%) = \frac{\text{The quantity of drug contained in nanoparticles}}{\text{sample of nanoparticles weighed and examined}} x100$$

$$Entrapment\ efficiency(\%) = \frac{\text{The actual loading of drugs}}{\text{Drug loading in theory}} x100$$

Zeta Potential (ZP) measurement and particle size analysis:

Using Malvern NANO ZS90 technology, the size, dispersion, and zeta potential of PPEGF nanoparticles loaded with docetaxel were investigated. This apparatus uses dynamic light scattering (DLS) and a solid-state laser to measure these properties. It is possible to determine the average size of the hydrodynamic particles, the size distribution, the polydispersity index, and the zeta potential of the particles by sonicating freeze-dried nanoparticles together in double-distilled water [17, 18].

Surface morphology using transmission electron microscopy (TEM) and scanning electron microscopy (SEM):

A Hitachi SEM (S-3600N) scanning electron microscope was used to analyse the form and morphology of the produced nanoparticles in order to evaluate their surface morphology. Double-sided sticky carbon tape was used to mount the nanoparticle sample on the metal stubs in order to attain the proper quantity of nanoparticles. The tape was then broken with a razor blade. Gold was sputter-coated onto the samples, and morphology was evaluated using a secondary electron emissive SEM in an argon environment.

It was shown that transmission electron microscopy (TEM) JEM CX 100 working at 200 kv with point-to-point resolution could view and depict the fine morphology of nanoparticles. A 2% aqueous uranyl acetate solution is used to adversely stain the samples after they have dried on carbon-coated grids. It is demonstrated that PPEGF nanoparticles can be produced and scaled similarly to other nanoparticles by combining multi-mode and bright field imaging at different magnifications [17, 19]

***In Vitro* Drug Release Study:**

The drug release from the generated nanoparticles was examined using phosphate buffer pH 7.4 (Jana et al., 2014a). Two millilitres of phosphate buffer were added to Eppendorf tubes holding five milligrammes of freeze-dried nanoparticles, and the tubes were then incubated at 37°C. After the samples were shaken for 0, 1, 3, 6, 9, 12, 24, 36, and 48 hours at a rate of 125 revolutions per minute, they were centrifuged, and 0.5 millilitres of the supernatant were removed. Fresh phosphate buffer solution was combined with 0.5 ml of the extracted samples to preserve the sink conditions. A spectrophotometer calibrated at 231 nm was used to perform the drug assay and ascertain the release from the samples.

***In Vitro* Drug Release Kinetic Study:**

Evaluating the mechanism and related kinetics of drug release from nanoparticles is crucial to comprehending the pharmacokinetic behaviour of a drug. Numerous kinetic equations, including zero order and first order, were used to interpret the data from the in vitro drug release investigations. Graphs were then created using the results of these equations. The associated linear plots were subjected to a regression analysis in order to get the values of r2 and k [20].

Cytotoxicity evaluation usingMTT assay:

As mentioned earlier, the cytotoxicity of PPegF-NPs and the free drug on MCF7 breast cancer cells was assessed using the MTT assay. [21-23].

Statistical analysis

The data is represented as the mean ± Standard Deviation (SD). The Tukey-Kramer test and one-way ANOVA based on $p < 0.05$ statistical differences between the groups were used to assess the results as post hoc analyses. The software used in this investigation was GraphPad Prism (Version 8.01, GraphPad Software, San Diego, USA).

RESULTS:

Study of drug excipient compatibility:

An FTIR study was conducted on the drug by itself, on individual excipients, on physical combinations of the drug and the excipient, and on polymeric nanoparticles loaded with docetaxel in order to examine the compatibility of the drug and the excipients. Figure 1 shows the FTIR spectra of the medication and excipient mixture that was physically mixed. The findings suggested that the drug, docetaxel and all the utilized excipients were compatible in the formulation without indicating any forms of interactions observed.

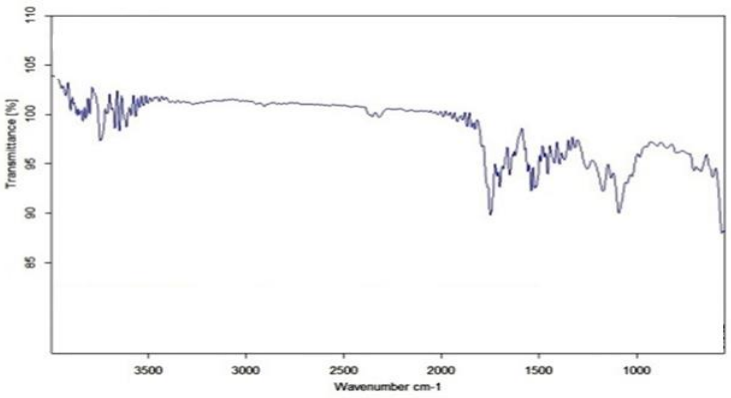

Figure 1. FTIR spectra of the drug in combination with the excipients docetaxel, FOL, PVA, and PLGA

Formulation of Docetaxel loaded PPegF nanoparticles:

By using the PPegF polymer and stabilizing it with PVA, polymeric nanoparticles loaded with docetaxel were produced using a modified nanoprecipitation process supported by solvent evaporation. The different stabilizer concentrations and varied drug polymer ratio concentrations were employed during the formulation process. Following preparation, the formulations' size, surface, and release properties were evaluated.

Assessment of drug loading and entrapment efficiency:

The nanoparticles (PVAF1–PVAF6) had entrapment efficiency (%) and drug loading (%) ranging from 57.19±0.93% to 66.32±0.91% and 6.24±0.74% to 14.38±0.59%, respectively. Table 2 displays all of the findings.

Table 2. Characterization of the fabricated nanoparticles:

Code for Formulation	Particle size (nm)	Zeta potential (mV)	Polydispersity index (PDI)	Entrapment efficiency (%)	Drug loading (%)
				(Mean ± SD) *	
PVAF1	386.5	-11.77	0.584	63.52±0.65	6.61±0.76

PVAF2	298	-9.24	0.461	58.44±0.87	6.24±0.74
PVAF3	281	-9.53	0.432	62.36±0.84	6.59±0.84
PVAF4	222	-15.77	0.438	66.32±0.91	14.38±0.59
PVAF5	322	-12.34	0.349	57.19±0.93	12.33±0.88
PVAF6	215.5	-16.29	0.613	65.28±0.97	13.57±0.91

*n=3

Particle size distribution and surface properties:

According to Table 2, the particle size distribution of the developed PPegF nanoparticles (PVAF1–PVAF6) ranges from 215.5 nm to 386.5 nm.

Examination of the surface morphology of the nanoparticles: SEM and TEM study

The smooth and spherical surfaces of the nanoparticles are depicted in Figures 3 and 4 based on the SEM and TEM pictures.

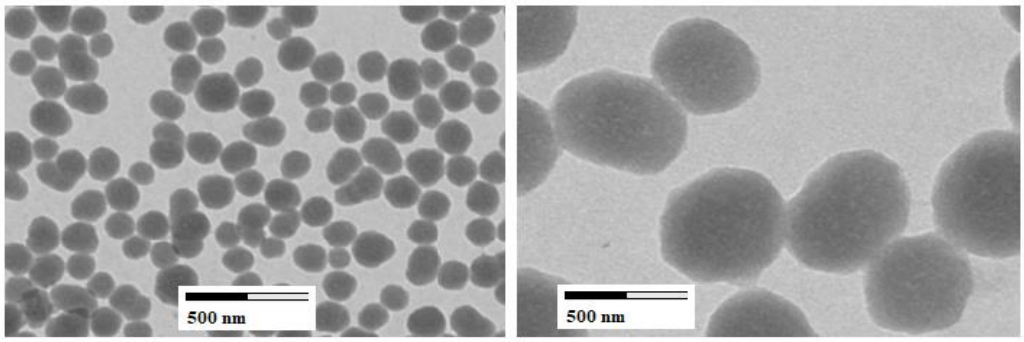

Figure 3. TEM images of Docetaxel loaded Polymeric Nanoparticles (PVAF4)

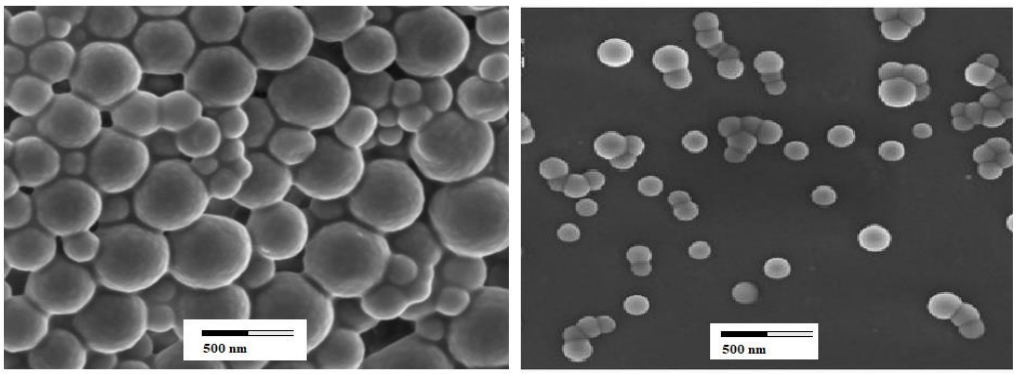

Figure 4. SEM pictures of Docetaxel-loaded Nanoparticles (PVAF4)

In vitro drug release and pharmacokinetic modelling:

In phosphate buffer (pH 7.4), the drug release from polymeric nanoparticles loaded with docetaxel was examined. The computed cumulative percentage of medicines released over time is displayed in Table 3. A cumulative percentage of drugs released against time profile graph was shown in Figure 5.

Table 3. The in vitro drug release from PPegF nanoparticles

Time (hours)	**The cumulative percentage of drug release (Mean ±SD) ***

	PVAF**1**	PVAF**2**	PVAF**3**	PVAF**4**	PVAF**5**	PVAF**6**
0	0	0	0	0	0	0
1	22.96±0.10	22.26±0.16	21.84±0.14	25.28±0.09	20.98±0.14	24.57±0.08
3	46.36±0.07	44.30±0.11	43.29±0.12	50.99±0.14	41.29±0.04	50.06±0.06
6	48.11±0.11	46.63±0.12	46.93±0.16	56.34±0.09	42.58±0.13	53.87±0.10
9	52.75±0.10	50.04±0.09	51.35±0.14	60.63±0.11	45.48±0.15	56.78±0.07
12	56.41±0.17	53.15±0.08	53.98±0.08	62.77±0.12	48.54±0.17	59.34±0.12
24	61.58±0.12	56.22±0.10	58.43±0.18	67.77±0.07	51.76±0.19	63.47±0.10
36	67.67±0.09	60.37±0.14	63.46±0.11	73.52±0.16	55.46±0.18	68.89±0.06
48	71.96±0.11	64.04±0.11	67.11±0.13	78.12±0.12	58.57±0.19	75.90±0.09

*n=3

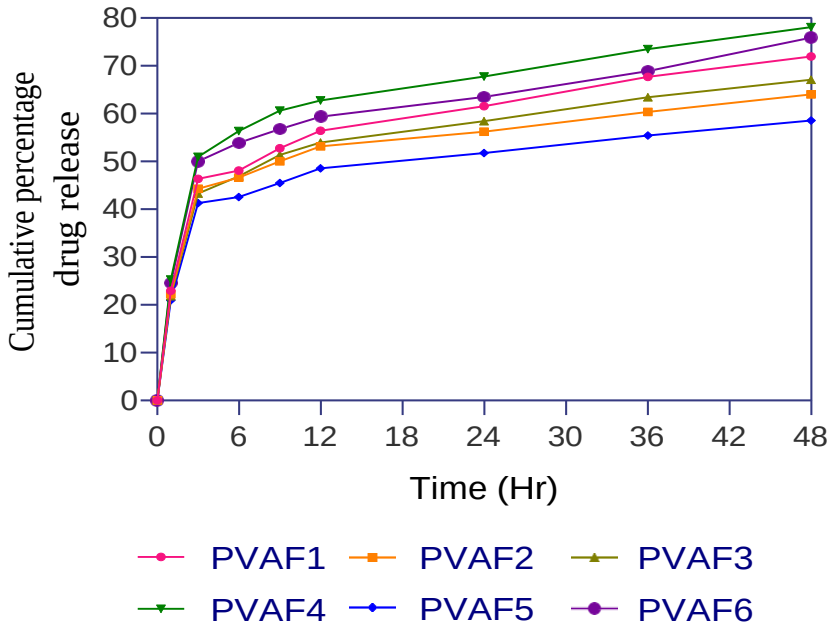

Figure 5. Time profile of the nanoformulations versus cumulative percentage of drugs released

Table 4. Below is a comparison of the different rate constants and release exponents that were determined using drug release data in accordance with several kinetic models.

Table 4. Specifications of various kinetic models

Formulation Code	**Zero Order Model**	**First Order Model**	**Hixon-Crowell Model**	**Higuchi Model**	**Korsmeyer-Peppas Model**	
	R^2_Z	**R^2_F**	**R^2_{HC}**	**R^2_H**	**R^2_{KP}**	**n**
PVAF1	-0.537	0.329	0.268	0.596	0.969	0.216
PVAF2	-0.801	0.004	0.297	0.469	0.958	0.190

PVAF3	-0.619	0.191	0.285	0.560	0.966	0.209
PVAF4	-0.668	0.482	0.291	0.533	0.960	0.204
PVAF5	-0.831	-0.144	0.249	0.455	0.960	0.187
PVAF6	-0.679	0.333	0.299	0.522	0.958	0.201

Discussion:

There were no chemical interactions between the drug and excipients, based on the final formulation, physical mixing, and the interpretation of the individual drug and excipient FTIR spectra. This is due to the fact that both the polymeric nanoparticles containing docetaxel and the drug plus excipient mixture displayed all of the significant drug peaks. Since there were no interactions that would have altered the drug's uniqueness as a result of the present formulations, in the current formulas, the components work well together to create the final result. Six formulations of PPegF nanoparticles with PVA as a stabilizing agent were developed using a modified nanoprecipitation procedure to attain the necessary entrapment efficiency, size, zeta potential, polydispersity index, and in vitro drug release characteristics. This was done so as to formulate Docetaxel loaded polymeric nanoparticles with the optimal size, entrapment efficiency, and characteristics. Compared to other formulations, the PVA stabiliser-formulated nanoparticles (PVAF4) showed a higher level of drug loading and entrapment efficiency. The percentages of drug loading and entrapment efficiency in each formulation ranged from 6.24±0.74% to 14.38±0.59% and 57.19±0.93% to 66.32±0.91%, respectively. It was shown that the values of entrapment efficiency and drug loading were significantly influenced by the drug polymer ratio and stabiliser concentration. This result implied that there is no direct relationship between the amount of polymer employed in the formulation and the drug's loading and entrapment ratio. Numerous factors, including the optimal drug-to-polymer ratio, homogenisation speed, stabiliser, and other important variables, influence this process [15]. The findings of the particle size data demonstrated that the ratio of drug polymer and the surfactant concentration significantly affected the size of the nanoparticles. Consequently, all of the drug-loaded formulations (PVAF1 through PVAF6) had average diameters between 215.5 and 386.5 nm. According to this research, PVA might also be a useful stabiliser for the synthesis of nanoparticles with the proper particle size.

The average polydispersity index of the medication formulation was found to range between 0.432 to 0.613. The PDI value of the nanoparticles made it clear that their distribution was consistent throughout the production process. Zeta potential (ZP) measurement can be utilised to evaluate the docetaxel-loaded PPegF nanoparticles' surface charge [24]. The nanoparticles PVAF1 through PVAF6 had zeta potentials that ranged from -9.24 to -16.29. The nanoparticles did not quickly aggregate to form a cluster and did not maintain their initial size for a significantly longer period of time, as indicated by the zeta potential range of -30 mV to +30 mV [15].The measured zeta potential, however, indicates that depending on their sizes, synthesised and produced nanoparticles can stay intact without aggregating, hence facilitating medication absorption in biological systems [25].To assess the stability of the PPegF nanoparticles and their destiny in vivo, its zeta potential was measured [26]. It has been suggested that the polymer PPegF's negative carboxylic group is what causes the zeta potential, or negative charge. This group may have dissociated hydrogen ions during the preparation of the nanoparticles [27]. It is evident from looking at the SEM images of the docetaxel-loaded nanoparticles that they were uniformly distributed throughout and submicron in size. In agreement with the polydispersity index results, TEM images demonstrate that the drug has been dispersed in particulate form over the nanoparticle surfaces.

The in vitro drug release for each formulation varied between 20.98±0.14 and 25.28±0.09 at one hour and between 41.29±0.04 and 50.99±0.14 at three hours. The information gathered also showed that medication release increases gradually after three hours of the in vitro test, rather than exploding during the first three hours. This release pattern might be the consequence of the PPegF conjugate gradually diffusing up to 78.12±0.12% at 48 hours after initial degrading. When compared to other formulations, formulation (PVAF4) exhibited the maximum drug release at 48 hours, with a rate of 78.12±0.12%. When the release kinetic pattern of this in vitro drug release data was examined, the R2 values revealed zero order kinetics following robust linearity in the

Korsmeyer-Peppas plot. The release from a polymeric formulation is confirmed by kinetic modelling of the in vitro release data using the Korsmeyer-Peppas model, which illustrates its release process. Additionally, based on the n value of 0.204, the release mechanism for formulation PVAF4, which produced the greatest release, is determined to be Fickian diffusion. This data clearly indicates that drug diffusion from the polymeric system is accompanied by zero order release. It was shown that the concentration of the reagent employed in the MTT experiment affected PVAF4's IC50 (50 percent inhibition of cell growth) against MCF7 cells. The results of this research, which used a range of PVAF4 concentrations, are shown in table 5 and figure 6. PVAF4 dosages ranging from 100 nM to 2000 nMwere shown to significantly effect MTT tests and MCF7 cells in comparison to the control and free drug concentrations. The study found that the maximum concentration of PVAF4, 2000 nM, had a viability rate of 5.57±2.67% of the cells after examining the concentrations of PVAF4 that shown the greatest cytotoxicity against the MCF7 cell. The growth inhibition % was found to increase as the concentration of PVAF4 rose, and the IC50 value was found to be 69.79 µg/ml.

Table 5. Comparing the PPegF-NPs' cytotoxicity to that of free docetaxel

Concentration (nM)	Docetaxel	PPegF-NPs (PVAF4)
0	99.95±3.09	99.99±3.29
100	99.01±2.91	72.47±2.49
200	98.54±2.62	59.27±2.64
300	99.69±2.64	40.47±2.24
400	87.76±2.24	37.77±2.45
500	66.81±2.45	31.77±2.67
750	48.80±2.67	27.57±1.72
1000	41.78±2.65	20.67±2.64
1250	33.64±2.59	18.47±2.24
1500	32.40±2.56	5.76±2.45
2000	20.95±1.81	5.57±2.67

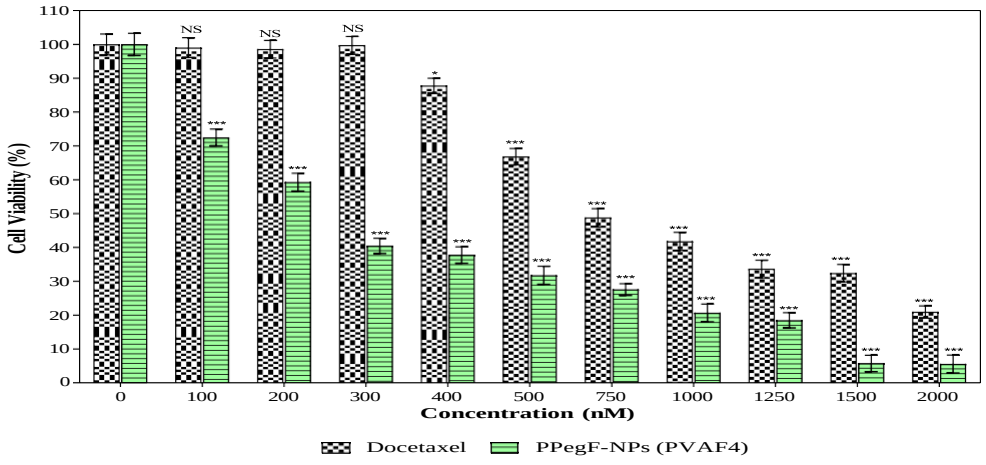

Figure 6. Comparing the PPegF nanoparticles' cell viability (%) to that of free Docetaxel in a cytotoxicity study

CONCLUSION:

In this present work, the physiochemical characteristics of docetaxel-loaded PPegF nanoparticles were assessed after they were fabricated utilizing the modified nanoprecipitation method with PVA acting as stabilizer. Formulation (PVAF4) was chosen as the best optimal formulation after being characterised based on its features. Additionally, the morphological characteristics of the optimal formulation were further characterised using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). The TEM and SEM images showed that the polymeric nanoparticles were spherical. In comparison to the other formulations, the total amount of medication released from PVAF4's lyophilised Docetaxel-loaded polymeric nanoparticles was determined to be 78.12±0.12% after 48 hours. R2 values for formulation PVAF4 indicated zero order kinetics followed by a more linear Korsmeyer-Peppas plot, according to in-vitro drug release kinetics modelling. The results showed that the drug released from the matrix type nanoparticle formulation underwent "Fickian diffusion," with the drug release exponent (n value) on the Korsmeyer-Peppas plot being less than 0.5. An in-vitro drug release investigation determined that the PVAF4 formulation was the best and most optimal nanoformulation. Thus, it can be said that PPegF nanoparticles loaded with docetaxel could be a potent and promising anticancer drug delivery method.

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