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Formulation and Evaluation of Lipo-Nanosphere Loaded Docetaxel Drug

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Abstract

As nanotechnology advances, Nano liposphere or Lipo-Nanosphere is being considered as a possible drug carrier to enhance the bioavailability of some lipophilic drugs. Lipospheres are often employed to deliver hydrophobic agents because lipids can make pharmaceuticals more soluble and release them in a controlled manner. Antineoplastic medication Docetaxel (DCX) is useful for treating a variety of complicated malignancies, particularly cancers of the breast and ovary. Because of it is highly hydrophobicity, first-pass metabolism with P-glycoprotein efflux pumps that prompts low bioavailability with extreme gastrointestinal toxicity of DCX if provided orally, it was only developed for intravenous infusion on the market at a dose of 100 mg/m^2 every three weeks (Taxotere®). The creation of lipo-nanospheres (LPNS) as docetaxel carriers is discussed in this work; by using the melt dispersion method the lipidic physical combination comprising lipid, phospholipids etc., is created then the physical combination is emulsified into a hot, external aqueous phase that is kept at that temperature and of lipidic phase contains the appropriate surfactant. Usually the developed lipo-nanospheres, which are made of biodegradable and biocompatible lipids, are described for surface morphology, crystallinity, and release studies. Due to delayed drug diffusion from lipo-nanospheres, docetaxel's in vitro release behaviors from the created lipo-nanospheres showed a biphasic pattern, with a quick initial release and a slower, continuous release over the course of 24 hours.

Keywords: Anticancer drugs, Docetaxel, Lipo-Nanospheres, Triglycerides

Introduction

Alternative carrier substances, such as lipidic materials, are used instead of synthetic polymer matrix materials because the polymeric matrix frequently have a determinate effect on the incorporated drugs, particularly during formulation manufacturing or polymer erosion. The polymeric matrix may exhibit toxic effects through impairment of the Reticulo Endothelial System (RES) or after human macrophages and granulocytes phagocyte the particles [(1)].Better physical stability, inexpensive ingredient costs, ease of preparation, high dispersibility in an aqueous medium, increased entrapment of hydrophobic medicines, and prolonged release of entrapped medications are just a few advantages of the Lipospheres carrier system [(2).]A single layer of phospholipid contains a solid lipid core that makes up the lipo-nanosphere (LPNS) ; the general structure of lipospheres was explained in Figure.1 .

Using the appropriate emulsifier, the medication is partitioned across lipids to form a homogeneous coat around the core. The exterior lipid coat's tensile strength is developed with the addition of an aqueous plasticizer, and it depends on the kind and characteristics of the stabilizer that is used [(3).] Lipospheres in general are one of the most promising solid lipid particulate drug delivery technologies available for increasing the release rate at which water-insoluble medications dissolve.Originally described as a particulate dispersion of solid spherical particles with a diameter ranging from 0.2 to 100 micrometer; lipospheres are composed of a solid hydrophobic fat core, such as triglycerides or fatty acid derivatives, stabilized by a phospholipid monolayer. LPNS are a novel class of fat-based encapsulation systems designed for topical and parenteral delivery of bioactive substances. They have been applied to the delivery of vaccines, local anesthetics, antibiotics, anticancer drugs, proteins, and peptides as well as anti-inflammatory substances [(4)].

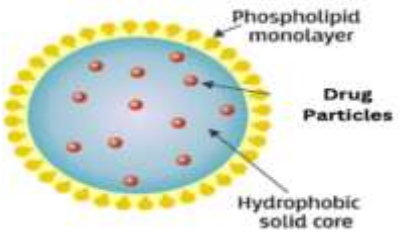

Figure 1. Structure of Lipo-Nanosphere [(5]

Docetaxel (DCX) is a semi-synthetic analogue of Paclitaxel, an anticancer medication from the second generation of the taxoid family; Figure. 2 the chemical structure of DCX. Applying the chemical formula $C_{43}H_{53}NO_{14}$ which translates to a molecular weight of 807.89 Da, it is generated semi-synthetically from 10-deacetylbaccarin-III, an inactive precursor molecule derived from the needles of a rare Pacific yew tree, *Taxus baccata*. The compound's log-P and PKa values of 4.1 and 10.97, respectively. The skin permeability (1 X 10^{-6} cm/second) and poor aqueous solubility (0.025 µg/ml). DCX falls under the dissolution/permeability limited group of pharmaceuticals due to its low solubility and permeability, class IV in the Biopharmaceutical classification system (BCS) and its melting point between (167-169 ºC) [6]; the above physiochemical properties for anhydrous docetaxel that differ from trihydrate DCX.

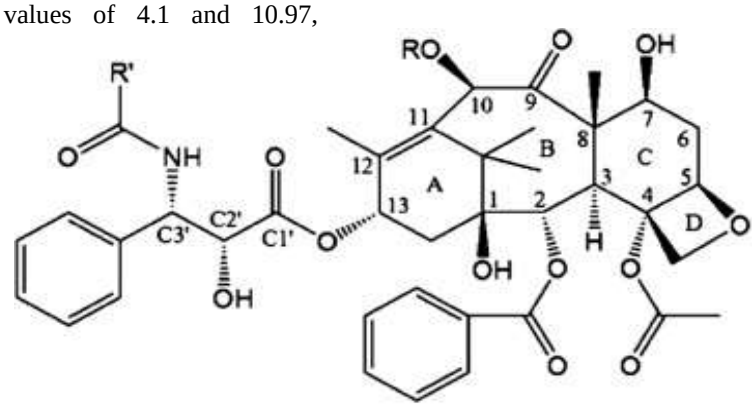

Figure 2. The chemical structure of Anhydrous Docetaxel [7].

Inducing tubulin monomer polymerization and preventing depolymerization are two effects of DCX that can cause mitotic cell arrest in the G2/M phase of the cell cycle and ultimately result in cell death. It can also cause apoptosis in cells by promoting bcl-2 phosphorylation. Due to its non-specific targeted behavior and associated side effects, DCX's clinical usefulness is still restricted. Due to the serious side effects such as neutropenia, hypersensitivity responses, peripheral neuropathy, musculoskeletal toxicity, and nasolacrimal duct stenosis are associated with the commercial formulations of DCX that are now available [8]. Improving DCX's permeability and solubility is the goal of the project. These drugs, such as paclitaxel and Docetaxel, have limited permeability and low water solubility, which prevents them from reaching the tumor site at the prescribed therapeutic dose. Additionally, the market's available dose forms had a high rate of negative effects and little to no benefits.

Materials and Methods

Materials

Docetaxel procured from Hangzhou Hyper Chemicals Ltd. China, phospholipid 80H and phospholipid 90G, both supplied from Henan Guange Biotechnology Co., Ltd. China, cetyl alcohol, paraffin wax Alpha Chemika, India. stearic acid from Panreac Co., Spain. Tricaprine, Tristearin and Hydrogenated Soybean oil come from Pharmaffiliates Analytics and Synthetics Ltd., India. Beeswax, polyvinyl alcohol, tween 80, and Phosphate Buffer Saline PH.7.4 are all provided by HIMEDIA company, India. Ethanol is 100% HPLC gradefrom CHEM-LAB company, Belgium.

Methods

Formulation Technique and Composition

The emulsion melt dispersion process was utilized to prepare Lipo-Nanosphere loaded with DCX.First; the bioactive chemical was added to the lipidic mixture or the exterior phase (core and coat); all were dissolved together at 70°C with a minimum amount of ethanol by utilizing a hot plate magnetic stirrer (JOANLAB ,China) at 950 RPM. Also, by employing the same magnetic stirrer with the same speed; a reasonable amount of Deionized water (DIW) dissolve both surfactant (tween80) and cosurfactant (polyvinyl alcohol) this external aqueous hot phase was heated approximately until 75°C. To gain lipidic emulsion by gradual adding of the hot melted oil phase drop wisely by (disposable5 ml syringe) to the aqueous phase, while stirring on the hot plate magnetic stirrer with identical temperature and speed of preparation for both already made phases [9].

In order not to lose sight of the fact that the primarly homogenous Lipo-Nanosphere (O/W) emulsion both phases must be in the same temperature during the blending step; also must be hold on the same temperature with magnetic stirring for 15 minutes after composition [10].After the the liquid is quickly cooled to less than 20°C

by submerging the primary LPNS inside ice bath while stirring continually by using a homo dispenser(homogenizer; JOANLAB ,China); this operation stay approximately For 60 minutes ; to create homogenous dispersion; the homogenous LPNS emulsion fabricated also kept at 4 °C after placed in the ultrasonic probe (Shimadzu, Japan)for 10 minutes with 50 seconds of work and 10 seconds of rest at 40% watts[11], this procedure was explained briefly in Figure.3 and Table1.

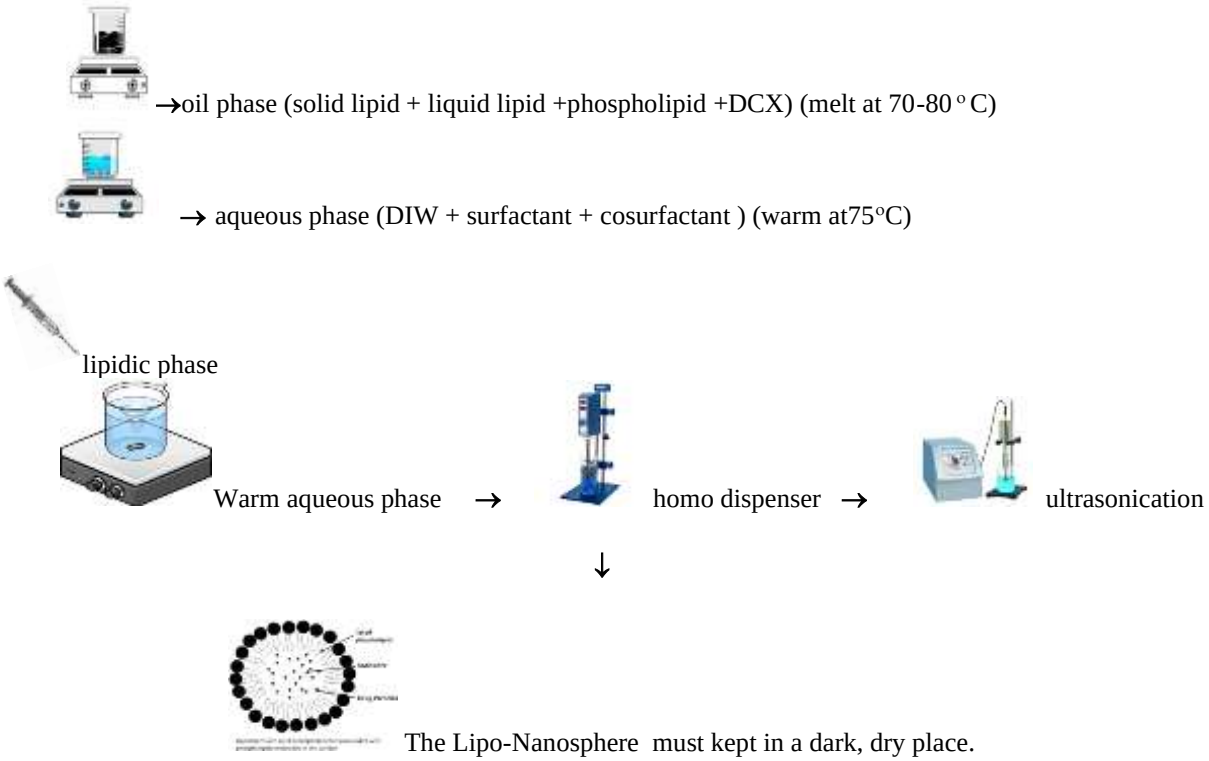

Figure 3. Schematic Presentation of Formulation DCX Loaded Lipo-Nanosphere by Melt Dispersion Technique.

Table 1. Trail batches for selection of best LPNS.

Substance	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**Speed rpm**
DCX(mg)	16	16	16	16	16	16	16	16	1000
Tricaprine(ml)	-	-	4.5	4.5	4.5	4.5	4.5	4.5	1000
Paraffin wax(mg)	25	25	-	-	-	-	-	-	1000
Hydro. Soybean oil * (mg)	-	-	-	-	-	-	25	25	1000
90G*(mg)	10	-	10	-	10	-	10	-	1000
80H*(mg)	-	10	-	10	-	10	-	10	1000
Cetyl alcohol(mg)	25	25	25	25	-	-	-	-	1000
Ethanol (ml)	10	10	10	10	10	10	10	10	1000
Hydro. Olive oil* (ml)	-	-	-	-	1.8	1.8	-	-	1000
PVA*(mg)	5	5	5	5	5	5	5	5	1000
Tween 80(ml)	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1.9	1000
DIW*	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	1000

Hydro. Soybean oil * mean hydrogenated soybean oil**, Hydro. Olive oil*** mean hydrogenated olive oil, **Phospholipon 90G*** represent, soybean Phosphatidylcholine while **Phospholipon 80H*** represent Hydrogenated soybean Lecithin, **PVA*** mean Polyvinyl Alcohol and **DIW*** represent deionized water**.**

Characterization of lipo-nanosphere

Vesicle size, polydispersity index, and zeta potential determination

Due to the lipids that provided the mixture's high viscosity, all eight recipes were diluted up to 100 times with deionized water and stirred at 37 °C with a magnetic stirrer. This dilution makes it simple and easy to get clear, fair results like particle's sizes and charges. Using a particle size analyzer (Malvern Zetasizer, USA), the dynamic light scattering method was used to examine the final vesicle size of each nanoemulsion, and the PDI was then calculated [12]. The zeta potential was also ascertained for only the selected liquid LPNS formulations [13]; this selection depends on the drug entrapment efficiency the amount of drug that content and loaded inside the lipid core.

Fourier transform infrared spectroscopy (FTIR)

An FTIR (Sigmadz1800, Japan) pressed-disk technique was used to produce the FTIR spectrum. a tiny quantity of untreated DCX, a chosen formula, and blank formula. After KBr powder was used to grinds with the solid formula, the mixture was compressed into a disc. The produced disc was examined with FTIR spectroscopy within a wavelength range of 4000-400 cm [14]. While the liquid formulas was examined by deposition of the sample on IR transparent material (silicon), then left to dry and form a film that can easily examined.

Determination of drug entrapment efficiency and Drug loading capacity

The filtration/centrifugation method indirectly measured the loading capacity and the proportion of DCX encapsulated within LPNS. By using volumetric flask containing PBS 7.4: ethanol (7:3) was filled with the LPNS Liquid state and placed in a magnetic stirrer for five minutes after completing the volume to 10 mL. Then, the appropriate amount was added to the upper chamber of an Amicon® Ultra Centrifugal tube with a molecular cut off size (MWCO) of 10 kDa, and the tube was centrifuged for thirty minutes at 4,000 rpm. The medication that had not been entrapped soon gathered in the filtrate in the lower chamber. Using PBS (pH 7.4): ethanol (7:3) as a blank, the clear solution was obtained, filtered using a 0.22 µm filter syringe, diluted, and detected using a UV spectrophotometric; the drug entrapment efficiency was measured in triplicate, with average values being utilized [15].; also drug loading inside the lipid vesicles can be calculated using the following equations;(n=3) [16].

$$EE\% = \frac{WT-WF}{WT} * 100 \text{....Eq1}$$

$$DL\% = \frac{WT-WF}{WL} * 100 \text{....Eq2}$$

Where:

WT = weight total $drug$ is the weight of the initial drug used,

WF = weight $free\ drug$ is the weight of the free drug detected in ultrafiltration of the aqueous dispersion.

WL = weight $lipid$ is the total weight of the lipid used. Results are expressed as average values ± S.D [17]

Docetaxel content

One milliliter of the DCX-loaded Lipo-Nanosphere (or 0.08milligrams of DCX) was dissolved in ethanol. The drug was completely extracted at 50°C by adding 10 mL and stirring it for 10 minutes at 750 rpm on a hot plate magnetic stirrer [18]. After diluting the resultant solution with ethanol according to the instructions, it was filtered through a 0.22 µm filter syringe and the concentration of DCX was measured using spectrophotometry. After that, a UV-visible spectrophotometer (Shimadzu, Japan) was used to analyze it spectrophotometrically in ethanol at its λ max (299 nm) [19].

in vitro release

Five milliliters of recently made DCX Lipo-Nanosphere dispersion were put into a dialysis bag; with 3500 Da molecular weight threshold [20], the dialysis membrane put in the releasing medium phosphate buffer slain with PH 7.4 and ethanol; (70:30) ml; stirred with a magnetic stirrer [21]. The dialysis bag a was allowed to float freely while the Hot plate magnetic stirrer (JOANLAB, China) at 100 rpm and 37°C [22]. pulling of 5 mL of the dissolving medium at intervals of 30 minutes and 1 hr., 2 hr., 3hr, 4hr till 24 hr. To keep the volume constant; the same volume of newly produced release medium was added again. Using the calibration curve and a UV-Visible spectrophotometer (Shimadzu, Japan) set to 232 nm, the concentration of DCX was ascertained [23].

Field Emission Scanning Electron Microscopy Method (FESEM)

This technique was created to count, size, and help with focus and act as an internal control for particle sizing, unconjugated gold particles were combined with each sample after incubation. The particles were then fixed, dyed, and prepared for image analysis on carbon-coated copper grids [24, 25].

Selection of the optimum formula

Based on the zeta potential, vesicle size, PDI and particularly the in -vitro drug release experiments will support the selection of the best formulas [26].

Statistical analysis of data

The experimental results are presented as the mean of three replicate models ± standard deviation. They were subjected to a one-way analysis of variance (ANOVA) to ascertain whether the changes in the applied factors are statistically significant at the level of ($P < 0.05$) and non-significant at the level of ($p > 0.05$) [27].

Results and Discussion

The Composition and Formulation Method

Since the emulsion melt dispersion approach offered spherical particles with higher mechanical qualities, it was thought to be the ideal way to prepare LPNS as seen in Figure. 4; similar outcomes were noted in the case of lipospheres preparation as carriers for bioactive compounds [28]; evaluating several liposphere preparation techniques and concluding that the emulsion melt dispersion approach is the best. The preparation of lipid nanoparticulate using homogenization and probe-sonicator to create nanosized lipospheres facilitates the use of common surfactants like tween 80 and an organic solvent that is miscible with all constituents During the preparation of oral cyclosporin nanoparticulate lipospheres [29]. The most effective way to create equally sized nanocarriers is to use cavitation technology, which involves high shear homogenization and the aid of ultrasound vibrations produced by a probe-sonicator; one advantage of the energy-efficient method is that it can be operated without the need for specialized staff. They study this effect on the production of ritonavir nanostructure lipid carriers with multiple systematic processes to optimize their in-vitro release is by using the probe-sonicator and homogenizer [30]; as illustrated in Figure.5.

Figure 4. The color and appearance of Docetaxel-loaded LPNS for all prepared formulas

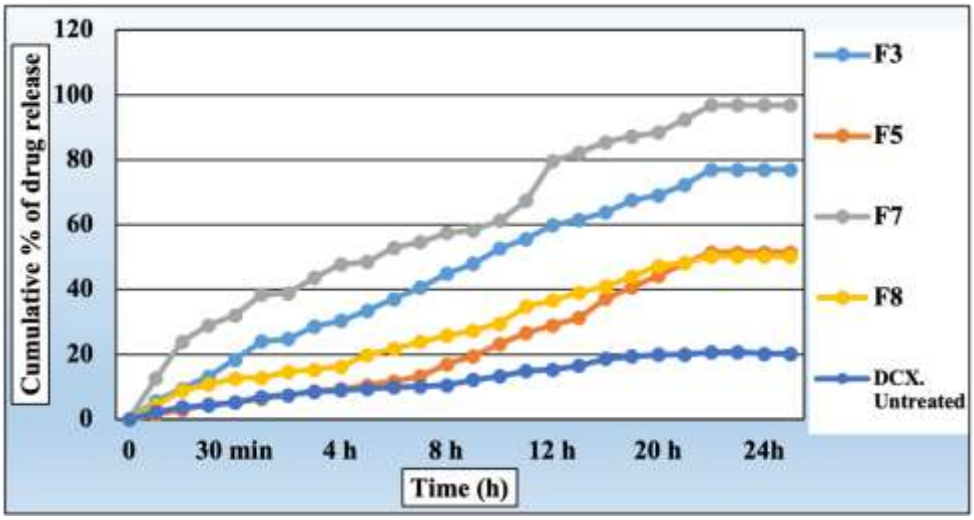

Figure 5. Dissolution profile of LPNS-DXC (F3, F5, F7, F8 and Pure drug)

Docetaxel particle size

The DCX particle size with F1 and F2 was 80.74±7.121nm and 73.75±12.55nm with paraffin wax, respectively as seen in Figure. 6; this is smaller than the particle sizes obtained with F3, F5, F6, F7, and F8, which are larger. This can be explained by the compatibility of paraffin wax with cetyl alcohol (fatty alcohol), which is thought to be a polar wax modifier and stabilizer. The same observation was notified during the peptide liposphere manufacturing process [31].

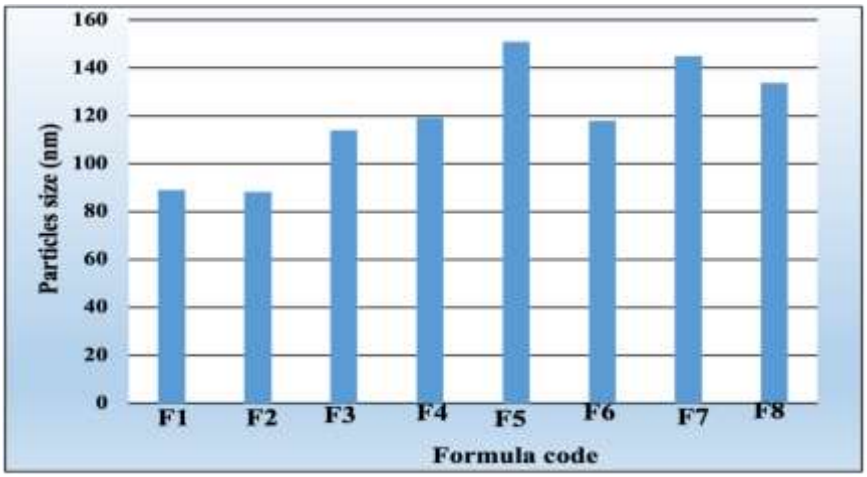

Figure 6. Histogram shows the particle size distribution of the formulas.

Docetaxel content and loading

Liquid lipids were added to the solid ones to maintain the same overall ratios. When creating LPNS, they considered as a single factor that would improve drug loading with the time-ordered explosion of DCX time . The same results were notified during the liposphere formation process that contained celecoxib [32]. Because the medication migrates out of the lipospheres and crystallizes in the solution when incompatible solid core is used, compatibility between the encapsulated drug and the solid core material is essential for keeping the drug inside LPNS particles [33]. The same is evident in F3, F5, F7, and F8 where we employ Tricaprine (triglycerides), which offer better DCX entrapment and content than Paraffin Wax F1 and F2. This is accurate since low melting point triglycerides have been shown to be superior Docetaxel solubilizers [34].

Table 2. Some Physical Properties of Lipo-Nanosphere

Formula code	Particle size (nm)*	Polydispersity index*	%Entrapment efficiency	Drug content (%)	Loading Capacity (%)	Zeta Potetial (mV)
Docetaxel	3416	1.101	-	-	-	-1.987
F1	80.74±7.121	0.252±0.022	44.5±3.53	39.47±1.33	5.89±2.4	-
F2	73.75±12.55	0.2592±0.026	32±2.82	45.04±0.127	2.133±0.9	-
F3	127±15.394	0.164±0.011	95.75±2.29	93.82±0.33	9.8±2.251	-13.39
F4	136.11±15.07	0.143±0.012	70.125±0.17	68.34±1.03	4.05±0.83	-
F5	157.23±31.38	0.161±0.018	81.625±2.29	83.68±3.130	7.189±1.38	-16.94
F6	141.61±20.76	0.124±0.016	51.4625±2.06	54.73±0.36	0.632±1.02	-
F7	154.143±11.77	0.163±0.022	96.375±1.94	97.18±3.048	9.55±2.17	-27.33
F8	156.07±21.88	0.155±0.018	96.6875±1.68	98.303±0.53	9.675±2.21	-14.72

* Average ±Standard Deviation (n=3).

Fourier transform infrared spectroscopy (FTIR)

To look at Docetaxel entrapment inside the Lipo-Nanosphere's cores, FTIR analysis was carried out on untreated DCX, blank lipo-nanospheres, and DCX lipo-nanospheres. DCX. has the C-O stretch shifted from (1701.22 cm^{-1} to 1737.86 cm^{-1}), while the O-H bending group at (3639.68 cm^{-1} altered to 3523.95 cm^{-1}). The following modifications show that an ester group has formed between DCX and the LPNS components. the C-H stretches from (2980.02 cm^{-1} to 2924.09 cm^{-1}), alkane C-H from (1371.39 cm^{-1} to 1388.75 cm^{-1}), and the long chain C-H from (702.09 cm^{-1} to 717.52 cm^{-1}). The Tricaprine, soyabean oil (the core components) and 90G phospholipid (the coat), which are important components of F7A and B, successfully encapsulate the DCX drug inside the Lipo-Nanosphere vesicles. As a result, the significant peaks of DCX were significantly lowered. similar results noticed during the preparation of the DCX-PLGA nanocarrier [35].

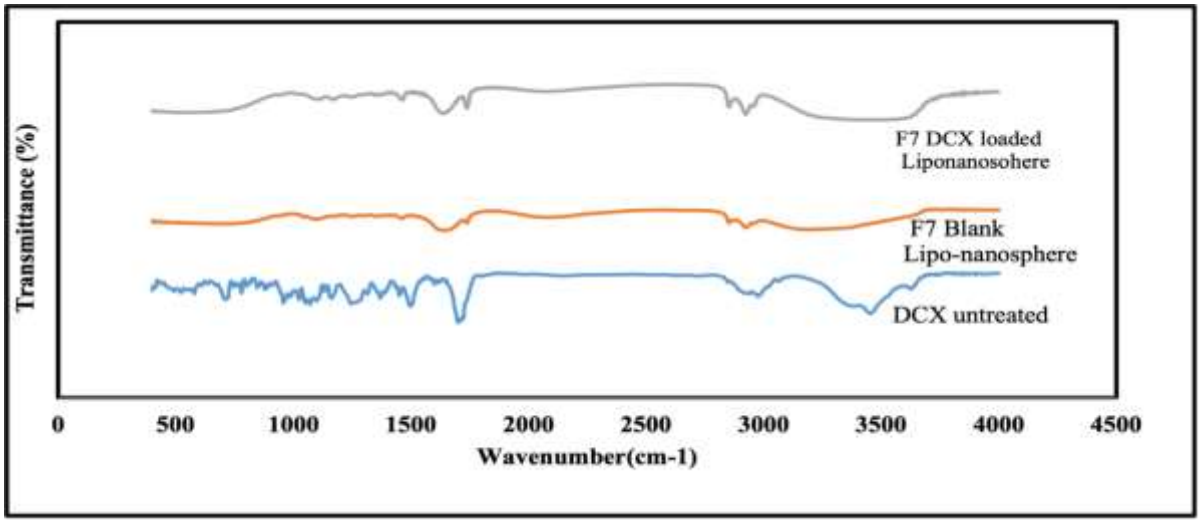

Figure 7. Qualitative FTIR analysis for Docetaxel Lipo-Nanosphere FTIR of Docetaxel untreated; FTIR of blank F7and F7 DCX Lipo-Nanosphere

(FESEM)study

From Figure. 8 A, B,C and D; the creation of smooth, spherical, and nanosized LPNS was greatly aided by the concentrations of Tween 80; the similar outcomes [36] were observed with the nebivolol lipospheres preparation . It is also the same since a higher yield and the creation of extremely small lipospheres were made possible using PVA as a stabilizer, when Ofloxacin lipospheres were being produced also achieved similar findings [37]

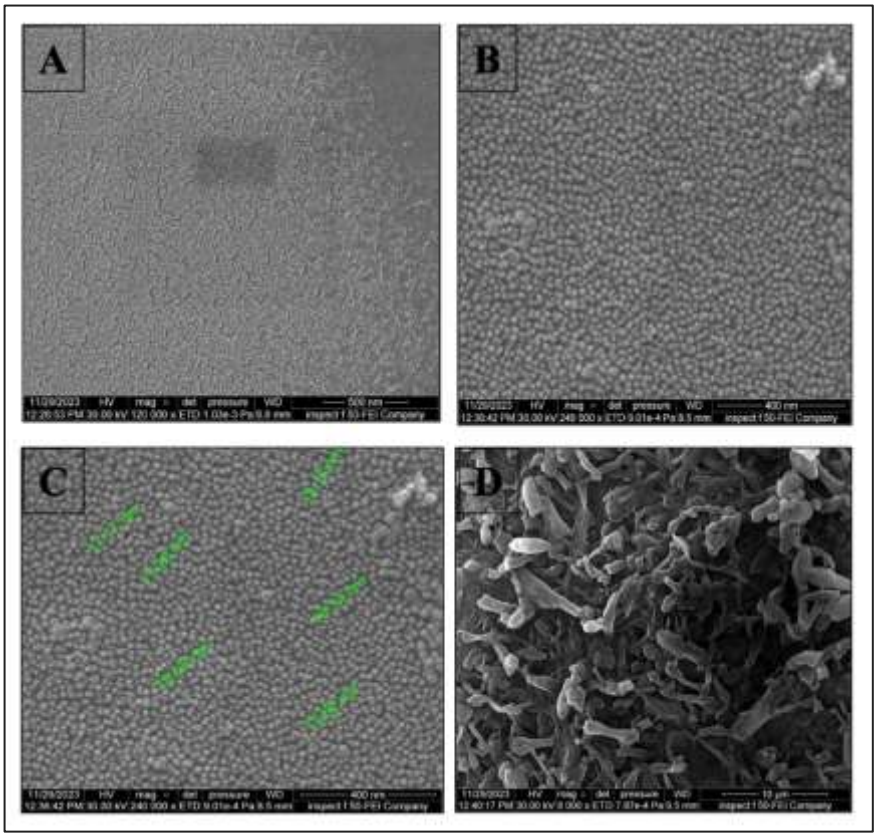

Figure 8. FESEM images of F7 Docetaxel Lipo-Nanosphere that gave spherical shape particle with different resolution. A.X. 120 000, B. and C. X 240 000 and D. Docetaxel untreated.

The optimized formula

The DCX-loaded LPNS exhibit the quickest rate of breakdown, releasing roughly 96% of the medication from F7 in 24h. Furthermore, DCX dissolved at a rate of 76%, 51%, and 50% for F3, F5, and F8. In the meantime, the untreated DCX offers a 24-hour, roughly 20% extended-release rate. According to this information, the introduction of DCX, an alkaloid anticancer from the terpenoids class [38]; that is a weak basic compound, which

restricted the release of Docetaxel in PBS7.4; the similar outcomes was observed, showing that 40% of DCX was released in basic medium and 80% in acidic medium, at PH 5 [39].

Conclusion

Soybean oil, DCX, and low melting point triglycerides have a high degree of compatibility, which results in an ideal 24-hour sustained-release formula, with high drug content and entrapment efficiency. Vesicles with spherical, nanoscale shapes were arranged on a smooth surface via the lipid carrier system, which F7 displays. The development of the Lipo-Nanosphere was able to extend the drug's duration of action, which is an important requirement in cancer chemotherapy. The FTIR study showed that DCX was entrapped inside the LPNS and that the drug was transformed into an amorphous form; also, the formulation was able to sustain the drug release.

Lipospheres in micro size solid lipid particulate(vesicles) system, it is a novel kind of fat-based encapsulating technology that already preparade in nanosized in this article , consequently to distinguish it from solid lipid nanoparticle (produced by melting fat and mixed with an aqueous surfactant) and nanostructure lipid carrier(created by combining liquid lipid oils with solid lipids). ; the nanosized lipospheres or nanoliposphere or Lipo-nanosphere all gave the same meaning composed of a monolayer of phospholipid stabilizing a solid or liquid hydrophobic fat core, such as triglycerides or fatty acid derivatives and waxes. The medication is either dissolved or distributed in a solid fat matrix within the liposphere's interior core [40, 41].

In the previously mentioned formulas especially F3, F4, F5, F6 and F7, using liquid and solid lipids, fats ,waxes , fatty alcohol and hydrogenated oils, all are used to discover the best formula, which was F7 that contain liquid lipid Tricaprine, solid hydrogenated soybean oil with phospholipon 90G (soybean Phosphatidylcholine); this compensation gave better sustained release for the anticancer medication that can be taken parentally, topically and rectally .

The production of Aceclofenac lipospheres as a carrier for a topical preparation [42] revealed the same formula's component variation; the same formula's component variation was also used while producing Naproxen lipospheres[43].By comparing F1 and F2 , the same between F3 , F4 and F5, F6 and F7, F8 to choose the best coat phospholipid which bring to light phospholipon 90G as the premier representing the coat of the LPNS, while the liquid triglycerides Tricaprine and the solid lipid hydrogenated soyabean oil as the best solid and liquid lipids these represent the core of the LPNS , these results fits with harmony of Figure 1 that represent the general structure of LPNS additionally Figure 8 B. FESEM images of F7 support our work outputs

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Conflicts of Interest

The authors stated no conflict of interest in the manuscript.

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Ethics Statements

There were no humans or animals used in all experiments.

Author Contribution

The author's responsibilities are described as follows: Preparation, collecting, and analyzing data: Maysam M. Abass. Designing, reviewing, and supervising the project : Shaima Nazar Abd Al Hammed. All authors reviewed the results and approved the final version of the manuscript.

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صياغة وتقييم الدواء المضاد للسرطان نافر للماء محمل بالليبو نانوسفير

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الخلاصة

اعتبار الغلاف النانوي بمثابة حامل محتمل للأدوية لتعزيز التوافر البيولوجي لبعض الأدوية المحبة للدهون. غالبًا ما تُستخدم الكريات الدهنية لتوصيل عوامل كارهة للماء لأن الدهون يمكن أن تجعل المستحضرات الصيدلانية أكثر قابلية للذوبان وتطلقها بطريقة خاضعة للرقابة. يعتبر دواء دوسيتاكسيل (DCX) المضاد للأورام مفيدًا لعلاج مجموعة متنوعة من الأورام الخبيثة المعقدة، وخاصة سرطانات الثدي والمبيض. نظرًا لأنه شديد الكارهة للماء، فإن استقلاب المرور الأول باستخدام مضخات تدفق البروتين السكري P يؤدي إلى انخفاض التوافر البيولوجي مع سمية الجهاز الهضمي الشديدة لـ DCX إذا تم تقديمه عن طريق الفم، وقد تم تطويره فقط للتسريب الوريدي في السوق بجرعة ١٠٠ مجم / م ٢ كل يوم. ثلاثة أسابيع (Taxotere®). تمت مناقشة إنشاء الجسيمات النانوية الدهنية (LPNS) كحاملات للدوسيتاكسيل في هذا العمل؛ باستخدام طريقة تشتيت الذوبان، يتم إنشاء التركيبة الفيزيائية الدهنية التي تشتمل على الدهون والفوسفوليبيدات وما إلى ذلك، ثم يتم استحلاب التركيبة الفيزيائية إلى طور مائي خارجي ساخن يتم الاحتفاظ به عند درجة الحرارة هذه ويحتوي الطور الدهني على المادة الخافضة للتوتر السطحي المناسبة. عادةً ما يتم وصف الجسيمات النانوية الدهنية المطورة، والمصنوعة من دهون قابلة للتحلل الحيوي ومقبولة حيويًا، لدراسات التشكل السطحي والبلورية والإطلاق. بسبب تأخر انتشار الدواء من الجسيمات النانوية الدهنية، أظهرت سلوكيات إطلاق الدوسيتاكسيل في المختبر من الجسيمات النانوية الدهنية التي تم إنشاؤها نمطًا ثنائي الطور، مع إطلاق أولي سريع وإطلاق مستمر أبطأ على مدار ٢٤ ساعة.

الكلمات المفتاحية: الأدوية المضادة للسرطان، الدوسيتاكسيل، الليبو نانوسفير، الدهون الثلاثية