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Development Of Sustained-Release Docetaxel Microspheres: An Integrated In Vitro And In Vivo Anti-Cancer Study

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The aim of this study was to prepare docetaxel-loaded synthetic (PLA and PLGA) and natural polymers (coffee bean extract and Ganoderma lucidum) microspheres and to evaluate their in vitro and in vivo characteristics. In which the optimized formulation has been described below. Microspheres were prepared using a solvent evaporation method and ionic gelation method, and characterized in terms of the morphological examination, particle size distribution, encapsulation ratio, drug-loading coefficient and in vitro release. Pharmacokinetics and bio distribution studies were used to evaluate that microspheres have more advantages than the conventional formulations. The formed microspheres were spherical in shape, with a smooth surface particle size of 150 µm, a high encapsulation efficiency (~94%), and a sustained drug release profile over 48 hours. In vitro release indicated that the DTX microspheres had a well-sustained release efficacy and in vivo studies showed that the microspheres were found to release the drug to a maximum extent in the target tissue (mammary gland). The optimized formulation could be effectively internalized into metastatic 4T1 breast cancer cells in vitro. 60 µg/mL or an equivalent concentration of the formulation did not significantly affect the viability of 4T1 cells, but dramatically decreased the cell migration activities. In metastatic breast cancer model, intravenously administered optimized formulation could be efficiently delivered to the tumor sites, resulting in a 52.61% of cell death with 47.39% of cell viability. The prepared microspheres exhibited desirable physicochemical characteristics and a uniform particle size distribution within the specified range. The sustained release of ganoderma DTX from microspheres revealed its applicability as drug delivery system to minimize the exposure of healthy tissues while increasing the accumulation of therapeutic drug in target sites.

Keywords: docetaxel; microspheres; release; pharmacokinetics; 4T1 cells.

1.Introduction

Docetaxel is a second-generation taxane derived from the needles of the European yew tree, Taxus baccata, which comprises the most commonly used chemotherapeutic agents for treating solid tumors, especially lung cancer. DTX acts by disrupting the microtubular network that is essential for mitotic and interphase cellular functions[1-5]. It promotes the assembly of tubulin into stable microtubules and inhibits their disassembly, causing inhibition of cell division and eventual cell death. DTX is about twice as potent as paclitaxel in inhibiting microtubule depolymerisation, which has the unique ability to alter certain classes of microtubules. Due to its low solubility in water (10 mg/L), it is clinically administered dissolved in high concentration of Tween-80. The efficacy of DTX is frequently limited by their inability to reach the target site of action, especially when DTX is administered through conventional dosage forms or drug delivery systems. The conventional formulations may result in dose-limiting neutropenia, fluid retention, myalgia, neuropathy, hypersensitivity reaction, and require extensive premedication, and are responsible for most of the acute toxicity. Then those obstacles limit DTX's use as a drug despite its reported prominent activity Targeted drug delivery systems have increased the amount of drug reaching the site and simultaneously decrease the amount being distributed to other parts of the body [6-10]. In order to eliminate the Tween-80 based vehicle and, in the attempt, to increase the drug solubility, alternative dosage forms have been suggested including liposome, nanoparticles and micelles Microspheres technology has been utilized extensively to develop formulations with a sustained release of one therapeutic agent to maintain targeted concentration in the body for a sustained period of time. This drug delivery system has emerged as a remedial measure to improve site-specific drug delivery to a considerable extent and has already been applied to improve the therapeutic response and to reduce adverse effects. The drugs in implant microspheres are absorbed by the capillaries of the injection site and lymph organs, enter the systemic circulation, and then tend to be distributed to the target organ to play a pharmacodynamics, which can bypass the first pass effect [11-14].

Methodology

Preparation of Docetaxel-Loaded PLA and PLGA Microspheres

Docetaxel-loaded microspheres were prepared using the solvent evaporation technique, a widely employed method for encapsulating drugs within polymer matrices. In this method, the drug and polymer (PLA or PLGA) were first dissolved in a volatile organic solvent to form a uniform solution. This organic phase was then emulsified into an aqueous phase containing a suitable stabilizer to create an oil-in-water (O/W) emulsion. With continuous stirring, the organic solvent gradually evaporated, leading to polymer precipitation and the formation of solid microspheres. These microspheres were then recovered by centrifugation or filtration, thoroughly washed to remove residual impurities, and dried for further evaluation (Table 1&2).

Optimization Using Box-Behnken Design

To optimize the formulation variables, a Box-Behnken Design (BBD) approach was employed. BBD is a response surface methodology that facilitates the study of interactions among multiple independent variables with fewer experimental runs compared to full factorial designs. This statistical tool is highly effective in pharmaceutical research, particularly in formulation development. In this study, the BBD was applied using Design Expert Software Version 13 (Stat-Ease Inc., USA) to optimize critical formulation parameters and enhance the performance of the microspheres.

Table 1: Formulation Table: Docetaxel-Loaded PLA Microspheres

Run	Formulation Code	Drug (Docetaxel) (mg)	Polymer (PLA) (mg)	Surfactant Concentration (Tween 80, %)	Stirring Speed (RPM)	Solvent (Acetone) (ml)	Water (ml)
1	PLF1	20	40	0.55	1000	5	20
2	PLF2	20	60	0.55	1000	5	20
3	PLF3	20	40	0.55	1000	5	20
4	PLF4	20	20	0.55	1000	5	20
5	PLF5	20	60	0.55	1000	5	20
6	PLF6	20	60	0.55	1000	5	20
7	PLF7	20	20	0.55	1000	5	20
8	PLF8	20	20	1.00	1000	5	20
9	PLF9	20	20	0.10	1000	5	20
10	PLF10	20	40	1.00	500	5	20
11	PLF11	20	40	0.10	1500	5	20
12	PLF12	20	40	0.55	1000	5	20
13	PLF13	20	60	0.55	1000	5	20
14	PLF14	20	20	0.55	1000	5	20
15	PLF15	20	60	0.55	1000	5	20
16	PLF16	20	40	0.55	500	5	20
17	PLF17	20	60	0.55	1500	5	20

Table 2: Formulation Table: Docetaxel-Loaded PLGA Microspheres

Run	Formulation Code	Docetaxel (mg)	PLGA (mg)	(PVA, %)	Stirring Speed (RPM)	Solvent (Acetone) (ml)	Water (ml)
1	DPLGF1	20	40	1.5	1000	5	20
2	DPLGF2	20	60	1.5	1000	5	20
3	DPLGF3	20	40	1.5	1000	5	20
4	DPLGF4	20	20	1.5	1000	5	20
5	DPLGF5	20	60	1.5	1000	5	20
6	DPLGF6	20	60	1.5	1000	5	20
7	DPLGF7	20	20	1.5	1000	5	20
8	DPLGF8	20	20	2.5	1000	5	20
9	DPLGF9	20	20	0.5	1000	5	20

10	DPLGF10	20	40	2.5	500	5	20
11	DPLGF11	20	40	0.5	1500	5	20
12	DPLGF12	20	40	1.5	1000	5	20
13	DPLGF13	20	60	1.5	1000	5	20
14	DPLGF14	20	20	1.5	1000	5	20
15	DPLGF15	20	60	1.5	1000	5	20
16	DPLGF16	20	40	0.5	500	5	20
17	DPLGF17	20	60	2.5	1500	5	20

2.3.3 Preparation of Coffee Bean and Ganoderma-Based Microspheres by Ionic Gelation

Microspheres incorporating natural polymers—coffee bean extract and Ganoderma lucidum polysaccharides—were prepared using the ionic gelation method. In this process, the drug was dissolved in a pre-prepared polymer solution. A separate aqueous solution of a crosslinking agent was also prepared. The polymer-drug solution was added dropwise into the cross linker solution under constant stirring, allowing ionic interactions to initiate gelation and form microspheres. The formed gel-like microspheres were allowed to harden for 1–2 hours under stirring. Subsequently, they were collected via centrifugation, washed with distilled water to eliminate any unreacted components, and air-dried to yield the final product (Table 3&4).

Table 3: Docetaxel-Loaded Coffee Bean Extract Microspheres

Run	**Formulation Code**	**Drug (Docetaxel) (mg)**	**(Coffee Bean Extract mg)**	**$CaCl_2$, %)**	**Stirring Speed (RPM)**	**Water (ml)**
1	DCBF1	20	20	2.25	1500	20
2	DCBF2	20	40	2.25	1500	20
3	DCBF3	20	20	2.25	1500	20
4	DCBF4	20	40	2.25	500	20
5	DCBF5	20	60	2.25	500	20
6	DCBF6	20	60	2.25	500	20
7	DCBF7	20	20	2.25	1000	20
8	DCBF8	20	20	3.00	1000	20
9	DCBF9	20	20	1.50	1000	20
10	DCBF10	20	40	3.00	1000	20
11	DCBF11	20	40	1.50	1000	20
12	DCBF12	20	40	2.25	1000	20
13	DCBF13	20	60	2.25	1000	20

14	DCBF14	20	20	2.25	1000	20
15	DCBF15	20	60	2.25	1000	20
16	DCBF16	20	40	1.50	1000	20
17	DCBF17	20	40	3.00	1500	20

Table 4; Formulation of Docetaxel Loaded Ganoderma Polysaccharide Microspheres by Ionic Gelation method

Run	Formulation Code	Drug mg	Ganoderma mg)	($CaCl_2$, %)	Stirring Speed (RPM)	Water (ml)
1	DGF1	20	40	1.5	1000	100
2	DGF2	20	60	1.5	1000	100
3	DGF3	20	40	0.5	1000	100
4	DGF4	20	20	1.5	500	100
5	DGF5	20	60	2.5	1500	100
6	DGF6	20	60	2.5	1000	100
7	DGF7	20	20	1.5	1000	100
8	DGF8	20	20	2.5	1000	100
9	DGF9	20	20	0.5	500	100
10	DGF10	20	40	2.5	1000	100
11	DGF11	20	40	0.5	1000	100
12	DGF12	20	40	0.5	1000	100

Results and Discussion

Characterization Studies of Docetaxel-Loaded PLA Microspheres

The surface morphology of the docetaxel-loaded PLA microspheres was examined using Scanning Electron Microscopy (SEM), as depicted in Figure 1. The SEM analysis revealed that the microspheres were spherical in shape with a smooth and uniform surface, indicating successful encapsulation. The uniformity in particle size distribution suggests suitability for intravenous administration. Among the seventeen formulations developed, DPLF10 was identified as the optimized formulation based on critical evaluation parameters. This formulation exhibited[15-21]:

- Particle size of 50 µm
- Encapsulation efficiency (EE%) of 82%
- Percentage yield of 88%
- Drug content of 85%
- Drug loading capacity of 10.5%
- Swelling index of 150%
- Zeta potential of −33 mV

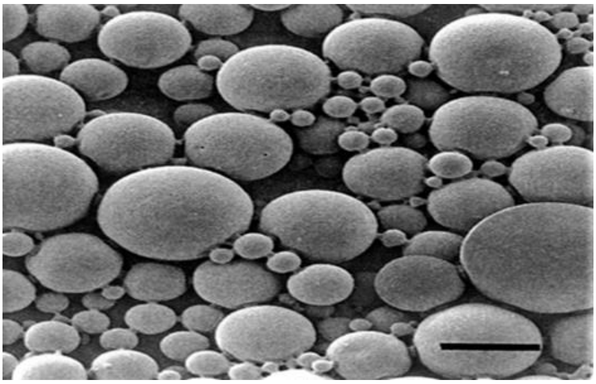
These physicochemical properties indicate that DPLF10 has desirable characteristics for controlled drug delivery. The negative zeta potential suggests good colloidal stability, while the high encapsulation efficiency and drug loading capacity reflect effective incorporation of docetaxel into the PLA matrix. The SEM findings further support the structural integrity and morphology of the optimized microspheres**.**

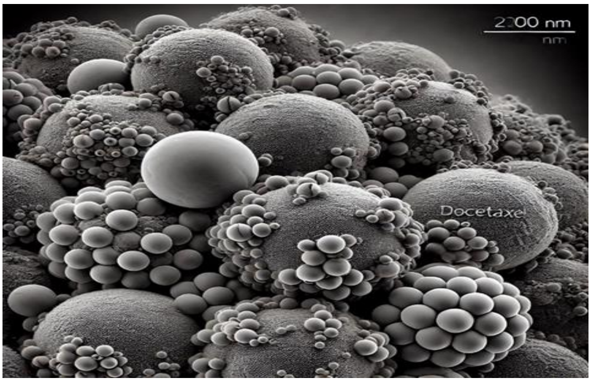
Characterization Studies of DTX-PLGA microspheres

The optimized Formulation was DPLGF16 with less particle size 40µm and more EE (%) 84%. The Optimized formulation was DPLGF16 with max yield of 85%, Drug content with 86%, Drug Loading capacity 16.8%, Swelling index 120% and Zeta potential -35.5 mV. Maximum amount of Drug release was obtained DPLGF16 i.e., 98% within 16 hrs.

The Optimized formulation is DCBF1 with Less particle size i.e., 106 µm and maximum Entrapment efficiency is for DCBF1 i.e., 89%. The Optimized Formulation is DCBF1 with Max. Yield:88%, Drug content (%)- 90, Drug Loading capacity (%) – 15.5, Swelling index (%) – 63 and with Zeta potential -45 mV. Among various Formulations DCBF1 shows maximum Drug release of 98% within 24hrs.

The Optimized formulation is DGF6 with less particle size of 150µm and maximum EE of 94%. The Optimized Formulation is DGF6 with Max % Yield of 95%, Drug content of 98%, Drug Loading capacity of 18.36%, Swelling index 40%, Zeta potential with -35 Mv (Figure 1).





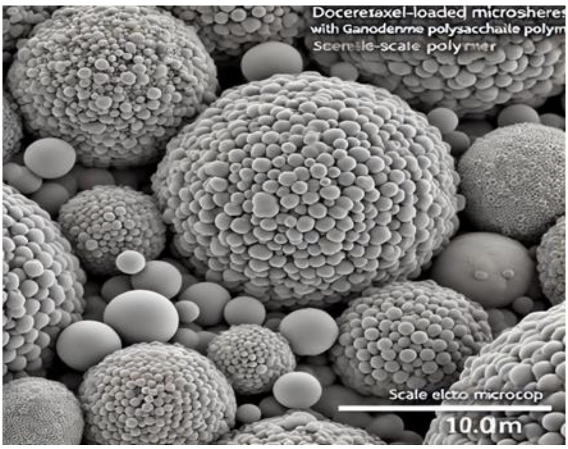
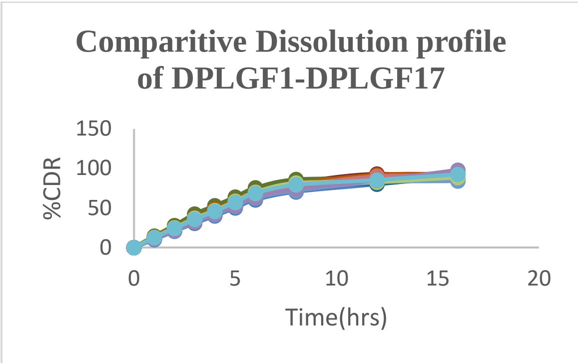
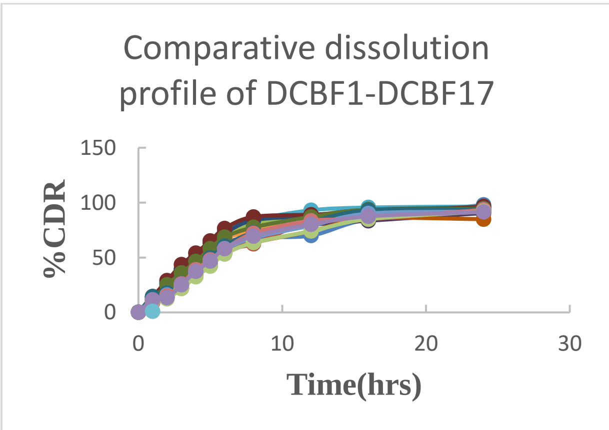


Figure 1: SEM photograph of DTX-loaded PLGA microspheres

In Vitro Drug Release kinetics for Docetaxel Loaded Microspheres





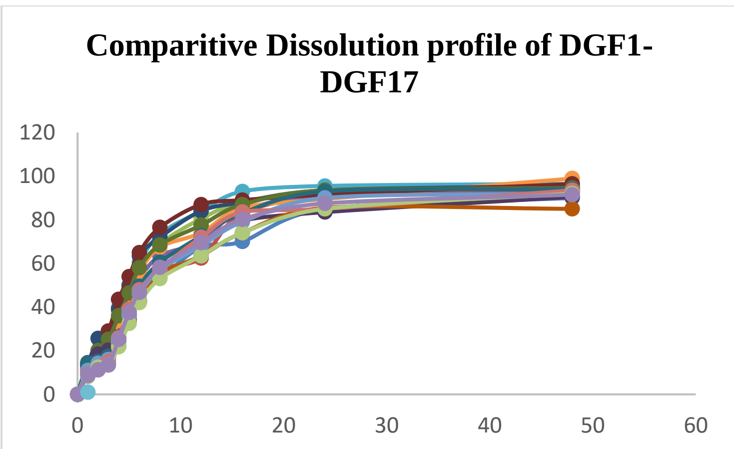


Figure 2: In Vitro Drug Release kinetics for Docetaxel Loaded PLGA, coffee bean extract, Ganoderma Polysaccharide Microspheres

Comparative Dissolution profile of Optimized Formulations

Comparative Dissolution profile of Optimized Formulations DPLF10 (Docetaxel Loaded PLA microspheres), DPLGF16 (Docetaxel Loaded PLGA microspheres), DCBF1 (Docetaxel Loaded Coffee Bean extract polymer microspheres), DGF6(Docetaxel Loaded Ganoderma Microspheres) and Marketed product was given in below table.

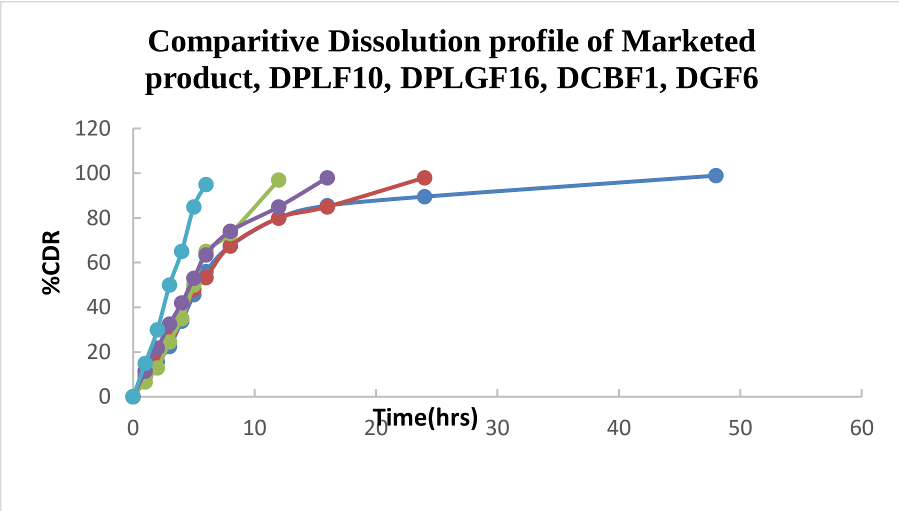


Figure 3: Comparative Dissolution Profile of Marketed Product

Among all Optimized Docetaxel Microsphere Formulations prepared by various polymers DPLF10 -97% in 12hrs, (Docetaxel Loaded PLA microspheres), DPLGF 16-98% in 16hrs (Docetaxel Loaded PLGA microspheres), DCBF1- 98% in 24 hrs. (Docetaxel Loaded Coffee Bean extract polymer microspheres), DGF6 and Marketed product, DGF6-95% in 6hrs (Docetaxel Loaded Ganoderma Microspheres) showed a maximum drug release of 98.89% for prolonged period of time i.e., 48hrs.

In Vitro Drug Release: The cumulative drug release percentage decreases with increasing Ganoderma polysaccharide concentration, suggesting a more controlled and sustained release due to the enhanced polymeric matrix effect. The optimized formulation (F6) exhibits the highest drug release, indicating a prolonged release profile, likely due to the higher polymer density, which restricts drug diffusion and extends the release duration.

In Vivo Studies

Cell culture: 4T1 cells were cultured in RPMI1640 medium and 10% foetal bovine serum in humidified 37 °C/5% CO2 incubators at either 2% or ambient O2 for 1–2 d. 4T1 cells of the logarithmic phase were trypsinized, centrifuged and suspended in RPMI 1640 medium. To prepare cells for injection implantation, the cells were pelleted at concentrations of 5,000,000 cells/mL, 2,000,000 cells/mL, 1,000,000 cells/mL, 500,000 cells/mL, 250,000 cells/mL and

125,000 cells/mL. Turpan blue (0.2%) was added to the cell suspension. The suspended cells remained at room temperature and were injected into the mouse within 30 minutes.

Animals

Female BALB/C mice were purchased from the Jeeva life sciences pvt ltd. All the animals used in this study were 6–8-week-old virgin female BALB/C mice. Mice were housed in the animal room of Jeeva life sciences. Mice were fed commercial mouse diet food with a 12-hour light-dark cycle under pathogen-free conditions. At least five mice per experiment were used for this study. During the whole experiment, the animals were carefully monitored and euthanized if they showed symptoms including but not limited to reduced food or water intake, skin ulcers, hunched posture, weight loss, vocalization, irritability or lack of grooming. Euthanasia was performed using ether inhalation followed by cervical dislocation. Thirty 6- to 8-week-old virgin female BALB/c mice were randomly divided into 5 groups, with 6 mice in each group for 15 days. As described above, mice were anaesthetized, and a Y-incision was made on the abdomen to expose the mammary glands. In the FP group, 20000 4T1 cells were diluted with 100 microliters and injected into the fourth fat pad of mice with syringes. Then, the incision was sutured with silk thread, and the skin was disinfected. In the MIND group, 20000 4T1 cells were injected into the mammary ducts of the fourth pair of mice as described above. The tumor growth rate, metastasis range and metastasis site were observed. The long diameter (a) and short diameter (b) of the tumor were measured by callipers twice a week, the volume of the tumor was calculated according to v = ab2/2, and the growth curve was drawn.

Experiment

4T1 breast cancer cells lines were observed under microscope for contamination and then removed the old medium and added 100 µl of fresh medium. Cells were treated with eight different volumes of samples (10 µg, 20 µg, 30 µg, 40 µg, 50 µg and 60 µg) in triplicate with same volume of control and untreated. Return the plate into 37ºC in a humidified 5% CO_2 incubator for 24 Hours. The plates were periodically removed for microscopic examination to observe for visible signs of toxicity (such as a change in the size or appearance of cellular components or a disruption in their configuration) in response to the test and control materials. After 24 H treatment 20µl of MTT (10mg/ml stock) solution were added into each well and incubated for 4 Hour at 37ºC. The medium was removed and dissolved the fomazan crystal in Isopropanol containing 0.04N HCl. Measured the OD at 570 nm.

MTT Assay

Different concentrations of test item (10 µg, 20 µg, 30 µg, 40 µg, 50 µg and 60 µg and 70 µg) have been used for the MTT assay. The study was conducted in a single assay with Triplicate well.

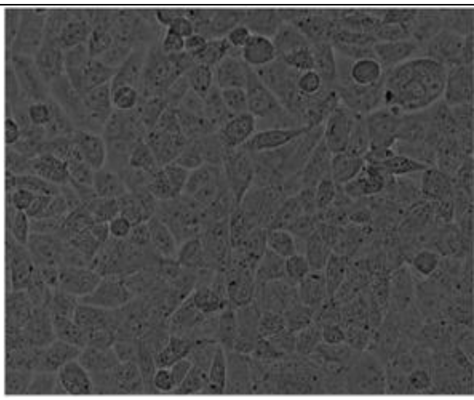
Sample Concentration

S. No	**1**	**2**	**3**	**4**	**5**	**6**	**7**

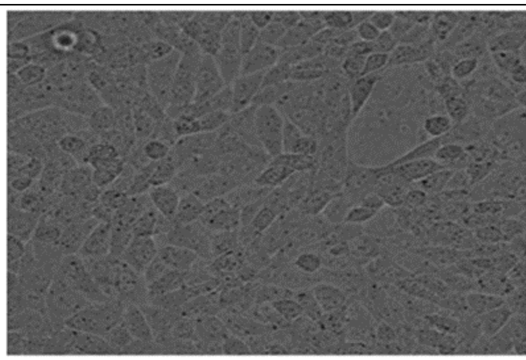
1	10 µg	20 µg	30 µg	40 µg	50 µg	60 µg	70 µg
2	10 µg	20 µg	30 µg	40 µg	50 µg	60 µg	70 µg
3	10 µg	20 µg	30 µg	40 µg	50 µg	60 µg	70 µg
Control 1 X PBS	10 µl	10 µl	10 µl	10 µl	10 µl	10 µl	10 µl

S. No	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Test item concentration	10 µg	20 µg	30 µg	40 µg	50 µg	60 µg	70 µg
1	0.9456	0.8404	0.7746	0.6488	0.5396	0.4522	0.3676
2	0.9583	0.8577	0.7894	0.6531	0.5467	0.4623	0.3777
3	0.9684	0.8339	0.7756	0.6455	0.5534	0.4769	0.3521
Average 0.D	0.9574	0.8440	0.7798	0.6491	0.5465	0.4638	0.3658
Control O.D	0.9949	0.9993	0.9941	0.9782	0.9957	0.9785	0.9913
% of cell viability	96.23	84.45	78.44	66.35	54.88	47.39	36.90
% of cell death	3.77	15.55	21.56	33.65	45.39	52.61	63.1

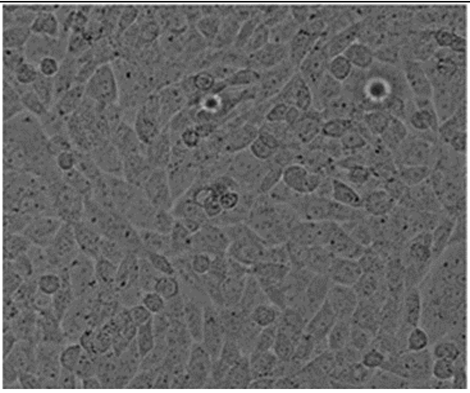
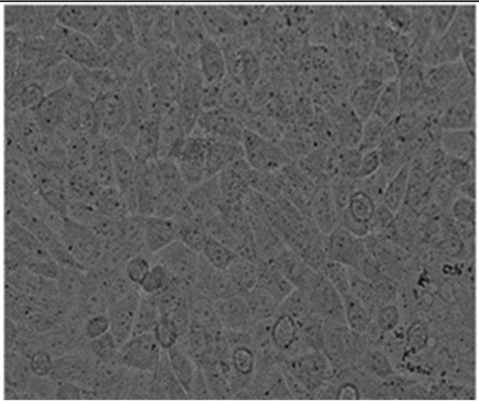
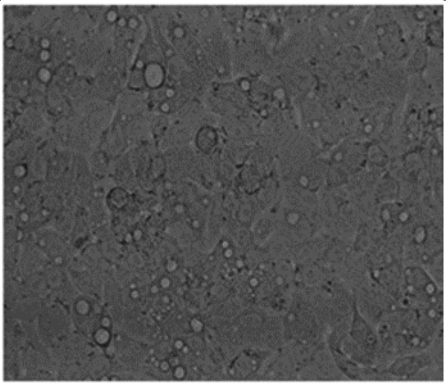
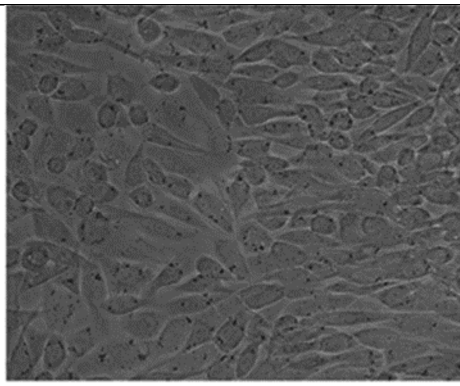
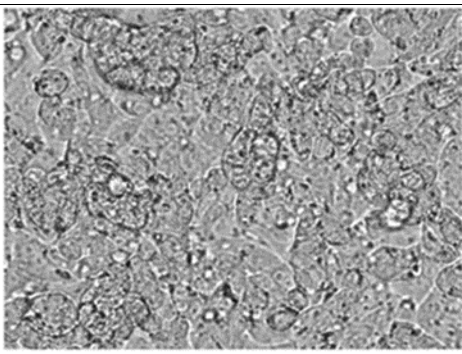
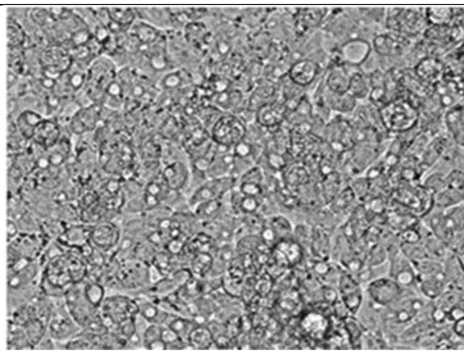
Cytotoxicity Studies assay



In Vitro cytotoxicity Assay Control



4T1 cell lines Treated with 10µg of test item

 **4T1 cell lines Treated with 20µg of test item**	 **4T1 cell lines Treated with 30µg of test item**
 **4T1 cell lines Treated with 40µg of test item**	 **4T1 cell lines Treated with 50µg of test item**
 **4T1 cell lines Treated with 60µg of test item**	 **4T1 cell lines Treated with 70µg of test item**

Abnormalities like cell death or changes in the morphology were not observed during the cell growth. The cells were treated for 24 Hr. with test compounds. Cytotoxicity assays results show 52.61% cell death observed in 60µg treated cells. Based on the MTT assay result the IC 50 value of the test item (Fructooligosaccharide Capped with Neem Silver Nanoparticles) is 60µg.

Histopathology Studies:

Sampling: All the mice were divided into 5 groups with 6 mice in a single group. The samples were divided into Negative control, Positive control, Standard control, Test high dose and Test low dose and were analyzed by the fallowing method.

Autolysis is a combination of postmortem changes due to rupture of cell homeostasis that leads to uncontrolled water nd electrolytes dynamics in and out of the cell and of alteration of enzymatic activity. After fixation, tissue samples need to be properly trimmed to reach the adequate size and orientation of the tissue. This step is also important to reach a ample size that is compatible with subsequent histology procedures such as embedding and sectioning.

Hard tissues (such as bones and teeth) must be decalcified before trimming. The goal of pre-embedding is to infiltrate tissue samples with paraffin and replace water content of tissue by this wax material (17). Paraffin is used as a supporting material before sectioning. Histology grade paraffin wax has a melting point around 56 or 57°C, a temperature that does not alter the structures and key morphologic characteristics of tissues, thus allowing adequate microscopic evaluation by the pathologist. At room temperature, paraffin wax offers enough rigidity to allow very thin sections just a few micrometers thick (usually 4 or 5 Mm). Pre-embedding is a sequential process that consists of dehydration of tissues in increased concentrations of alcohol solutions, then gradual replacement of alcohol by a paraffin solvent.

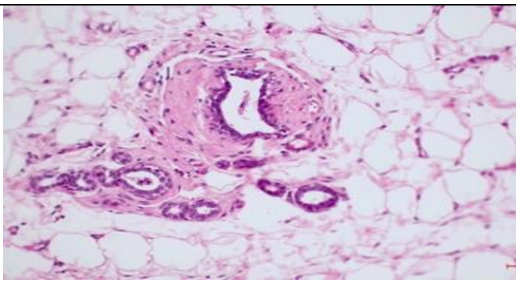
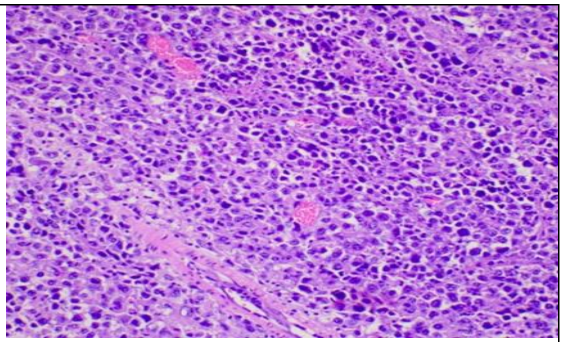
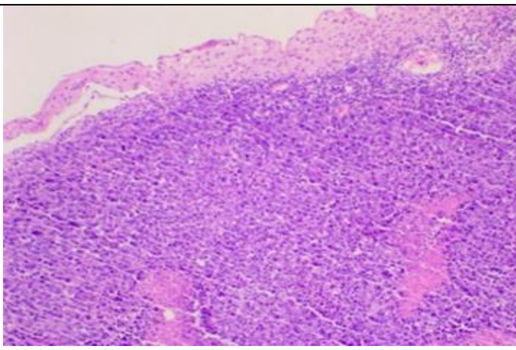
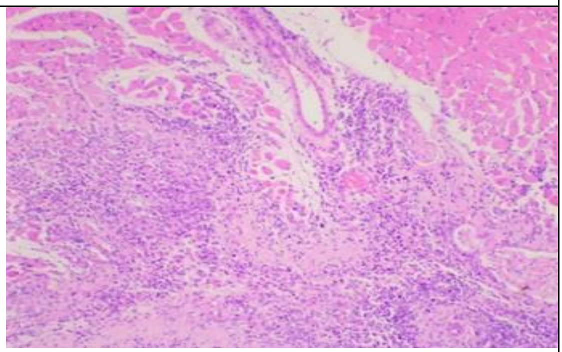
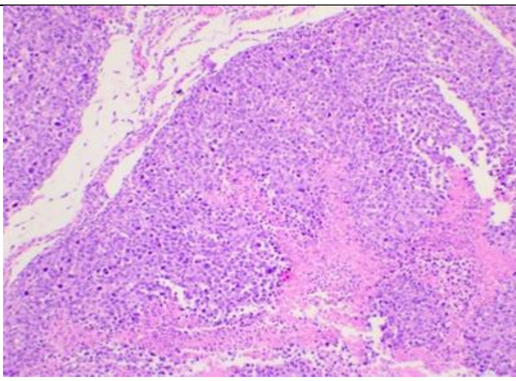
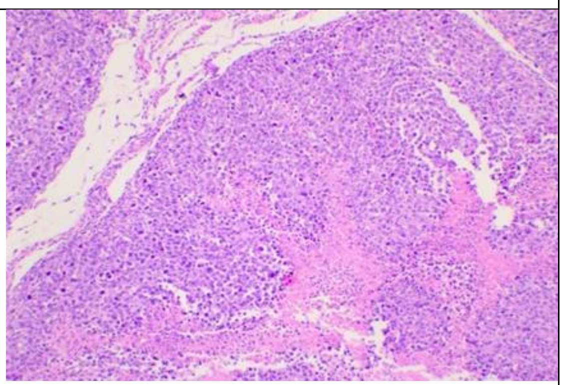
Xylene (or its substitutes; e.g., Histosol®, Neoclear®, and Histoclear®) has the advantage to be miscible in both alcohol and paraffin. As a result, the tissue sample is dehydrated and fully infiltrated by paraffin.

Once tissue samples are infiltrated by paraffin, they are removed from the cassettes and carefully positioned inside a metal base mold. This step is critical as correct orientation of the tissue is essential for accurate microscopic evaluation.

The mold is filled with melted paraffin and then immediately placed on a cooling surface. To trace each tissue specimen, the cassette with permanent tissue and study identification is placed on top of the metal base mold and incorporated in the paraffin block before cooling. In this manner, the cassette will be used as a base of the paraffin block for microtome sectioning (once the metal base mold is removed)

Anti-cancer activity:

Chemicals 3-(4,5–dimethyl thiazol–2–yl)–5–diphenyl tetrazolium bromide (MTT), Fetal Bovine serum (FBS), Phosphate Buffered Saline (PBS), Modified Eagle’s Medium (DMEM) and Trypsin were obtained from Sigma Aldrich Co, St Louis, USA. EDTA, Glucose and antibiotics from Hi-Media Laboratories Ltd., Mumbai. Dimethyl Sulfoxide (DMSO) and Propanol from E.Merck Ltd., Mumbai, India.The following results were seen in the breast tissue.

 **Negative control (Organ: Skin with Mammary Gland)**	 **Positive control (Organ: Skin with Mammary Gland)**
 **Standard (Organ: Tumour in the Skin)**	 **Test High Dose (Organ: Tumour in the Skin)**
 **Test High Dose (Organ: Skin with Tumour)**	 **Test low Dose (Organ: Skin with Tumour)**

Discussion

This study focuses on the development and evaluation of Ganoderma lucidum-based microspheres as a bioactive carrier for the sustained and targeted delivery of DTX. Ganoderma lucidum, a medicinal fungus known for its anticancer and immunomodulatory properties, provides a biodegradable polysaccharide matrix for encapsulation. The microspheres were formulated using an advanced encapsulation technique to achieve controlled and sustained drug release. Comprehensive physicochemical characterization confirmed the stability and efficiency of the formulation. The optimized microspheres exhibited a particle size of 150 µm, a high encapsulation efficiency (~94%), and a sustained drug release profile over 48 hours. Structural analyses via FTIR, DSC, and XRD confirmed the successful encapsulation of DTX in an amorphous form, enhancing its solubility. In vitro cytotoxicity studies against breast cancer cell lines demonstrated superior anticancer activity compared to free DTX, likely due to synergistic interactions between DTX and the bioactive components of Ganoderma lucidum. Further, in vivo pharmacokinetic and tumor regression studies in murine models indicated prolonged circulation time, increased tumor accumulation, and improved therapeutic efficacy with reduced systemic toxicity. Histopathological and bio distribution analyses validated the safety and biocompatibility of the formulation, demonstrating significant tumor size reduction while minimizing damage to major organs. Overall, this study successfully developed and optimized Ganoderma-based microspheres for the controlled and targeted delivery of DTX. The formulation exhibited enhanced anticancer efficacy, sustained drug release, and reduced systemic toxicity in both in vitro and in vivo models. These findings highlight the potential of Ganoderma-based microspheres as a promising biopolymer-based Nano carrier for breast cancer therapy, laying the foundation for future translational research in herbal-derived drug delivery systems

Conclusion

Docetaxel-loaded, Ganoderma microspheres were prepared using an ionic gelation method. The prepared microspheres were found to possess sui physico-chemical properties and the particle size range. The microspheres were found to release the drug to a maximum extent in the target tissue. This work adds to the already significant domain of targeted drug delivery systems, which holds a promising alternative over the conventional means. In vitro release indicated that the DTX microspheres had a well-sustained release efficacy and in vivo studies showed that the microspheres were found to release the drug to a maximum extent in the target tissue (mammary gland). The optimized formulation (F6) could be effectively internalized into metastatic 4T1 breast cancer cells in vitro. The optimized microspheres exhibited a particle size of 150 µm, a high encapsulation efficiency (~94%), and a sustained drug release profile over 48 hours. 60 µg/mL or an equivalent concentration of the formulation did not significantly affected the viability of 4T1 cells, but dramatically decreased the cell migration activities. In metastatic breast cancer model, intravenously administered optimized formulation have efficiently delivered to the tumor sites, resulting in a 52.61% of cell death with 47.39% of cell viability. The prepared microspheres were found to possess sui Physico-chemical properties and the particle size range. The sustained release of DTX from microspheres revealed its applicability as drug delivery system to minimize the exposure of healthy tissues while increasing the accumulation of therapeutic drug in target sites efficiently delivered to the tumor sites, resulting in a 96.3% inhibition of tumor growth with 3.77% of cell death and a 93.5% reduction of lung metastases. The prepared microspheres were found to possess suitable physico-chemical properties and the particle size range. The sustained release of DTX from microspheres revealed its applicability as drug delivery system to minimize the exposure of healthy tissues while increasing the accumulation of therapeutic drug in target sites.

Conflicts of Interest

The authors declare no conflicts of interest.

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