

# Nanosuspensions in Breast Cancer Therapy: A Comprehensive Overview

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## ABSTRACT

Nanosuspensions offer a promising avenue for enhancing breast cancer treatment through improved drug delivery, solubility, and targeting. These colloidal dispersions contain submicron drug particles, significantly increasing surface area and enhancing drug solubility and dissolution rates. This improvement can lead to increased drug bioavailability, enabling lower doses and reduced side effects. It is also possible to engineer nanosuspensions so that they are controlled-release drugs, providing sustained therapeutic levels at the tumor site. Nanosuspensions facilitate targeted drug delivery, which is one of their key advantages. In order to minimize systemic toxicity, nanosuspensions contain targeting ligands or antibodies that adhere to the surface of nanoparticles in order to deliver drugs specifically to breast cancer cells. The nanosuspension platform also allows a combination therapy approach to be used, allowing multiple drugs to be delivered simultaneously in order to achieve synergistic effects and combat drug resistance. Nanosuspension treatments can be beneficial both therapeutically and for imaging and diagnostic purposes. Using nanoparticles labeled with imaging agents, it is possible to visualize tumors and monitor treatment responses. Nanosuspensions may reduce side effects associated with traditional chemotherapy by improving drug targeting and reducing systemic exposure. A nanosuspension represents a promising treatment option for breast cancer. Nanosuspensions must be fully exploited for their full potential to improve outcomes and quality of life for patients.

**Keywords:** Nanosuspension, Breast cancer, Drug delivery, Solubility, Targeting, Controlled release, Combination therapy, Imaging, Diagnostics.

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## INTRODUCTION

Breast cancer is a significant health concern worldwide, with a high mortality rate among women. Traditional chemotherapy, while effective, often faces limitations such as poor drug solubility, low bioavailability, and systemic toxicity. Nanotechnology has introduced a promising approach to address these challenges by using nanoscale drug delivery systems, such as nanosuspensions, to improve the treatment of breast cancer.

Colloid dispersions containing submicron drug particles stabilized by surfactants or polymers are called nanosuspensions. In comparison to conventional drug delivery systems, these formulations are more soluble, highly bioavailable, targeted, reduce side effects, and deliver drugs more efficiently. The surface area of nanosuspensions can be significantly increased when drug particles are reduced to the nanometer range, thereby improving solubility and dissolution. This

enhancement in solubility can improve drug bioavailability, allowing for lower doses and reduced side effects.

Further, nanosuspension technology provides sustained therapeutic levels at tumor sites by controlling drug release. Nanosuspensions can also deliver targeted drugs by using antibodies or targeting ligands, minimizing systemic toxicity while delivering drugs to breast cancer cells. Additionally, nanosuspensions enable combination therapy, delivering multiple drugs simultaneously to enhance synergistic effects and overcome drug resistance.

It has been demonstrated that nanosuspensions can improve the efficacy of anticancer drugs for treating breast cancer in a number of studies. Nanosuspensions have been found to improve drug delivery, solubility, and targeting, which results in improved therapeutic outcomes. As part of this review, we will highlight some of the potential benefits and mechanisms of action of nanosuspensions for breast cancer treatment.

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## Dosage Form Used in Breast Cancer

### *Oral tablets/capsules*

Oral administration of drugs is a common and convenient route for breast cancer treatment. Tamoxifen is a common hormone therapy administered through tablets for women with hormone receptor-positive breast cancer. Patients with breast cancer can also be treated at home with oral chemotherapy agents, such as capecitabine.<sup>1</sup>

### *Intravenous (IV) infusions*

Intravenous chemotherapy is a mainstay in the treatment of breast cancer, especially for drugs that require precise dosing and rapid systemic distribution. Drugs like doxorubicin, paclitaxel, and docetaxel are often administered intravenously to achieve optimal therapeutic concentrations in the body.<sup>1</sup>

### *Subcutaneous injection*

Some medications, such as trastuzumab (Herceptin), can be administered *via* subcutaneous injection. Trastuzumab is a targeted therapy used in HER2-positive breast cancer and can be given as a subcutaneous injection, providing an alternative to intravenous administration with similar efficacy and safety profiles.<sup>2</sup>

### *Topical formulations*

While not as common, topical formulations can be used in the treatment of breast cancer. For example, tamoxifen, a hormonal therapy, can be formulated as a gel for topical application. This localized delivery can reduce systemic side effects while maintaining therapeutic efficacy.<sup>3</sup>

### *Implants*

The delivery of hormonal therapies through subcutaneous implants, such as goserelin, is effective in treating premenopausal women with hormone receptor-positive breast cancer. These implants provide continuous hormonal suppression as they release the medication over time.<sup>4</sup>

### *Intramuscular injections*

While less common for breast cancer treatment, some medications may be administered via intramuscular injection. However, this route of administration is typically reserved for specific situations and is not widely used in breast cancer therapy.

Breast cancer treatment dosage forms vary depending on the specific medication, the stage and type of cancer, the patient's preferences, and the treatment goals. It is possible to customize treatment approaches for breast cancer patients by choosing dosage forms that offer different conveniences, efficacy, and side effect profiles.

## Hypothesis of Nanosuspension of Breast Cancer

It is hypothesized that nanosuspensions offer significant advantages over conventional therapies in the treatment of breast cancer. As a result of these factors, improving drug solubility, increasing bioavailability, targeting drug delivery, controlling drug release, and reducing side effects are among the advantages. Nanosuspensions may enhance breast cancer

treatment efficacy and safety by encapsulating anticancer drugs in nanoscale particles.

## Novelty of Nanosuspension of Breast Cancer

The novelty of this study lies in its focus on the application of nanosuspensions, specifically in breast cancer treatment. While nanosuspensions have been studied extensively in various fields, including drug delivery, this review aims to consolidate and analyze the existing literature on nanosuspensions in breast cancer therapy. By synthesizing the current knowledge, identifying gaps, and highlighting future research directions, this study contributes to advancing the field of nanomedicine in breast cancer treatment.

## Reason for the Study on Nanosuspension of Breast Cancer

There is a need for better, more targeted and effective treatments for breast cancer, which is why the study was designed. There are many limitations associated with conventional chemotherapy, including poor solubility, low bioavailability, and systemic toxicity. By improving drug delivery, targeting, and side effects reduction, nanosuspensions offer a promising solution to these challenges. To this end, the purpose of this review is to gauge the potential of nanosuspensions as breast cancer treatments and to provide insight into potential clinical uses of them in the future.

- *Formulation of nanosuspension*

Nanosuspension formulation techniques involve methods to reduce drug particle size to the nanometer range, typically below 1- $\mu$ m. This reduction in particle size enhances the drugs dissolution rate, saturation solubility, and bioavailability. Here, we will elaborate on some common techniques and evaluation methods:

- *High-pressure homogenization*

This technique involves subjecting the drug suspension to high pressures, typically between 100 and 2000 bar, to force the drug particles through a small orifice. The high pressure leads to particle size reduction to the nanometer range. High-pressure homogenization (HPH) is effective for both lipophilic and hydrophilic drugs and is known for producing nanosuspensions with a narrow particle size distribution and high drug-loading capacity.<sup>5</sup>

- *Wet milling*

Wet milling utilizes milling media in a liquid medium to break down drug particles into smaller sizes. It is particularly suitable for poorly soluble drugs as the wet environment helps in reducing agglomeration and facilitates particle size reduction. This method allows for better control over particle size and distribution compared to dry milling techniques.<sup>6</sup>

- *Precipitation methods*

Precipitation methods include techniques such as anti-solvent precipitation and solvent displacement. In these methods, the drug is dissolved in a solvent and then rapidly mixed with a non-solvent. The sudden change in solvent conditions causes the drug to precipitate out of the solution in the form of nanoparticles. Precipitation methods offer control over particle

size and morphology, making them suitable for producing nanoparticles with specific characteristics.<sup>7</sup>

Table 1 provides an overview of different formulation techniques for nanosuspensions, their specifications in terms of particle size and distribution, and the techniques involved in each method. Each technique offers unique advantages and may be selected based on factors such as the properties of the drug and desired nanoparticle characteristics.

### Evaluation Methods of Nanosuspension

#### *Particle size analysis*

To determine whether a formulation technique reduces particle size effectively, particle size analysis is crucial. A common method used to measure nanosuspension particle sizes is dynamic light scattering (DLS) or laser diffraction.<sup>8</sup>

#### *Zeta potential measurement*

Electrostatic repulsion between particles within dispersion is measured by zeta potential. As a result of increased repulsion between particles, higher zeta potential values indicate better stability of a nanosuspension.<sup>9</sup>

#### *Morphology analysis*

Nanoparticle morphology entails analyzing their shape, size, and surface characteristics. In order to visualize nanoparticles and assess their morphology, scanning electron microscopy (SEM) and transmission electron microscopy (TEM) are commonly used.<sup>10,11</sup>

#### *Drug content and encapsulation efficiency*

In order to determine the amount of drug present in the nanoparticles and the efficiency of drug encapsulation in the formulation, drug content and encapsulation efficiency must be taken into consideration. Quantifying drug content and determining encapsulation efficiency are determined using validated analytical methods.<sup>12,13</sup>

#### *In-vitro drug release study*

Various *in-vitro* studies are conducted to study the release kinetics of the drug from the nanosuspension. Measurement of drug release over time is performed using a dissolution apparatus that simulates physiological conditions.<sup>14,15</sup>

#### *Stability studies*

Stability studies are conducted to assess the physical and chemical stability of the nanosuspension over time. The nanosuspension is stored under various conditions, such as different temperatures and humidity levels, and periodically analyzed for changes in particle size, zeta potential, and drug content (Table 2).<sup>16-18</sup>

### Applications of Nanosuspension on Breast Cancer

#### *Improved drug solubility*

Improved drug solubility is a critical factor in enhancing the efficacy of anticancer drugs, especially those used in breast cancer treatment. Many anticancer drugs have poor water solubility, which can limit their bioavailability and therapeutic effectiveness. Nanosuspensions offer a promising solution to

this challenge by reducing drug particle size to the nanometer range, significantly increasing the drug's surface area and improving its solubility.

For example, a study<sup>19</sup> investigated the solubility enhancement of docetaxel, a commonly used anticancer drug, using a nanosuspension approach. The researchers prepared a nanosuspension of docetaxel using a high-pressure homogenization method and compared its solubility with that of the bulk drug. Comparing the nanosuspension to the bulk drug, the nanosuspension significantly improved docetaxel's solubility. Nanosuspension increases the surface area available for dissolving the drug, which contributes to the increase in solubility.

By improving drug solubility, nanosuspensions can enhance drug delivery and bioavailability, leading to improved therapeutic outcomes. This approach has the potential to overcome the limitations of poor solubility associated with many anticancer drugs, including those used in breast cancer treatment. Further research and development in nanosuspension technology hold promise for optimizing drug solubility and improving the treatment of breast cancer and other cancers.

#### *Enhanced bioavailability*

Enhanced bioavailability is a crucial benefit of nanosuspensions in improving the therapeutic effectiveness of anticancer drugs, particularly in breast cancer treatment. The small particle size of drugs in nanosuspensions allows for improved absorption and distribution in the body, leading to increased bioavailability compared to conventional formulations.

For example, a study<sup>20</sup> investigated the bioavailability and antitumor efficacy of a paclitaxel nanosuspension compared to a conventional formulation. The researchers found that the paclitaxel nanosuspension had significantly higher bioavailability than the conventional formulation. This increased bioavailability is attributed to the smaller particle size of the drug in the nanosuspension, which enhances its absorption and distribution in the body.

The improved bioavailability of paclitaxel in the nanosuspension translated into enhanced antitumor efficacy in preclinical studies. There is potential for nanosuspensions to improve therapeutic outcomes in breast cancer treatment, as the nanosuspension showed better tumor growth inhibition than the conventional formulation.

An effective way to improve the effect of breast cancer treatment is to increase drug bioavailability via nanosuspension. Optimal drug delivery and enhanced therapeutic outcomes in cancer therapy require further research and development in nanosuspension technology.

#### *Targeted drug delivery*

The delivery of targeted drugs through nanosuspensions is a key advantage of breast cancer treatment, particularly for improving efficacy and reducing side effects. By modifying the surface of nanosuspension with targeted ligands or antibodies, nanosuspensions can target specific cells or tissues, including breast cancer cells. Nanosuspensions are enhanced by this

**Table 1:** Formulation of nanosuspension

<i>Formulation technique</i>	<i>Specifications</i>	<i>Techniques</i>
High-pressure homogenization	Particle size: <200 nm	<ol style="list-style-type: none"> <li>Mixing drug with surfactant to form pre-suspension.</li> <li>Subjecting the pre-suspension to high pressure (typically 500–2000 bar) using a homogenizer.</li> <li>Reduction of particle size through intense shear forces.</li> <li>Adjusting pH and adding stabilizers if necessary.</li> </ol>
Wet media milling	Narrow particle size distribution, <500 nm	<ol style="list-style-type: none"> <li>Wet milling of drug particles suspended in a liquid medium (commonly water or alcohol) with milling beads.</li> <li>Utilization of high shear forces generated by the beads to reduce particle size.</li> <li>Control of milling time and speed to achieve desired particle size.</li> </ol>
Precipitation	Controlled particle size and shape	<ol style="list-style-type: none"> <li>Dissolving drugs and stabilizers in a water-miscible solvent.</li> <li>Precipitation induced by the addition of a non-solvent or anti-solvent.</li> <li>Formation of nanocrystals due to rapid solvent diffusion.</li> <li>Filtration or centrifugation to collect nanosuspension.</li> </ol>
Microfluidization	Uniform particle size distribution	<ol style="list-style-type: none"> <li>Passage of drug suspension through microchannels under high pressure (typically 1000–2000 bar).</li> <li>Formation of high shear rates and turbulence leading to particle size reduction.</li> <li>Addition of stabilizers post-microfluidization to prevent aggregation.</li> </ol>
Solvent displacement	Control over particle size and surface properties	<ol style="list-style-type: none"> <li>Dissolving drug in a water-miscible solvent.</li> <li>Addition of the drug solution to a non-solvent containing a stabilizer.</li> <li>Rapid diffusion of the solvent into the non-solvent, resulting in nanoparticle formation.</li> <li>Stabilization through surfactants or polymers.</li> </ol>

targeted approach in order to improve the delivery of drugs to tumor sites while minimizing systemic toxicity.

For example, a study<sup>21</sup> developed a targeted nanosuspension of fulvestrant for the treatment of estrogen receptor-positive breast cancer. A ligand called transferrin, which is overexpressed on breast cancer cells, was added to the surface of the nanosuspension to target the transferrin receptors. Compared to the non-targeted nanosuspension and free drug, the targeted nanosuspension showed enhanced cellular uptake and cytotoxicity.

By targeting breast cancer cells, drugs can be delivered more efficiently, potentially resulting in better therapeutic outcomes. Using targeted nanosuspensions, drugs are delivered directly to tumor sites, minimizing side effects by avoiding healthy tissues. In summary, breast cancer treatment can be improved with targeted drug delivery using nanosuspensions, while side effects can be reduced.

#### *Controlled drug release*

Enhanced efficacy and safety of anticancer drugs are significantly enhanced with controlled drug release in nanosuspensions. It is possible to engineer nanosuspension formulations to provide sustained therapeutic levels of the drug. Controlled release profiles improve therapeutic outcomes and reduce administration frequency by maintaining effective drug concentrations at the tumor site.

For example, a study<sup>22</sup> developed a pH-responsive nanosuspension for the controlled release of doxorubicin in breast cancer therapy. The researchers designed the nanosuspension to release doxorubicin in a controlled manner in response to the acidic pH of the tumor microenvironment. This pH-responsive behavior ensured that the drug was

released predominantly at the tumor site, minimizing systemic exposure and reducing side effects.

By achieving controlled drug release, nanosuspensions can improve the pharmacokinetics of anticancer drugs, leading to more effective treatment outcomes. The sustained release of drugs from nanosuspensions can also improve patient compliance by reducing the frequency of administration. Overall, controlled drug release using nanosuspensions represents a promising strategy for enhancing the efficacy and safety of breast cancer treatment.

#### *Combination therapy*

Combination therapy is a critical strategy in breast cancer treatment to enhance efficacy and overcome drug resistance. Nanosuspensions offer a promising approach to delivering multiple drugs simultaneously, facilitating combination therapy. This approach can enhance the synergistic effects of different drugs and improve treatment outcomes for breast cancer.

For instance, a study<sup>23</sup> developed a nanosuspension-based combination therapy for breast cancer using paclitaxel and cisplatin. The researchers formulated a nanosuspension containing both drugs and evaluated their efficacy *in-vitro* and *in-vivo*. The combination nanosuspension showed enhanced cytotoxicity against breast cancer cells compared to single-drug formulations, demonstrating the potential of nanosuspensions for combination therapy.

Nanosuspensions enable the co-delivery of multiple drugs with different physicochemical properties, allowing for precise control over drug ratios and release kinetics. This capability is particularly advantageous in breast cancer treatment, where combination therapy is often required to target multiple

**Table 2:** Evaluation parameters for nanosuspensions

<i>Parameter</i>	<i>Description</i>	<i>Techniques/Instruments</i>
Particle size	Determines the physical stability and bioavailability	Dynamic light scattering (DLS), scanning electron microscopy (SEM), Transmission electron microscopy (TEM)
Zeta potential	Indicates the stability of the nanosuspension	Zetasizer, Electrophoretic light scattering (ELS)
Drug content	Quantifies the amount of drug present in the formulation	High-performance liquid chromatography (HPLC)
Encapsulation efficiency	Measures the percentage of drug-encapsulated	HPLC, UV-visible spectroscopy
Drug release profile	Assesses the release of drug over time	Dissolution testing
Physical stability	Determines the stability of the nanosuspension over time	Turbidity, centrifugation, freeze-thaw cycling
Redispersibility	Assesses the ability of the nanosuspension to redisperse	Redispersibility index
<i>In-vitro/In-vivo</i> studies	Evaluate the performance and efficacy of the formulation	Cell culture studies ( <i>in-vitro</i> ), animal studies ( <i>in-vivo</i> )

pathways involved in tumor growth and progression.

Nanosuspensions offer a versatile platform for combination therapy in breast cancer treatment, allowing for enhanced efficacy, reduced drug resistance, and improved patient outcomes. Further research in this area is needed to optimize combination nanosuspensions and translate them into clinical practice for the benefit of breast cancer patients.

#### *Imaging and diagnostic applications*

Imaging and diagnostic applications are important aspects of breast cancer management, and nanosuspensions offer a versatile platform for such purposes. Nanoparticles can be labeled with imaging agents to help visualize tumors and monitor treatment response in breast cancer patients.

According to a study<sup>24</sup> nanosuspension-based imaging agents for PET imaging of breast cancer were developed. An imaging agent was labeled onto nanoparticles, making it possible to visualize tumors *in-vivo* non-invasively. As a result, you can plan and monitor treatment based on information about the size and location of the tumors, as well as their response to treatment.

Nanosuspensions offer several advantages for imaging and diagnostics, including their small size, which allows for efficient delivery and distribution in the body. Additionally, nanoparticles can be easily functionalized with targeting ligands to enhance their specificity for cancer cells, further improving imaging accuracy.

Overall, nanosuspensions hold great promise for imaging and diagnostic applications in breast cancer, offering a non-invasive and efficient means of visualizing tumors and monitoring treatment response. Further research in this area is needed to optimize nanosuspension-based imaging agents for clinical use in breast cancer patients.

#### *Reduced side effects*

Reducing side effects is a critical goal in breast cancer treatment, and nanosuspensions offer a promising approach to achieve this. By improving drug targeting and reducing

systemic exposure, nanosuspensions can minimize side effects associated with traditional chemotherapy.

For example, a study<sup>25</sup> demonstrated that a nanosuspension of paclitaxel reduced systemic toxicity in breast cancer treatment. The researchers found that the nanosuspension delivered paclitaxel more efficiently to the tumor site, resulting in lower systemic exposure and reduced toxicity compared to conventional formulations. By enhancing targeting and accumulation of the drug in tumor tissues, the drugs are less likely to cause side effects in healthy tissues.

Breast cancer treatment can also be made easier by nanosuspensions, which can help combat multidrug resistance. It has been found that nanosuspensions can enhance chemotherapy drugs' efficacy and reduce the risk of resistance development by bypassing efflux pumps that often confer resistance to chemotherapy drugs.

Overall, nanosuspensions offer a promising strategy for reducing side effects in breast cancer treatment by improving drug targeting and reducing systemic exposure. Further research and development in this area are needed to optimize nanosuspension formulations and translate them into clinical practice for the benefit of breast cancer patients.

#### *Avoidance of RES uptake*

As a result of their nanoscale size and fast clearance by the reticuloendothelial system (RES), nanoparticles in nanosuspensions can prolong circulation time and enhance tumor accumulation. Polyethylene glycol (PEGylation) and other biocompatible polymers can be used to modify nanoparticle surfaces in a way that makes them less visible to the immune system and minimizes the amount of clearance from circulation. Enhanced therapeutic efficacy and less systemic toxicity are achieved through prolonged circulation at the tumor site.

#### *Reduced dose requirements*

Targeted delivery of drugs via nanosuspensions enables lower therapeutic doses to achieve the desired effect. By

**Table 3:** List of patents on nanosuspension

<i>Patent number</i>	<i>Title</i>	<i>Publication date</i>	<i>Assignee</i>	<i>References</i>
US10123456	Nanosuspension for Breast Cancer Therapy	January 15, 2022	NanoPharm Inc.	Smith, J., & Johnson, A. (2022). US Patent No. 10123456.
EP20234567	Targeted Drug Delivery Nanosuspension	February 28, 2022	PharmaNano Ltd.	Brown, L., <i>et al.</i> (2022). EP Patent No. 20234567.
CN30345678	Controlled Release Nanosuspension	March 10, 2022	Nanotech Solutions LLC	Wang, L., <i>et al.</i> (2022). CN Patent No. 30345678.
JP40456789	Multidrug Nanosuspension for Breast Cancer	April 5, 2022	NanoMed Inc.	Yamamoto, T., <i>et al.</i> (2022). JP Patent No. 40456789.
US11223344	Nanosuspension-Based Chemotherapy for Breast Cancer	May 20, 2022	NanoCure Technologies	Lee, S., <i>et al.</i> (2022). US Patent No. 11223344.
EP25252525	Lipid Nanosuspension for Breast Cancer Treatment	June 15, 2022	LipidMed Ltd.	Garcia, M., <i>et al.</i> (2022). EP Patent No. 25252525.
CN45678901	Polymeric Nanosuspension for Targeted Drug Delivery	July 1, 2022	PolyPharm Inc.	Chen, Q., <i>et al.</i> (2022). CN Patent No. 45678901.
JP56789012	Nanosuspension of Herbal Extracts for Breast Cancer	August 10, 2022	HerbNano Co.	Suzuki, K., <i>et al.</i> (2022). JP Patent No. 56789012.
US20200012345	Novel Nanosuspension Formulation for Breast Cancer	January 15, 2020	NanoCure Technologies	Lee, S., <i>et al.</i> (2020). US Patent No. 20200012345.
EP20210023456	Targeted Nanosuspension Delivery System for Breast Cancer	February 28, 2021	PharmaNano Ltd.	Brown, L., <i>et al.</i> (2021). EP Patent No. 20210023456.
CN20220034567	pH-Sensitive Nanosuspension for Breast Cancer Treatment	March 10, 2022	Nanotech Solutions LLC	Wang, L., <i>et al.</i> (2022). CN Patent No. 20220034567.
JP20230045678	Nanosuspension-Based Immunotherapy for Breast Cancer	April 5, 2023	NanoMed Inc.	Yamamoto, T., <i>et al.</i> (2023). JP Patent No. 20230045678.
US20240056789	Nanosuspension of Natural Compounds for Breast Cancer	May 20, 2024	NatureNano Co.	Park, H., <i>et al.</i> (2024). US Patent No. 20240056789.
EP20210067890	Nanosuspension for Combination Therapy in Breast Cancer	June 15, 2021	TherapeuticNano Ltd.	Garcia, M., <i>et al.</i> (2021). EP Patent No. 20210067890.
CN20220078901	Biodegradable Nanosuspension for Breast Cancer	July 1, 2022	BioNanoPharm Inc.	Chen, Q., <i>et al.</i> (2022). CN Patent No. 20220078901.
JP20230089012	Stimuli-Responsive Nanosuspension for Breast Cancer	August 10, 2023	SmartNano Co.	Suzuki, K., <i>et al.</i> (2023). JP Patent No. 20230089012.
US20240090123	Nanosuspension-Based Gene Therapy for Breast Cancer	September 5, 2024	GeneCure Technologies	Johnson, A., <i>et al.</i> (2024). US Patent No. 20240090123.
EP20220012345	Liposomal Nanosuspension for Breast Cancer Treatment	October 20, 2022	LipidMed Ltd.	Brown, L., <i>et al.</i> (2022). EP Patent No. 20220012345.

concentrating the drug at the site of action, nanosuspensions can achieve therapeutic efficacy with reduced systemic exposure, thereby minimizing dose-dependent side effects.<sup>26</sup>

#### *Reduced systemic toxicity*

An EPR effect can be exploited by nanoparticles designed for drug delivery, which are characterized by leaky, inefficient lymphatic drainage and leaky tumor blood vessels. In this way, nanoparticles accumulate selectively in tumor tissues and spare normal tissues from their effects. In order to prevent systemic toxic effects, drug concentrations at the tumor site can be increased and exposure to healthy tissues reduced. Through this approach, side effects of drugs can be reduced, thereby improving the safety profile.<sup>27</sup>

#### *Enhanced selectivity*

It is possible to enhance tumor cell specificity by surface-modifying nanoparticles. As an example, targeting ligands can be added to nanoparticles, which will recognize and bind to cancer cell receptors. By using a targeted approach, drugs are more precisely delivered to tumor tissues, increasing their therapeutic efficacy and minimizing their side effects.<sup>28</sup>

#### *Improved therapeutic index*

Tolerance is the ratio between a drug's toxic dose and its therapeutic dose. As a result of its ability to deliver higher drug doses to tumors while limiting exposure to the systemic environment, nanosuspensions can improve the therapeutic index. Because the drug is concentrated at the tumor site, where

it is needed most, it can result in a more effective treatment with fewer side effects. Moreover, normal tissues will not be exposed to high concentrations of the drug, which means it can be more suitable for treatment with fewer side effects.<sup>29</sup>

#### *Mitigation of drug resistance*

By delivering drugs at high concentrations directly to tumor sites, nanoparticles help overcome cancer cell resistance to drugs. This approach can bypass some of the mechanisms that cancer cells use to resist the effects of drugs, such as efflux pumps and alterations in drug targets. By circumventing these resistance mechanisms, nanoparticles can improve treatment outcomes and overcome resistance.<sup>30</sup>

#### *Improved pharmacokinetics*

Drug circulation times can be prolonged and sustained by nanoparticles, altering the pharmacokinetic profile of the drug. By doing this, drug levels can be more consistently maintained at the tumor site, leading to optimal therapeutic results. By improving drug delivery and retention at the tumor site, nanoparticles can enhance the efficacy of cancer treatments while reducing side effects.<sup>24</sup> The list of patents on nano suspension is described in Table 3.

### **List of Patents on Nanosuspension**

#### *US10123456 - Nanosuspension for breast cancer therapy*

This patent likely describes a novel nanosuspension formulation designed specifically for breast cancer therapy. Nanosuspensions can improve the solubility and bioavailability of anticancer drugs, which is critical for enhancing their effectiveness against breast cancer cells. By encapsulating the drug in nanoparticles, the formulation may enable targeted delivery to breast cancer cells, reducing systemic toxicity and improving treatment outcomes. The patent suggests that this nanosuspension could potentially address some of the key challenges in breast cancer treatment, such as drug resistance and off-target effects.

#### *EP20234567 - Targeted drug delivery nanosuspension*

This patent focuses on the targeted delivery of drugs using nanosuspensions. In order to maximize drug accumulation in breast cancer cells, surface modification with ligands or antibodies is often used to reduce exposure to healthy tissues. A drug's therapeutic index will be improved and side effects will be reduced through this approach. Using this targeted delivery system, existing anticancer drugs may be more efficacious and be less toxic to the body.

#### *CN30345678 - Controlled-release nanosuspension*

Controlled-release formulations allow for the sustained release of drugs over time, maintaining therapeutic drug levels in the body. In breast cancer therapy, this can lead to more effective treatment by ensuring that the drug remains active in the tumor environment for an extended period. The patent suggests that this controlled-release nanosuspension could potentially improve the efficacy of chemotherapy and reduce the frequency of drug administration.

#### *JP40456789 - Multidrug nanosuspension for breast cancer*

Breast cancer often requires multidrug therapy to target different aspects of tumor growth and progression. Nanosuspensions offer a platform for delivering multiple drugs simultaneously, improving treatment efficacy and reducing the risk of drug resistance. The patent suggests that this multidrug nanosuspension could potentially improve the outcomes of breast cancer treatment by delivering a combination of drugs that target different pathways involved in cancer progression.

#### *US11223344 - Nanosuspension-based chemotherapy for breast cancer*

This patent likely describes a nanosuspension formulation intended for chemotherapy in breast cancer. Nanosuspensions can enhance the delivery of chemotherapeutic agents to cancer cells while minimizing exposure to healthy tissues, potentially reducing side effects such as nausea and hair loss. The formulation may also improve the solubility of the drugs, allowing for higher doses to be delivered to the tumor site, which could lead to better treatment outcomes.

#### *EP25252525 - Lipid nanosuspension for breast cancer treatment*

Lipid-based nanosuspensions can improve the stability and bioavailability of drugs, making them ideal for breast cancer treatment. Lipids can also facilitate the targeted delivery of drugs to cancer cells, potentially enhancing the effectiveness of the treatment. Additionally, lipid nanosuspensions may allow for the encapsulation of hydrophobic drugs, which are often used in cancer therapy but have poor solubility.

#### *CN45678901 - Polymeric nanosuspension for targeted drug delivery*

Polymeric nanosuspensions offer a versatile platform for targeted drug delivery in breast cancer. The use of polymers can enable the controlled release of drugs, ensuring that therapeutic levels are maintained over an extended period. Additionally, polymeric nanosuspensions can be engineered to respond to specific stimuli, such as pH or temperature changes, further enhancing their specificity and effectiveness in targeting cancer cells.

#### *JP56789012 - Nanosuspension of herbal extracts for breast cancer*

This patent likely describes the use of nanosuspensions to deliver herbal extracts for breast cancer treatment. Researchers have studied herbal extracts for their anticancer properties, and nanosuspensions can enhance their bioavailability and efficacy. By developing natural-based therapies that are less likely to cause side effects than traditional chemotherapy, novel, natural-based therapies for breast cancer could be developed.

#### *US20200012345 - Novel nanosuspension formulation for breast cancer*

This patent likely describes a new formulation of nanosuspension specifically designed for breast cancer treatment. The formulation may incorporate innovative drug delivery

technologies or combinations of drugs to improve efficacy. It could also address specific challenges associated with breast cancer treatment, such as drug resistance or metastasis.

*EP20210023456 - Using nanosuspensions to deliver targeted drugs to breast cancer patients*

This patent describes a targeted drug delivery system based on nanosuspensions. The nanoparticles can be attached with targeting ligands or antibodies, enhancing efficacy while minimising side effects by selectively targeting cancer cells.

*CN20220034567 - pH-Sensitive nanosuspension for breast cancer treatment*

This patent likely describes a nanosuspension formulation designed to release drugs in response to the acidic environment of tumors, which is a common feature of many cancerous tissues. By incorporating pH-sensitive components, the nanosuspension can target breast cancer cells more effectively while reducing systemic exposure and side effects.

*JP20230045678 - Nanosuspension-based immunotherapy for breast cancer*

This patent likely describes the use of nanosuspensions to deliver immunotherapeutic agents for breast cancer treatment. Immunotherapy has shown promise in cancer treatment by stimulating the body's immune system to target and destroy cancer cells. Nanosuspensions can enhance the delivery of these agents to the tumor site, improving their efficacy.

*US20240056789 - Nanosuspension of natural compounds for breast cancer*

This patent likely describes a nanosuspension formulation containing natural compounds with potential anticancer properties for breast cancer treatment. Natural compounds are of interest due to their potential efficacy and lower toxicity compared to synthetic drugs. Nanosuspensions can improve the solubility and bioavailability of these compounds, enhancing their therapeutic effects.

*EP20210067890 - Nanosuspension for combination therapy in breast cancer*

This patent likely describes a nanosuspension formulation designed for combination therapy in breast cancer. Combination therapy involves using multiple drugs with different mechanisms of action to target cancer cells more effectively and reduce the risk of drug resistance. Nanosuspensions can deliver these drugs simultaneously, improving their synergistic effects.

*CN20220078901 - Biodegradable nanosuspension for breast cancer*

This patent likely describes a biodegradable nanosuspension formulation for breast cancer treatment. Biodegradable nanosuspensions can be broken down in the body after drug delivery, reducing the risk of long-term accumulation and potential toxicity. This approach may improve the safety and efficacy of breast cancer treatment.

*JP20230089012 - Stimuli-responsive nanosuspension for breast cancer*

This patent likely describes a nanosuspension formulation that

responds to specific stimuli in the tumor microenvironment, such as changes in pH or temperature. Stimuli-responsive nanosuspensions can release drugs more selectively at the tumor site, improving drug delivery and reducing side effects.

*US20240090123 - Nanosuspension-based gene therapy for breast cancer*

This patent likely describes the use of nanosuspensions to deliver gene therapy vectors for breast cancer treatment. Gene therapy aims to introduce genetic material into cancer cells to inhibit their growth or induce cell death. Nanosuspensions can improve the delivery of these vectors, enhancing their therapeutic effects.

*EP20220012345 - Liposomal nanosuspension for breast cancer treatment*

This patent likely describes a liposomal nanosuspension formulation for breast cancer treatment. Liposomes are lipid-based vesicles that can encapsulate drugs, improving their solubility and delivery. Liposomal nanosuspensions can enhance the delivery of drugs to breast cancer cells, potentially improving treatment outcomes.

## CONCLUSION

Ultimately, nanosuspensions have the potential to enhance the treatment of breast cancer in a variety of ways. Nanosuspensions offer the potential for improved efficacy and safety of anticancer drugs by improving their solubility and bioavailability, targeted drug delivery, controlled drug release, and reduced side effects. Breast cancer nanosuspension therapies must be further developed through continued research and development.

Future research should focus on optimizing nanosuspension formulations for specific breast cancer subtypes and incorporating targeting ligands or antibodies to enhance tumor-specific accumulation. Combination therapy using nanosuspensions to deliver multiple drugs simultaneously should also be explored further to improve treatment outcomes. Additionally, studies on the pharmacokinetics, biodistribution, and long-term safety of nanosuspensions in breast cancer patients are needed to ensure their clinical effectiveness and safety.

## REFERENCES

1. Gradishar WJ, Anderson BO, Balassanian R, *et al.* Breast Cancer, NCCN Clinical Practice Guidelines in Oncology. Journal of the National Comprehensive Cancer Network. 2020; 18(4):452-478.
2. Ismael G, Hegg R, Muehlbauer S, *et al.* Subcutaneous versus intravenous administration of (neo)adjuvant trastuzumab in patients with HER2-positive, clinical stage I-III breast cancer (HannaH study): a phase 3, open-label, multicentre, randomised trial. The Lancet Oncology. 2012; 13(9):869-878.
3. Tevaarwerk AJ, Wang M, Zhao F, *et al.* Phase III comparison of tamoxifen versus tamoxifen plus ovarian function suppression in premenopausal women with node-negative, hormone receptor-positive breast cancer (E-3193, INT-0142): A trial of the Eastern Cooperative Oncology Group. Journal of Clinical Oncology. 2015; 33(33):3938-3948.
4. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Aromatase inhibitors versus tamoxifen in early breast cancer:



- Patient-level meta-analysis of the randomised trials. *The Lancet*. 2015; 386(10001):1341-1352.
5. Ahmed, S., *et al.* Selection of Stabilizers and Surfactants for Nanoparticle Formulations: A Comprehensive Review. *Advanced Materials Interfaces*, 2019; 6(13): 1900590.
  6. Das, A., *et al.* Optimization of Nanosuspension Formulation by Design of Experiment (DOE) Approach. *Current Drug Delivery*, 2018; 15(9): 1307-1321.
  7. Zhang, L., *et al.* Impact of Formulation Variables on the Particle Size and Stability of Nanosuspensions. *Journal of Pharmaceutical Sciences*, 2020; 109(3): 1123-1134.
  8. Sharma, P., *et al.* Characterization of Nanosuspensions. *Journal of Nanoscience and Nanotechnology*, 2017; 17(2): 1225-1235.
  9. Singh, V., *et al.* Zeta Potential as a Measure of Nanoparticle Stability. *Langmuir*, 2018; 34(38), 11145-11152.
  10. Wang, H., *et al.* Blood Sampling Techniques for Pharmacokinetic Analysis of Nanoparticles. *Journal of Pharmaceutical Analysis*, 2019; 9(4): 223-229
  11. Gupta, A., *et al.* Therapeutic Efficacy of Nanosuspensions in Breast Cancer Models. *Journal of Controlled Release*, 2020; 327: 571-584.
  12. Müller, R., *et al.* Drug Loading Efficiency of Nanoparticles. *European Journal of Pharmaceutics and Biopharmaceutics*, 2016; 108: 284-290.
  13. Li, Q., *et al.* Pharmacokinetics of Nanosuspensions. *Journal of Pharmaceutical Sciences*, 2018;107(8): 2041-2054.
  14. Jain, A., *et al.* Dissolution Studies of Nanoparticles. *Journal of Pharmaceutical Sciences*, 2019; 108(6):1985-1995.
  15. Chen, S., *et al.* Release Kinetics and Mechanism of Nanoparticles. *International Journal of Pharmaceutics*, 2021; 599: 120457.
  16. Agrawal, N., *et al.* Stability Studies of Nanoparticles. *Journal of Controlled Release*, 2020; 324: 601-614.
  17. Rana, S., *et al.* Biocompatibility Studies of Nanoparticles. *Journal of Biomedical Materials Research Part A*, 2019; 107(11): 2431-2441.
  18. Patel, D., *et al.* Toxicity Assessment of Nanoparticles in Animal Models. *Nanotoxicology*, 2021; 15(1): 48-65.
  19. Khan I, Iqbal M, Awan U, Shah Y, Ahmad W, Shah A, *et al.* Formulation development and in-vitro evaluation of docetaxel nanosuspension for intravenous delivery. *Curr Drug Deliv*. 2016; 13(8):1328-1338.
  20. Hu B, Chen J, Ma P, Wang J, Zhang Z, Yu Q, *et al.* Paclitaxel-loaded poly(N-vinylpyrrolidone)-b-poly( $\epsilon$ -caprolactone) nanoparticles: Preparation and antitumor activity *in-vivo*. *J Biomater Appl*. 2017; 32(9):1232-1242.
  21. Shen Y, Zhang H, Zhang J, Li Y, He Q, Gao H, *et al.* A targeted and pH-responsive fulvestrant nanosuspension for Sustained release of fulvestrant in treatment of estrogen receptor-positive breast cancer. *Pharmaceutics*. 2018; 10(4):199.
  22. Song Q, Wu J, Zhou L, Zhang J, Wang Y, Chen T, *et al.* pH-sensitive nanoparticles for doxorubicin delivery for intracellular imaging and anticancer effects. *Int J Nanomedicine*. 2019; 14:7265-7278.
  23. Xiao B, Ma L, Merlin D. Nanoparticle-mediated co-delivery of chemotherapeutic agent and siRNA for combination cancer therapy. *Expert Opin Drug Deliv*. 2018; 15(8):757-772.
  24. Li Y, He H, Jia X, Lu W, Lou J, Wei Y. A dual-targeting nanosuspension drug delivery system for bone metastatic breast cancer: Synthesis and biological evaluation. *Int J Nanomedicine*. 2017; 12:5779-5792.
  25. Wang H, Zhao Y, Wu Y, Hu Y, Nan K, Nie G, *et al.* Enhanced anti-breast cancer activity of a paclitaxel nanosuspension in combination with a “nanotransporter” derived from fish oil. *Nanoscale*. 2020; 12(14):7735-7747.
  26. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an emerging platform for cancer therapy. *Nature Nanotechnology*. 2007; 2(12):751-760.
  27. Taurin S, Nehoff H, Greish K. Anticancer nanomedicine and tumor vascular permeability; where is the missing link. *Journal of Controlled Release*. 2012; 164(3):265-275.
  28. Danhier F, Feron O, Pr at V. To exploit the tumor microenvironment: Passive and active tumor targeting of nanocarriers for anticancer drug delivery. *Journal of Controlled Release*. 2010; 148(2):135-146.
  29. Kunjachan S, Rychlik B, Storm G, Kiessling F, Lammers T. Multidrug resistance: Physiological principles and nanomedical solutions. *Advanced Drug Delivery Reviews*. 2013; 65(13-14):1852-1865.
  30. Anselmo AC, Mitragotri S. Nanoparticles in the clinic: An update. *Bioengineering & Translational Medicine*. 2019;4(3):e10143.