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Review Article

Nanotechnology based drug delivery in cancer treatment: enabling controlled and targeted release of medications

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ABSTRACT

The advent of nanotechnology in drug delivery has revolutionized cancer treatment, offering controlled and targeted release of therapeutic agents. This study investigates the impact and effectiveness of various nanoparticle-grounded drug delivery systems (DDSs) in cancer therapy. A qualitative analysis of secondary literature was conducted to explore the types, targeting mechanisms, and clinical applications of nanoparticles (NPs) in cancer treatment. The study categorized NPs into organic, inorganic, and hybrid types and examined their roles in passive and also active targeting of cancer cells. The findings reveal the significant diversity and efficacy of NPs in enhancing drug delivery efficiency while minimizing systemic toxicity. Notable examples of clinically approved nanotherapeutic formulation medications include Doxil®, Myocet®, and Abraxane®, which have shown improved drug pharmacokinetics and biodistribution. Nanotechnology offers transformative potential in cancer therapy, providing promising avenues for the development of advanced and personalized cancer therapeutics.

Keywords: Nanotechnology, Cancer Therapy, Nanoparticles, Targeted Drug Delivery, Nanomedicine

INTRODUCTION

Cancer remains one of the most formidable challenges in modern medicine, with its treatment often plagued by the limited efficacy and severe side effects of traditional therapies. In recent years, the advent of nanotechnology has offered new avenues for the development of targeted and efficient cancer therapies.[1]

The emergence of nanotechnology has ushered in a new era in cancer therapy, offering innovative approaches to drug delivery that promise enhanced efficacy and reduced side effects. Nanoparticles (NPs), with their unique properties, have become key players in this field, enabling precise and targeted delivery of therapeutic agents to cancer cells.[2]

Nanoparticles come in various forms, categorized into organic, inorganic, and hybrid types, each offering distinct advantages in cancer therapy. Targeting cancer cells utilising nanoparticles represents a promising strategy to improve treatment outcomes while minimizing systemic toxicity.[4] Two primary mechanisms are employed: passive targeting, exploiting tumor-specific characteristics for NP accumulation, and active targeting, where ligands on NPs interact with specific receptors on cancer cells, ensuring precise delivery of therapeutic payloads.[5]

This study also explores the role of magnetic fields in cancer treatment, leveraging magnetic nanoparticles guided by external fields for targeted drug delivery. Additionally, the discussion covers emerging and current nanomedicines, highlighting approved formulations and

those undergoing clinical trials across various cancer types.

METHODS

Study design

This research utilized a qualitative approach to examine secondary source data concerning nanoparticles' application inside targeted cancer cell therapy. Qualitative methods were selected to facilitate a comprehensive exploration and understanding of keywords such as nanoparticles, cancer therapy, targeted therapy, and nanomedicines within existing literature, reports, or datasets. This methodology aimed to provide in-depth insights and perspectives on the topic under investigation.

Study period

The study period for the data were 2018 to 2024. This study employed a qualitative approach to systematically examine and synthesize secondary source data concerning the application of nanoparticles in targeted cancer cell therapy. The qualitative approach was chosen to enable a detailed exploration and interpretation of the existing literature, allowing for the identification of key themes, patterns, and emerging trends. Through secondary analysis, we categorized and the data based on recurring concepts and relationships within the studies. This process involved iterative reading and re-reading of the selected articles to ensure a deep understanding of the content. The qualitative methodology facilitated an in-depth analysis that went beyond mere data aggregation, providing rich insights into the nuances of nanoparticle applications in cancer therapy. This approach allowed us to capture the complexity and context of the findings, thereby contributing to a more comprehensive and interpretative synthesis of the existing knowledge.

Inclusion criteria

For this study, studies included reports, or datasets that specifically addressed nanoparticles' application inside targeted cancer cell therapy from time period from 2018 to 2024. This study considered peer-reviewed journal articles, and conference papers, and research reports published within the last five years to explore the research questions in-depth., and datasets written in the English language and we focused on materials related to the keywords: nanoparticles, cancer therapy, targeted therapy, and nanomedicines.

Exclusion criteria

In our selection process, we excluded studies, reports, or datasets that were irrelevant to nanoparticles' application inside targeted cancer cell therapy. Duplicate publications, including multiple versions of the same study or dataset, were excluded. Additionally, materials lacking sufficient detail or relevance to our research objectives were excluded from consideration.

Data collection

Data for this research study were collected from secondary sources using a systematic search strategy. As following steps.

Systematic search strategy

A systematic search was conducted across several electronic databases, including PubMed, Web of Science, and Google scholar. Keywords and search strings related to nanoparticles, cancer therapy, targeted therapy, and nanomedicines were used to identify relevant literature, reports, and datasets.

Screening and selection

Identified records were screened for relevance based on inclusion and exclusion criteria. This process involved reviewing titles, abstracts, and full texts where necessary. Reference lists from selected articles were manually screened to include additional relevant studies not captured in the initial search.

Data Extraction

Relevant data were extracted from selected sources, focusing on information related to the application of nanoparticles in targeted cancer cell therapy. This included details on nanoparticle types, targeting methods, and clinical applications.

Outcome measure

For this study, the outcome measures were derived from the qualitative analysis of secondary source data pertaining to nanoparticles in targeted cancer cell therapy. These outcome measures aimed to provide a comprehensive understanding of the current landscape of nanotherapeutic formulations, targeting cancer cells, and potential future directions in utilizing nanoparticles for targeted cancer cell therapy. Additionally, the study sought to identify key themes, patterns, and emerging trends within the literature, reports, and datasets analyzed, thereby contributing to the body of knowledge in this field.

Data analysis

The collected secondary data underwent analysis to identify key parameters. This involved reviewing the data to understand the different types of nanoparticles (NPs), Target cancer cells and nanomedicine in clinical use. The findings were interpreted and synthesized to provide a comprehensive understanding of the role of nanotechnology in enabling controlled and targeted release of medications for cancer treatment.

RESULTS

The advent of nanotechnology has revolutionized cancer treatment by enabling controlled and targeted release of therapeutic agents, boosting drug efficacy while minimizing side effects. Nanoparticles (NPs) facilitate this by leveraging mechanisms such as passive targeting, which uses the enhanced permeability and retention (EPR) effect, alongside active targeting, which involves ligand-receptor interactions. Additionally, magnetic fields can guide magnetic NPs to tumor sites, further enhancing targeted drug delivery. These methods allow NPs to overcome biological barriers, selectively deliver drugs to tumor tissues, and improve treatment efficacy while reducing systemic toxicity. The table exemplifies the effectiveness of targeted nanomedicine, showcasing nano systems like liposomes and polymeric nanoparticles with targeting ligands, ensuring higher drug concentration at tumor sites and demonstrating ongoing advancements in cancer treatment.

Different types of nanoparticles for cancer therapy

Nanoparticles (NPs) are utilized in DDSs for cancer therapy, categorized into organic, inorganic, and hybrid NPs as shown in Figure 1.

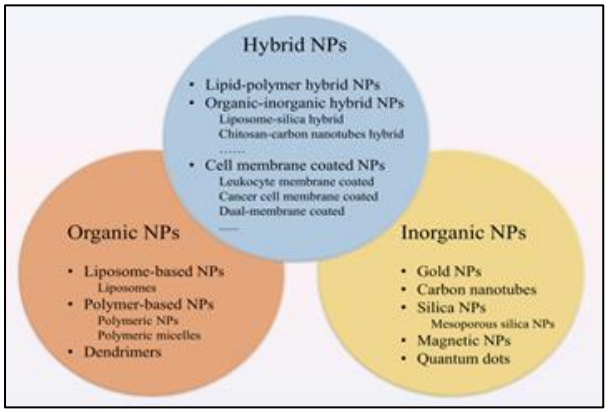

Figure 1: Different types of nanoparticles (NPs) for cancer therapy.

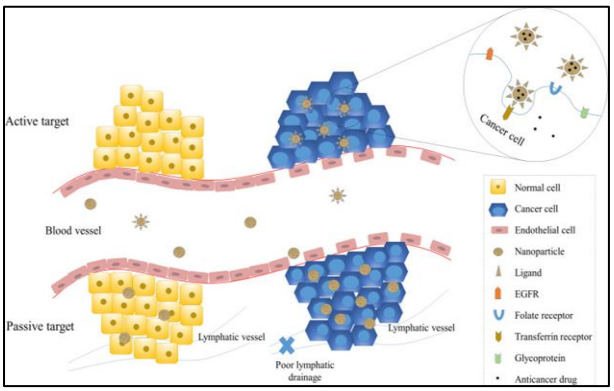

Figure 2: Passive and active targeting of NPs to cancer cells.

Targeting cancer cells with nanoparticles

Targeting cancer cells with nanoparticles (NPs) represents a promising approach in cancer therapy, aiming to enhance drug delivery efficiency while minimizing systemic toxicity. This strategy involves two primary mechanisms: passive targeting, leveraging tumor-specific characteristics to accumulate NPs within the cancerous tissue, and active targeting, where Magnetic fields are utilized in cancer treatment to guide magnetic nanoparticles to tumor sites, enabling targeted drug delivery and enhancing therapeutic outcomes.

Through these mechanisms, NPs can conquer biological barriers and selectively deliver drugs to tumor sites, improving treatment efficacy and dropping side effects. In this context, understanding the intricacies of NP targeting to cancer cells is indispensable for developing advanced and personalized cancer therapeutics.

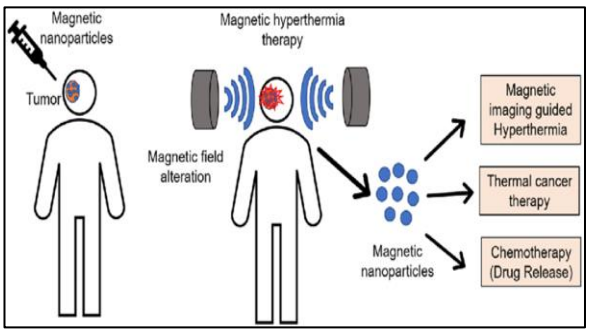

Figure 3: Magnetic field for cancer treatment.

Emerging and current nanomedicines and targeting methods: focus on cancer

The goal of achieving comprehensive cancer treatment is still challenging due to the diverse and unique characteristics of various malignancies, as well as the challenge of specifically focusing therapeutic interventions to cancerous areas without causing injury to healthy tissues. The majority of anticancer drugs that are now used in recognized therapy protocols are disseminated throughout the body, without specifically targeting cancerous tissue. The extensive diffusion of chemotherapeutics throughout the body results in both desired anticancer effects and unintended off-target deleterious effects.

Now, the FDA has only granted approval for a limited number of nanotherapeutic and diagnostic materials to be used in clinical settings. However, there are several more that are now undergoing preclinical and clinical development. Due to their lack of specific design for targeting biological entities, the majority of these products are classified as first-generation nanomedicines. This table 3 lists various nanotherapeutic formulations, including their type, active compound, therapeutic indication, and current status in clinical trials or approval.

The formulations encompass both liposomal and polymeric nanoparticle systems, highlighting their applications in different cancer types and stages of clinical development.

First generation of clinically approved nanomedicines

Among various nano systems, only a select few nanomedicines have gained approval for cancer treatment. Notable examples include Doxil®, Myocet®, DaunoXome®, Depocyt®, Abraxane®, Genexol-PM®, and Oncaspar®. These nanocarriers have significantly improved drug pharmacokinetics and biodistribution, enhancing drug accumulation in tumor tissues. However, challenges such as limited controlled release and stability persist with liposome-based nanocarriers. [6]

Despite these challenges, polymeric nanocarriers like Genexol-PM® show promise with their high drug-loading capacity along with controlled release capabilities. These advancements open avenues for the clinical translation of controlled-release polymeric nanoparticles, offering solutions for various challenges in nanomedicine. The development of biocompatible and biodegradable materials such as PLA, PLGA, PCL, poly (glutamic acid), and poly (amino acids) further enhances the potential of polymeric-based drug delivery systems.[7]

Targeted nanosystems in clinical use for anticancer therapy

This Table 4 exemplifies the effectiveness of targeted nanomedicine in cancer therapy by showcasing various nano systems designed for specific delivery of anticancer agents. Each entry demonstrates the use of liposomes and polymeric nanoparticles conjugated with targeting ligands, such as transferrin or antibody fragments, to direct therapeutic compounds like doxorubicin and siRNA to cancer cells.

These targeted approaches ensure higher drug concentration at the tumor site, enhancing treatment efficacy while minimizing systemic toxicity. The clinical phases of these nano systems further illustrate the ongoing advancements and validation of targeted nanotechnology in improving cancer treatment outcomes.

Table 1: Passive and active targeting of nanoparticles to cancer cells.

Targeting Method	Description
Passive Targeting	Achieved through the enhanced permeability and retention (EPR) effect, which takes advantage of increased vascular permeability and weakened lymphatic drainage in tumor tissues, allowing nanoparticles (NPs) to accumulate more in cancer cells passively.
Active Targeting	Involves interaction between ligands on NPs and specific receptors on cancer cells, such as transferrin receptors, folate receptors, glycoproteins (like lectins), and epidermal growth factor receptor (EGFR), enabling NPs to specifically target and deliver drugs to cancer cells more effectively.

Table 2: Magnetic field for cancer treatment.

Method	Description
Magnetic micro- and nanoparticles	Used as drug carriers for specific targeting, directed to tumor sites by external magnetic fields.
Superparamagnetic Fe3O4 nanoparticles	Synthesized with pentaerythritol poly(ε-caprolactone) micelles, these demonstrate effective doxorubicin (DOX) delivery under high-frequency magnetic fields, showing significant drug release (51.5%) and enhanced intercellular uptake within 0.5 hours of incubation.
Magnetically driven paclitaxel delivery systems	Incorporating iron oxide in a palmitoyl chitosan matrix, these systems leverage magnetic fields for precise drug delivery, inducing enhanced cell death through hyperthermic effects.
Silica magnetic nano capsules	Loaded with camptothecin and doxorubicin, these show dramatic changes in drug release when magnetic fields are toggled, effectively reducing tumor growth in mice.
Superparamagnetic nickel ferrite nanoparticles	Functionalized and conjugated with doxorubicin, these enhance drug release rates under magnetic fields by generating mechanical deformation, ejecting drug molecules effectively.

Table 3: Approved and investigational nanotherapeutic formulations for cancer treatment.

Name	Formulation	Bioactive compound	Indication	Status
Liposomes				
DaunoXome®	Non-Pegylated liposomes	Daunorubicin	Kaposi's sarcoma	Approved
Myocet®	Non-Pegylated liposomes	Doxorubicin	Breast cancer	Approved
Onco TCS®	Non-Pegylated liposomes	Vincristine	Non-Hodgkin's lymphoma	Approved
Depocyt®	Non-Pegylated liposomes	Cytarabine	Leukemia, Glioblastoma	Phase III, Phase I/II
Doxil®/Caelyx®	Pegylated liposomes	Doxorubicin	Breast cancer, ovarian cancer, multiple myeloma, Kaposi's sarcoma	Approved
Thermodox®	Pegylated liposomes	Doxorubicin	Liver cancer, breast cancer	Phase III
SPI-77	Pegylated liposomes	Cisplatin	Ovarian cancer	Phase II
NL CPT	Pegylated liposomes	Irinotecan	Glioma	Phase I
Polymeric nanoparticles				
Genexol-PM®	PEG-poly (lactic acid)	Paclitaxel	Breast cancer, lung cancer, ovarian cancer	Phase II
NK105	PEG-poly (aspartic acid)	Paclitaxel	Gastric cancer, breast cancer	Phase I, Phase III
NK911	PEG-poly (aspartic acid)	Doxorubicin	Various solid tumors	Phase II
Opaxio™	PGA-paclitaxel	Paclitaxel	Lung cancer, ovarian cancer	Phase III
CRLX101	PEG-cyclodextrin	Camptothecin	Non-small-cell lung cancer	Phase II
NC-6004	PEG-poly (glutamic acid)	Cisplatin	Pancreatic cancer	Phase II
Other				
ProLindac™	HPMA	DACH-Pt	Ovarian cancer	Phase II
Abraxane®	Albumin-based	Paclitaxel	Breast cancer	Approved
Paclical®	Micellar retinoid-derived	Paclitaxel	Ovarian cancer	Phase III
NC-4016	Micellar PEG/polyamino acid	Oxaliplatin	Various solid tumors	Phase I/II
Oncaspar®	PEG-L-asparaginase	Asparagine-specific enzyme	Acute lymphoblastic leukemia	Approved

DISCUSSION

The findings of this study underscore the transformative potential of nanotechnology in revolutionizing cancer therapy. By analyzing secondary source data, we gained valuable insights into the diverse applications of nanoparticles (NPs) in targeted cancer cell therapy. The discussion focuses on several key aspects highlighted by the study, including the role of NPs in enhancing drug delivery efficiency, the mechanisms of passive and active targeting, and the current landscape of nanotherapeutic formulations for cancer treatment. One of the significant contributions of NPs to cancer therapy lies in their ability to improve drug delivery efficiency while minimizing systemic toxicity. A study by Kumar et al.[2] Investigated the efficacy of liposome-based nanoparticles in delivering chemotherapeutic agents to tumor sites. Their findings demonstrated a significant improvement in drug accumulation within cancerous tissues, leading to enhanced therapeutic outcomes with reduced systemic toxicity. Research by Raj et al focused on the application of magnetic nanoparticles for targeted drug delivery in cancer therapy.[6] They reported successful localization of drug-loaded magnetic nanoparticles to tumor sites using external magnetic fields, resulting in precise drug delivery and improved treatment efficacy. Rodriguez et al explored the potential of cell membrane-coated nanoparticles in cancer therapy.[9] Their study highlighted the synergistic effects of combining organic and inorganic nanoparticles, leading to enhanced cellular uptake and improved anticancer activity in preclinical models. The study highlights diverse nanotherapeutic formulations in clinical use or under investigation for cancer treatment, including liposomes and polymeric nanoparticles, offering advantages in drug loading, controlled release, and biocompatibility.[12] Notable examples like Doxil®, Myocet®, DaunoXome®, Abraxane®, Genexol-PM®, and Oncaspar® have shown significant improvements in pharmacokinetics and biodistribution over conventional formulations. Recent findings by Parodi et al investigated the controlled release capabilities of polymeric nanoparticles in cancer therapy.[10] Their study demonstrated the potential of polymeric nanocarriers, such as Genexol-PM®, in overcoming challenges associated with liposome-based formulations, offering controlled drug release and enhanced therapeutic efficacy.[11]Nanomedicine has shown great promise in treating a variety of diseases, including cancer, by precisely targeting specific cells and tissues. However, the field is not without challenges. The main

challenge facing nanomedicine is the delivery of nanocarriers to the target site. Nanoparticles can undergo various mechanisms in the body, such as absorption by the reticuloendothelial system, which may lead to premature elimination.[13] Another challenge is the development of high-quality nanomaterials. Besides producing nanomaterials that require precise control of size, shape and surface properties, which can be difficult to achieve, the scalability of nanofabrication processes is another challenge that needs to be addressed role.[14]

In terms of safety and toxicity, there are concerns about the potential adverse effects of nanomaterials on living organisms. More research is needed on the toxicity and biocompatibility of different nanomaterials. Furthermore, the development of nanoparticles that can specifically target cancer cells is a challenging task. There is a need for a better understanding of the biological mechanisms of carcinogenesis and the development of nanoparticles that can effectively target and destroy cancer cells. Although nanomedicine shows great promise in the treatment of various diseases, many challenges remain to be overcome. Further research is needed to develop effective and safe nanomaterials, as well as to better understand their biological interactions. In summary improving drug loading efficiency, targeting specificity, and pharmacokinetics of NPs is crucial for advancing nanomedicine, with emerging technologies like nanotechnology-enabled diagnostics and theranostics offering promising personalized cancer treatment, though further interdisciplinary research and collaboration are necessary to address challenges and realize its full potential.

CONCLUSION

In conclusion, the results underscore the transformative impact of nanotechnology on cancer therapy, especially in enhancing targeted drug delivery. The study highlights the diversity and effectiveness of various nanoparticles (NPs) including organic, inorganic, and hybrid types in improving drug delivery efficiency and minimizing systemic toxicity. It elucidates both passive and active targeting mechanisms, demonstrating how NPs can exploit tumor-specific characteristics and ligand-receptor interactions for precise drug delivery. The exploration of magnetic field-guided magnetic nanoparticles further emphasizes the potential for targeted therapeutic outcomes. Additionally, the study sheds light on approved and investigational nanotherapeutic formulations, such as Doxil®, Myocet®, and Abraxane®, which have improved drug pharmacokinetics and biodistribution. Overall, the findings illustrate the significant advancements and promising future of nanotechnology-based cancer therapeutics.

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