Review Article

Exploring the potential of Nano carrier for cancer immunotherapy: A comprehensive review

Pavithra P.[1*], Raga Priya S.[1], Pritha K.[1], Priyanka S.[1], Rema A.[1], Pavazhaviji P.[2], Jayaraman Rajangam[1]

[1]*Department of Pharmacology, Shri Venkateshwara College of Pharmacy, Ariyur, Puducherry-605102*

[2]*Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Sciences, Technology and Advanced Studies, Pallavaram, Chennai, Tamil Nadu-600043*

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Abstract

The host immune system possesses an intrinsic ability to target and kill cancer cells in a specific and adaptable manner that can be further enhanced by cancer immunotherapy, which aims to train the immune system to boost the antitumor immune response. This review consists of various types of nano carriers used for cancer therapy. Several different categories of cancer immunotherapy have emerged as new standard cancer therapies in the clinic, including cancer vaccines, immune checkpoint inhibitors, adoptive T cell therapy, and oncolytic virus therapy. Despite the remarkable survival benefit for a subset of patients, the low response rate and immunotoxicity remain the major challenges for current cancer immunotherapy. Over the last few decades, nanomedicine has been intensively investigated with great enthusiasm, leading to marked advancements in nanoparticle platforms and nanoengineering technology.

***Keywords*:** Nanomedicine, immunotherapy, nanoengineering, vaccines, cancer

Introduction

Cancer presents considerable health risk with a significant mortality rate worldwide; according to American Cancer Society, around 1.9 million people were diagnosed with cancer in 2021, and the cancer-associated mortality is expected to reach 22 million by the year of 2030. Conventional cancer treatment methods, such as surgery, chemotherapy, and radiotherapy, have limited efficacy, particularly against advanced cancers with metastasis. Since William B. Coley reported the first systemic study of immunotherapy using bacterial toxins for the treatment of sarcoma in 1891 cancer immunotherapy has become a new treatment option for many different cancers. Cancer immunotherapy harnesses the host immune system by training immune cells to specifically recognize and kill cancer cells (García-Domínguez et al., 2024). Although radiotherapy and surgery are the most appropriate and beneficial therapies for non-metastatic and local malignancies, they are ineffective when the tumour cells are spread to other parts of the body. Cancer medications (such as biological, chemotherapy and hormonal treatments) may reach each organ in the body through the circulation; they are the present treatment of options for metastatic cancers (Kenchegowda et al., 2022). Currently, chemotherapeutic drugs are primarily administered to cancer patients via traditional oral and parenteral routes, which often encounter problems such as first-pass hepatic metabolism, poor bioavailability, severe systemic side effects, and patient incompliance (Liu and Falconer, 2025).

Nanocarriers

Nanocarriers can protect nucleic acids from enzymatic degradation, extend in vivo circulation, and enhance targeted delivery and cellular absorption for effective transcriptional regulation. Moreover, nanocarriers can be actively targeted by functionalization with tumor affinity ligands or passively targeted by increased permeation and rate (Song et al., 2017). For example, NP formation was shown to enhance the local transport of immuno adjuvants into peripheral lymphoid organs while limiting systemic distribution, maximizing immunological activity, and minimizing systemic immunotoxicity and can efficiently accumulate in lymphoid

Address for Corresponding Author:
Pavithra P.
Department of Pharmacology, Shri Venkateshwara College of Pharmacy, Ariyur, Puducherry-605102
Email: pavithrapharmacologist@gmail.com

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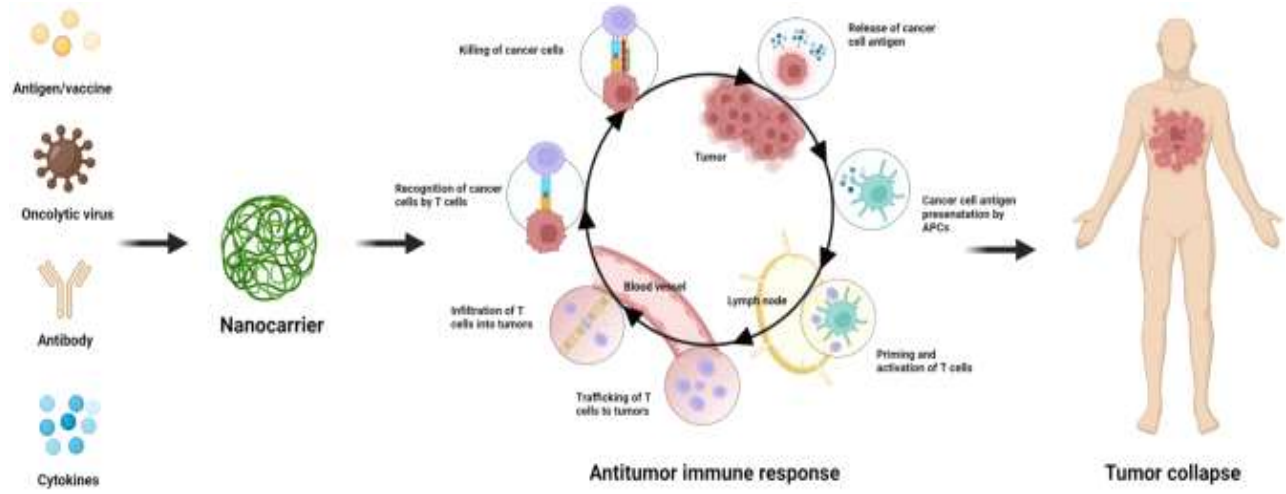

Figure 1. Mechanism of Nanocarrier (Rana et al., 2022)

organs and other immune target sites (Gurunathan et al., 2024).

Types of nano carriers

- Conjugates
- Polymeric
- Nanoparticles
- 4.lipid-based carriers
- Carbon nanotubes
- Dendrimers
- Gold nanoparticles.

Cancer vaccine

"Vaccines can be categorized into types based on the technology that they use to initiate an immune response". This technology is referred to as a 'vaccine platform'. Cancer vaccines are classified into cell-, peptide-, viral-, and nucleic acid-based ones (Gurunathan et al., 2024).

Different types of cancer vaccines

Cell-based cancer vaccines

Typically, whole or fragmented cells are used to create cell-based cancer vaccines, which almost contain tumor antigens and trigger stronger immune responses. DC

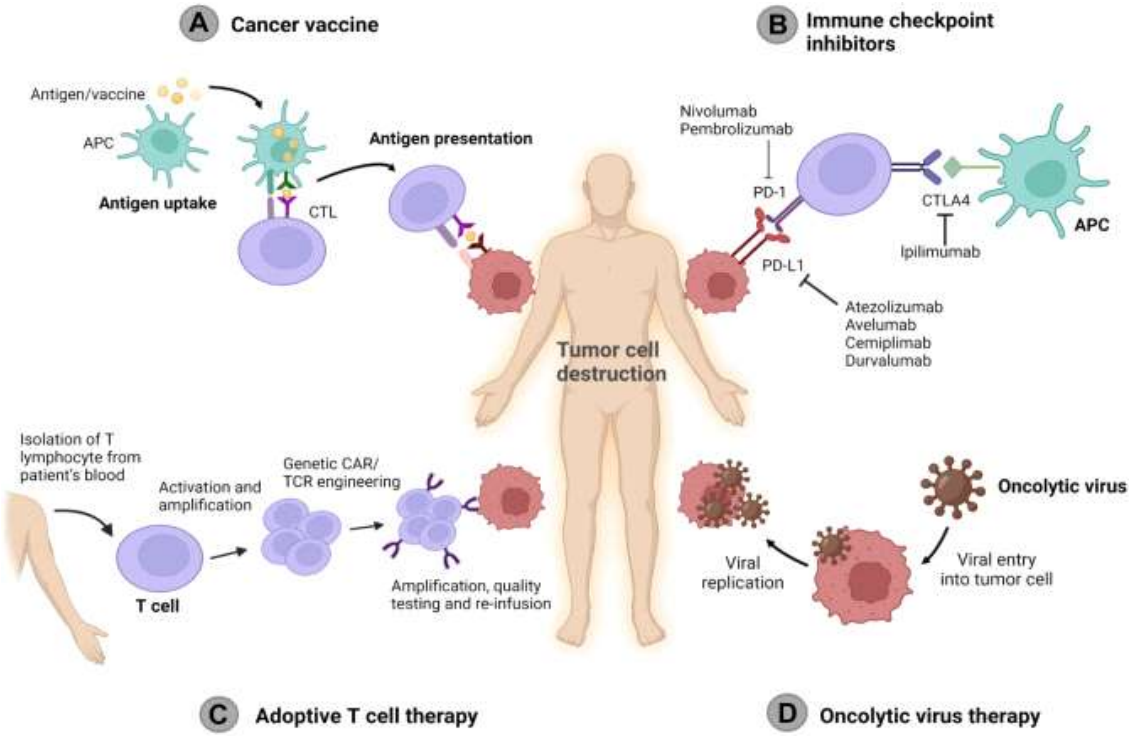

Figure 2. Cancer vaccine (Rana et al., 2022)

vaccines are a crucial subset of cell-based vaccines. Customized neoantigen cancer vaccines based on DCs have shown promising antitumor effects in clinical trials. However, DC vaccine development is constrained by laborious procedures and high costs. Tumor cell–based vaccination is a simple technique that uses allogeneic or autologous tumor cells obtained from patients to create cellular vaccines (Chiang et al., 2015). DCs derived from monocytes (Mo-DCs) and leukemia cells (DCleu) are the two primary types of DCs used in DC vaccines. DC cancer vaccines have been investigated in phase I, II, and III clinical trials because a sufficient number of DCs can be cultured (Gurunathan et al., 2024).

Virus-based cancer vaccines

Numerous viruses have immunogenic properties, and their genetic makeup can be altered to include TA-encoding genes. Consequently, viruses serve as the foundation for cancer vaccination. Adenoviruses, poxviruses, and alpha viruses are the most commonly used vaccine vectors (Hollingsworth and Jansen, 2019). Vaccines made from modified viruses can expose the immune system to numerous tumor antigens and thus achieve antitumor immunity. Vectors can also be created using oncolytic viruses. In addition to supplying tumor antigens, viruses can lyse tumors, release tumor antigens, boost vaccine efficiency, and create a long-lasting immunological memory (Gurunathan et al., 2024).

Nanotechnology in cancer diagnosis

Cancer diagnostic and therapeutic strategies are targeted at early detection and inhibition of cancerous cell growth and their spread. Notable among the early diagnostic tools for cancers is the use of positron emission tomography (PET), magnetic resonance imaging (MRI), computed tomography (CT) and ultrasound. These imaging systems, however, are limited by their inadequate provision of relevant clinical information about different cancer types and the stage. Hence it makes it difficult to obtain a full evaluation of the disease state based on which an optimum therapy can be provided (Jin et al., 2020)

Nanotechnology in cancer therapy and types of nanocarriers

1. OMV's nanocarriers

OMVs, i.e., nanosized proteoliposomes produced from the outer membranes of gram-negative bacteria, have average sizes of 50–300 nm and are therefore suitable carriers for the intracellular transport of antigens to APCs and lymph nodes, drawing considerable interest in cancer immunotherapy. From a safety perspective, OMVs are non-replicating particles that are safe and free of live bacterial cells. OMVs carrying RNA, DNA, endotoxins, proteins, and virulence compounds are representative examples of biochemical signaling involving the transport of bacterial OMVs. Given that bacterial OMVs contain immune stimulating danger signals as lipopolysaccharides, lipoproteins, and flagellin, which stimulate TLR4 and TLR5, respectively, they can be used as carriers and adjuvants for vaccine development (Hayashi et al., 2001). The development of OMV-based tumor nanovaccines depends on various factors, including the type of strain, OMV heterogeneity, efficacy of tumor antigen loading, immunogenicity, safety, and suitability for mass production (Gurunathan et al., 2024).

2. Biogenic nanocarriers

Biogenic nanocarriers, i.e., nanomaterials produced by organisms, exhibit high potential biocompatibility, high biodegradability, and low toxicity. Bacterial outer membrane vesicles (OMVs) and exosomes are prominent examples of biogenic nanocarriers. EVs, including exosomes, microvesicles, ectosomes, oncosomes, and apoptotic bodies, are lipid-based vesicles containing lipids, proteins, and nucleic acids generated by various cells and released into the surrounding environment (Raposo and Stoorvogel, 2013). Commensal and pathogenic bacteria create EVs that are classified as either micro vesicles (MVs) or OMVs, depending on whether they are produced by gram-positive or -negative bacteria, respectively. EVs produced by bacteria can influence the human immune system and induce pro-inflammatory reaction (Gurunathan et al., 2024).

3. Exosomes

Exosomes are nanovesicles with sizes of 30–150 nm. The phospholipid bilayer structures of exosomes enable stable drug transport, extend drug half-life during delivery, and protect drugs from enzymatic degradation. Additionally, exosome membranes can easily bind to target cells and thus increase the bioavailability of the loaded drugs. Compared to conventional drug carriers, such as liposomes, exosomes have poor immunogenicity and toxicity profiles (Yang et al., 2015). Commensal and pathogenic bacteria create EVs that are classified as either micro vesicles (MVs) or OMVs, depending on whether they are produced by gram-positive or -negative bacteria, respectively. EVs produced by bacteria can influence the human immune system and induce pro-inflammatory reaction (Gurunathan et al., 2024).

4. Cell membrane–coated nanocarriers

Cell membrane–coated nanocarriers hold considerable promise for biological applications. Depending on the type of the employed cell membrane, the resulting biomimetic nanoformulation has several properties that are typically associated with the source cell, including improved biocompatibility, immune evasion, and tumor targeting

Table 1: Nanomaterial-carrying drugs in clinical trials of cancer treatment

Nanocarriers	Year	Drugs	Disease	Findings
Liposome	OSOOME 2015	Doxorubicin	Platinum-Sensitive Ovarian Cancer	favorable risk-benefit profile
		Paclitaxel	Non-Small Cell Lung Cancer	considerable disease response, resection rate with acceptable toxicity
		Ursolic acid	Advanced Solid Tumors	tolerable, manageable toxicity, improving patient remission rates
		Mitomycin C	advanced cancer	long circulation time, tolerable, effective
	2016	miR-34a Mimic	Advanced Solid Tumors	Effective
		Vincristine Sulfate	Refractory Solid Tumors or Leukemias	without dose-limiting neurotoxicity
		5-fluorouracil and Leucovorin	Advanced Solid Tumors	lower peak plasma concentration, longer half-life, increased area
		Cytarabine	Childhood Acute Lymphoblastic Leukemia	no permanent adverse neurological sequelae
	2017	Amphotericin	Acute Lymphoblastic Leukaemia	Effective
		Irinotecan	Recurrent High-Grade Glioma	no unexpected toxicities
	2018	Cytarabine and Daunorubicin	Newly Diagnosed Secondary Acute Myeloid Leukemia	significantly longer survival rate
		Curcumin	Locally Advanced or Metastatic Cancer	Durable
		Daunorubicin	Pediatric Relapsed/ Refractory Acute Myeloid Leukemia	well-tolerated and showed high response rates
		Lipovaxin-MM	Malignant Melanoma	well-tolerated and without clinically significant toxicity
		Vincristine Sulfate	Acute Lymphoblastic Leukemia	provided a meaningful clinical benefit and safety
		Oligodeoxynucleotide	Refractory or Relapsed Haematological Malignancies (Jin et al., 2020)	well-tolerated, effective
	2019	Eribulin	Solid tumours	Well tolerated with a favourable pharmacokinetic profile
Polymeric materials	2017	Epirubicin	Solid tumours	Well tolerated in patients with various solid tumours and exhibited less toxicity than conventional equirubicin formulations
	2018	Genexol-PM plus carboplatin	Ovarian cancer	Non-inferior efficacy and well tolerated toxicities
	2019	Paclitaxel	Breast cancer	NK105 had a better PSN toxicity profile than PTX

(Feng et al., 2022). CNPs feature a synthetic nanoparticulate core covered by a layer of naturally derived cell membranes and therefore efficiently operate in complex biological environments. Cell membrane coating is more efficient in producing multifunctional and multiantigenic NPs than conventional functionalization techniques (Gurunathan et al., 2024). Cell membrane camouflage is another nanocarrier type used as a bioinspired platform for medication delivery. After the target cell membrane has been removed, as in the case of cancer cells, it is coated onto NP surfaces or used as a building block to create nanocarriers (Gurunathan et al., 2024).

5. Dendrimer NPs

Dendrimer NPs are thread-like polymers composed of dendritic repeating units with a central core. Typically, dendrimer NPs have optical size (1–100 nm), highly ordered structure, including a central core, multiple repeating branching units surrounding the central core, and terminal functional groups. It is worth mentioning that

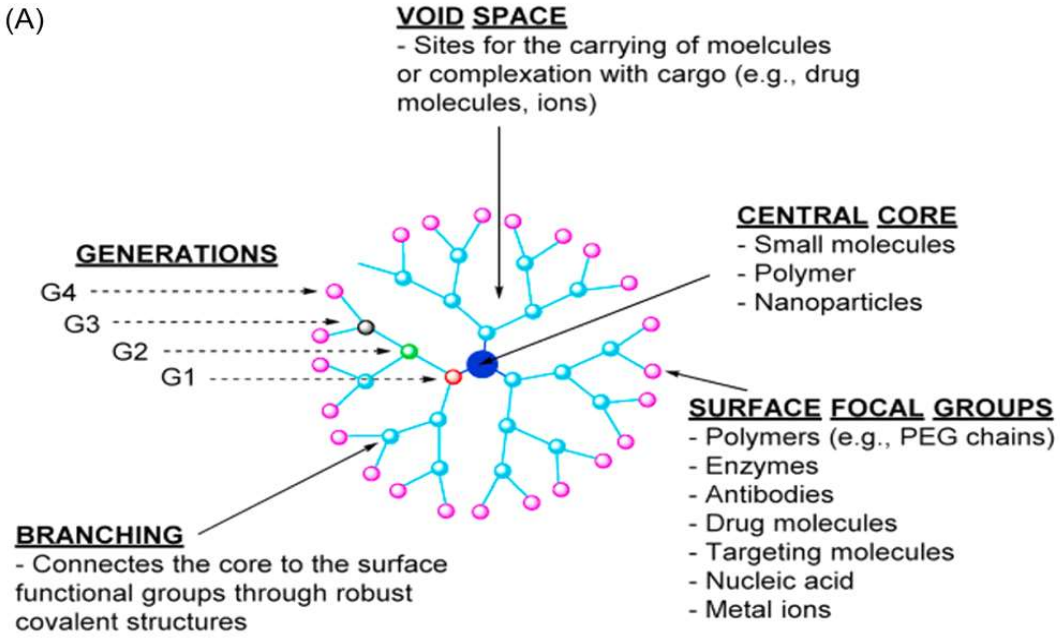

Figure 3. Dendrimer NPs

dendritic polymers have specific structures and properties that benefit drug delivery. For example, dendritic polymers have surface groups and internal cavities, which have allowed their widespread application as nanodelivery carriers in cancer therapy. With the help of hydrogen bonds, electrostatic or hydrophobic interactions, drugs can be encapsulated in dendritic cores. Additionally, drugs can be covalently linked to the terminal groups of dendritic polymers by chemical coupling, allowing for more stable drug delivery (Huang et al., 2024).

6. Biomimetic Nanoparticles

Biomimetic nanoparticles (BMNPs) are innovative nanovehicles that replicate the properties of naturally occurring extracellular vesicles, facilitating highly efficient drug delivery across biological barriers to target organs and tissues while ensuring maximal biocompatibility and minimal-to-no toxicity. BMNPs can be utilized for the delivery of therapeutic payloads and for imparting novel properties to other nanotechnologies based on organic and inorganic materials. The application of specifically modified biological membranes for coating organic and inorganic nanoparticles has the potential to enhance their therapeutic efficacy and biocompatibility, presenting a promising pathway for the advancement of drug delivery technologies. This manuscript is grounded in the fundamentals of biomimetic technologies, offering a comprehensive overview and analytical perspective on the preparation and functionalization of BMNPs, which include cell membrane-coated nanoparticles (CMCNPs), artificial cell-derived vesicles (ACDVs), and fully synthetic vesicles (fSVs). This review examines both "top-down" and "bottom-up" approaches for nanoparticle preparation, with a particular focus on techniques such as cell membrane coating, cargo loading, and microfluidic fabrication. Additionally, it addresses the technological challenges and potential solutions associated with the large-scale production and clinical application of BMNPs and related technologies (Tikhonov et al., 2024).

Conclusion

Genetic mutations can cause changes in the synthesis of certain biomolecules leading to uncontrolled cell proliferation and ultimately cancerous tissues. Cancers can be classified as either benign or malignant. Benign tumors are confined to the origin of cancer while malignant tumors actively shed cells that invade surrounding tissues as well as distant organs. The comprehensive examination of nanotechnology in cancer diagnostics indicates a potential area for customized treatment. Nanoparticles offer distinct benefits in targeted drug delivery, advanced imaging tools, and novel treatment approaches, such as photothermal therapy and controlled drug release. Their capacity to selectively target cancer cells while reducing adverse effects marks a paradigm leap in cancer treatment. However, challenges such as biocompatibility, toxicity, and integration with existing medicines remain, necessitating further research and development. Future prospects lead to predictive oncology, where nanotechnology might play a critical role in early detection, precision therapy, and improved cancer outcomes. Nanotheranostics has the potential to transform cancer therapy by linking diagnostics and treatments, enabling more effective, less invasive, and highly tailored methods (Al-Thani et al., 2024). In drug delivery, achieving optimal pharmacokinetics and

biodistribution is a significant challenge. The size, shape, surface charge, and surface chemistry of NPs can affect their interactions with biological systems and their ability to target specific cells or tissues. Additionally, there is a need for more effective methods for controlling the release of drugs from NPs and for optimizing their drug loading and encapsulation efficiency. While promising, animal studies and clinical trials highlight the potential of NP-based therapies. However, further research is imperative to thoroughly examine toxicity, clearance, scalability, regulation, stability, and biodistribution. Investigating the long-term safety and efficacy of NP-based therapies, along with assessing their reproducibility and cost-effectiveness, is crucial. This extensive research is essential to address regulatory challenges and ensure thorough safety and efficacy testing before the clinical approval of NP-based therapies.

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