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The Role of Excipients and Nanoparticles in Improving Cancer Treatments: A Review

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Abstract:

Nanoparticle-based drug delivery systems have emerged as an approach to combat the issues associated with conventional cancer treatments. These systems improve drug delivery by enhancing bioavailability, targeting cancer cells more effectively, and reducing side effects. Excipients, traditionally considered inactive ingredients, play a critical role in optimizing these systems by influencing drug absorption, pharmacokinetics, and therapeutic efficacy.

This review will evaluate recent advancements in the use of excipients and nanoparticles in cancer treatment, with a focus on chitosan-based nanoparticles, tannic acid-paclitaxel nanoparticles (TAP NPs), and fully active pharmaceutical ingredient nanoparticles (FAPINs). Chitosan nanoparticles exhibit excellent safety profiles and efficient drug delivery, making them suitable as lipophilic anticancer drug carriers and targeting colon cancer cells. TAP NPs tackle challenges like poor drug solubility and toxicity, particularly in breast cancer treatment, and FAPINs combine treatment and imaging in one system, making it easier to target tumors. The strengths, limitations, and suggested future actions for these approaches are discussed to provide an understanding of their potential in cancer therapy.

Keywords: Cancer, nanoparticles, excipients, chitosan, drug delivery, paclitaxel

Introduction

Cancer remains to be one of the leading causes of death on a global scale. There has yet to be a definitive cure for cancer, and there is still ongoing research to find more effective methods of treatment. Many treatments that are used to combat cancer today include chemotherapy, radiation therapy, stem cells, transplants, and many more. In this review, there is a greater focus on specific chemicals and emerging technology such as nanoparticles as an option to combating cancer.

There are two main components of formulated drugs: excipients and active pharmaceutical ingredients (API). In pharmaceutics, the active pharmaceutical ingredient is often studied to determine how it interacts with cells in the body. On the other hand, excipients are the inactive ingredients that act as

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fillers or structural support for the API and make up most of the mass of the drug. For example, lactose, pectin, and xanthan gum stabilizes the API in pill form, propyl gallate improves shelf life, and sodium lauryl sulfate acts as a detergent that solubilizes the API. [1] Excipients are tested for obvious toxicity and symptoms in the body, but are not studied closely for specific interactions with molecular targets of cells. [2] While it has been mostly overlooked, recent studies with a focus on the activity of excipients is expanding, giving a greater context of how it affects the body in conjunction with the API.

Furthermore, nanoparticles are small materials ranging from 1 to 100 nm and having many unique properties due to the differences in size, shape, and structure. Due to their intermediate size, there are many applications of nanoparticles including medical applications, imaging, and energy-based research. Nanotechnology has introduced ways to combat challenges that come with other past cancer therapeutics. Nanoparticle-based drug delivery systems have been engineered to improve drug solubility, stability, and targeted delivery. Excipients can be integrated into these systems to enhance treatment and maximize efficiency. [3] This review evaluates research on the role of excipients and nanoparticles in cancer treatment, focused on chitosan-based systems, tannic acid-paclitaxel nanoparticles, and fully active pharmaceutical ingredient nanoparticles (FAPINs).

Chitosan-Based Nanoparticles

Chitosan is a naturally derived polysaccharide that has been extensively studied for its potential in drug delivery due to its biocompatibility, biodegradability, and mucoadhesive properties. The development of chitosan-based nanoparticles for delivering lipophilic anticancer drugs was explored by Abruzzo. [4] The nanoparticles were formulated with multiple excipients such as cyclodextrins and hyaluronic acid, which improves drug encapsulation and solubility. Cyclodextrins are cyclic oligosaccharides and have a hydrophilic outer surface, so it could form complexes with hydrophobic molecules to become more stable and soluble. This ultimately leads to a greater efficiency for delivering lipophilic drugs.

Despite the promising in vitro results, there was not much in vivo data, limiting the understanding of how these nanoparticles would perform in a clinical setting. Transitioning to an in vivo study requires thorough exploration to ensure safety and efficacy. Additionally, the scalability of chitosan-based nanoparticles for production and distribution was not thoroughly addressed in the study. For the future, research should be expanded towards in vivo studies to investigate the pharmacokinetics and long-term safety of the chitosan-based nanoparticles in animals and eventually humans.

Tannic Acid-Paclitaxel Nanoparticles

Paclitaxel is a widely used chemotherapeutic agent that presents challenges such as poor solubility and potential systemic toxicity. The study by Chowdhury focuses on creating a nanoparticle formulation using tannic acid as a stabilizing and encapsulating agent, forming tannic acid-paclitaxel nanoparticles (TAP NPs). [5] TAP NPs have been shown to significantly increase the cellular uptake and solubility of paclitaxel, leading to greater anticancer efficacy. Chowdhury's work with TAP NPs has achieved a high encapsulation efficiency of 96%, which is a significant indication of effective delivery of paclitaxel. This means a greater proportion of the drug reaches the target site and has a greater effect while reducing the dosage required. Compared to other plain drug formulations, TAP NPs enhanced the uptake of paclitaxel by breast cancer cells significantly because the tannic acid interacts with the cell membrane to facilitate the entry of nanoparticles into the cells.

The scope of this study seems to be limited to targeting breast cancer cells. For future investigations and research, applying the concept of TAP NPs to other cancer cells would increase its usability. The study did well in investigating the most optimal size of nanoparticle for the most effective drug delivery; however, it did not fully consider optimizing the lower number of available binding sites and lower binding rate that comes with altering the size.

Fully Active Pharmaceutical Ingredient Nanoparticles (FAPINs)

Unlike the other approaches mentioned previously, fully active pharmaceutical ingredient nanoparticles (FAPINs) integrate both therapeutic and imaging functions within a single nanoparticle system. The research conducted by Xue introduces FAPINs that do not require additional carrier materials and are composed of entirely active pharmaceutical ingredients. The nanoparticle component of the FAPIN system is made completely out of imaging agents, which helps visualize the tumor during surgery due to its dual-color fluorogenic property. [6] Near-infrared fluorescence imaging and magnetic resonance imaging are methods that could be used for imaging FAPINs.

Xue also engineered nanoscale drug delivery systems, which focus on targeted delivery and controlled release of the chemicals. However, there are drawbacks due to low drug loading capacity and the ineffectiveness of chemotherapy alone on inhibiting aggressive tumors. Thus, for future research, more potent alternatives or versions of FAPINs could be developed, while ensuring minimal toxicity within the subject.

Discussion

The studies used a diverse range of methodologies for advancing anticancer drug delivery using nanoparticles and

excipients.

Abruzzo's study employed a systematic approach to develop and characterize chitosan-based nanoparticles. This involved using other chemicals such as hyaluronic acid and sulfobutyl-ether-cyclodextrin to enhance drug encapsulation and stability. They also used technology such as the photon correlation spectroscopy to measure particle size and size distribution, and Atomic Force Microscopy (AFM) to observe nanoparticle morphology. [4]

Similarly, the paclitaxel nanoparticles were prepared with the solvent evaporation method in Chowdhury's study. The paclitaxel was dissolved in acetone due to its lipophilic nature then was allowed to form nanoparticles. A variety of technology was also used to characterize the particles. This includes Fourier Transform Infrared (FTIR) spectra and X-ray diffraction (XRD) on the freeze-dried samples to observe morphology and particle sizes. [5] Most of the studies utilized similar technology and methods described in Abruzzo and Chowdhury's studies, with the exception of using different chemicals.

Xue used an innovative approach with fully active pharmaceutical ingredient nanoparticles (FAPINs). It includes synthesizing pheophorbide A and irinotecan (PaIr) to form the nanoparticles. In addition to the usual technology used to characterize the nanoparticles, Xue's study also used fluorescence spectroscopy to verify the optical properties. They also used in-vivo methods to assess the therapeutic efficacy in real time. [6] This use of multimodal therapy integrates photothermal, photodynamic, and chemotherapeutic effects and targets tumors in multiple ways. Because this design is complex, it may be difficult to keep precise control over all the variables, posing the possibility of replication issues. It also uses many chemicals and technological resources to create, so the costs and benefits would need to be investigated further.

Like Xue's work, Mauro's study on carbon nanodots were observed for their photothermal and fluorescent properties, showing the potential of improving imaging in cancer care for the future. [7] Zaki's study focused on the cytotoxicity of hydroxycamptothecin-loaded nanoparticles and its effects on lung and colon cancer cells, so methods like confocal laser scanning microscopy and microfluorimetry assay were utilized. [8]

While these approaches offer significant advancements, there are still some challenges. For example, there are obstacles in the reproducibility of nanoparticle formulations and their scalability for clinical use. Techniques such as emulsion-solvent evaporation or nanoprecipitation may require optimization for large-scale manufacturing. Furthermore, in vitro studies provide valuable insights into the efficacy of drug delivery systems, but their translation to in vivo and clinical settings is not always straightforward due to differences in biological environments.

Moving forward, this field could benefit from combining various approaches from these studies. Different approaches resulting in different nanoparticle and drug characteristics could be experimented to best suit each individual's medical needs. Furthermore, the use of computational modeling and AI technology could be integrated to develop or plan the best nanoparticle and excipient combinations. As more nanotechnology research is conducted, there could be more precise or cost-effective methods of producing and analyzing nanoparticles, allowing for easier application to healthcare. Overall, the methodologies used in the observed studies present a strong foundation for research on nanoparticle use in anticancer applications.

Conclusion

The use of nanoparticles and excipients in anticancer treatments indicates significant advancements in drug delivery systems by presenting the potential of enhancing efficacy while minimizing toxicity and side effects. Chitosan-based nanoparticles, tannic acid-paclitaxel nanoparticles, and fully active pharmaceutical ingredient nanoparticles each bring unique strengths to the field of cancer therapeutics but also face specific challenges that must be addressed. Further research on in vivo applications, scalability, and safety will allow for more effective, safe, and available cancer treatments in the future.

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