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Advancing Cervical Cancer Treatment: The Promise of Nanotechnology

Thenmozhi A[*a], Abishek B [a], P.BavaDhareni[b], Venkateshan N [c]
[a] *ArulmiguKalasalingam College of pharmacy – Department of Pharmaceutical Analysis.*
[b] *ArulmiguKalasalingam College of pharmacy – Doctor of Pharmacy.*
[c] *ArulmiguKalasalingam College of pharmacy – Department of Pharmaceutical Chemistry.*
** Corresponding author :Thenmozhi A*

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ABSTRACT:
Background: Nanotechnology has revolutionized cancer treatment by enabling precise drug delivery and enhancing therapeutic efficacy while minimizing side effects. Nanoparticles (NPs) offer the advantage of selectively targeting cancer cells, overcoming many limitations of traditional therapies like chemotherapy, radiation, and surgery.
Objective: This review focuses on the role of various nanoparticles in the treatment of cervical cancer, emphasizing their impact on improving drug delivery, tumor targeting, and the overall effectiveness of current treatment strategies.
Methods: A review of the literature was conducted on several types of nanoparticles used in cervical cancer treatment, including carbon nanotubes (CNTs), liposomes, gold nanoparticles (GNPs), iron oxide nanoparticles (Fe3O4), human albumin-based nanoparticles, and curcumin-loaded nanoparticles. The review analyzes their drug delivery mechanisms, therapeutic efficacy, and advantages over conventional therapies**.**
Results: Functionalized CNTs provide efficient drug delivery and imaging capabilities, allowing precise targeting of cancer cells. Liposomes enhance drug stability, solubility, and selective delivery, improving therapeutic outcomes while reducing systemic toxicity. Gold nanoparticles (GNPs) facilitate photothermal therapy, utilizing their optical and thermal properties to treat tumors. Iron oxide nanoparticles (Fe3O4) serve as drug carriers and immune system activators, with potential applications in cancer vaccines. Human albumin-based nanoparticles, such as Abraxane, reduce chemotherapy-related toxicity and are already FDA-approved for clinical use. Curcumin-loaded nanoparticles enhance the bioavailability and stability of curcumin, demonstrating promising preclinical results in treating cervical cancer.
Conclusion: Nanotechnology offers significant improvements in cervical cancer treatment by enabling targeted, effective therapies with fewer side effects. While challenges remain, nanomedicine holds great potential for improving patient outcomes and quality of life

Keywords:
Nanotechnology, Cervical cancer, Drug delivery, Nanoparticles, Targeted therapy, Gold nanoparticles, Curcumin-loaded nanoparticles.

I. BACKGROUND

Cancer that starts in the cells of the cervix is called cervical cancer. The cervix is the lower part of the uterus that connects to the vagina. According to the WHO, it is the fourth most common cancer in women worldwide, with about 604,000 new cases and 342,000 deaths in 2020. Around 90% of new cases and deaths worldwide in 2020 will occur in low- and middle-income countries[1]. Cervical cancer is caused by the human papilloma virus. This type of cancer occurs in the age group of 30 to 49 years. Thus, people in this age group only need to have a cervical cancer screening test once. WHO recommends the best age for screening is 35–45 years old[2].

II. NANOTECHNOLOGY USED IN THE TREATMENT OF CERVICAL CANCER

Nanotechnology can be defined as the science and engineering concerned with the design, synthesis, characterization, and application of materials and devices with the smallest functional organization at the scale of a nanometer or one billionth of a meter[3]. In cancer treatment, the key issue is achieving the desired concentration of the therapeutic agent at the tumor site, thereby killing cancer cells while minimizing damage to normal cells. With this vision in mind, it is imperative to create unique agents with great potential to make important contributions to the prevention, detection, and treatment of cancer. In this regard,

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several ligand-targeted therapeutic strategies, including immunotoxins, radioimmunotherapy, and immune-drug conjugates, are being developed to overcome the problems associated with these conventional therapies. Chemotherapy drugs, therefore, provide additional tools in the cancer treatment arsenal. Although these conjugated agents have shown promising efficacy compared with conventional chemotherapy drugs, limitations in their use remain a major problem. Advances show that nanotechnology provides targeted therapy with minimal side effects and greater efficacy compared to conventional drug delivery systems[4]. In conventional treatment, one of the treatment options is surgery. In other words, remove the cancerous part. However, the limit is that we lose organs, and cancer can come back. Additionally, surgery is not possible for all types of cancer cases. The second option is radiation therapy. In it, cancer cells are burned by radiation of a specific frequency range and intensity. The limitation of this method is that even when healthy cells are burned, cancer cells burn unevenly, and the burned part may die and no longer function. The third option is chemotherapy. That is, cancer cells are killed by cytotoxic drugs either by preventing the cells from absorbing the nutrients they need to divide or by blocking the mechanism responsible for cell division. Often, a combination of drugs is given so that the drug affects all three aspects of cancer treatment. The drawbacks of this method are that the treatment is harmful to healthy cells, the method is rudimentary, and it is rarely effective if the cancer is at a late stage. In nanotechnology, some nanoparticles(NP) can be designed to preferentially absorb a certain wavelength of radiation and be heated. Such an NP, if it enters cancer cells, will burn if irradiated with radiation of the appropriate wavelength. It's a bit like radiotherapy. Nanotechnology can be used to create therapeutic agents that target specific cells and deliver toxins to kill them. The NP would circulate throughout the body, detect molecular changes associated with cancer, assist with imaging to release the therapeutic agent, and then monitor the effectiveness of the intervention[5]. The following nanoparticles are used in the treatment of cervical cancer:

2.1 CARBON NANOTUBES

Carbon is one of the most abundant minerals on Earth. It is a building block of a variety of important macromolecules, including sugars, proteins, DNA, etc[6]. Carbon nanotubes (CNTs) have been fully characterized as flat, well-organized, tubular, high-aspect-ratio distributed networks of carbon with diameters measuring at the nanoscale. In particular, exploiting their diverse properties and small size through bioinspired functionalization techniques has enabled a wide range of biomedical applications through molecules and cells. CNTs can be classified based on their structure as single-walled CNTs (SWCNTs). With diameters from 1 to 10 nm and multi-walled concentric CNTs (MWCNTs) with diameters from about 5 to 30 nm and lengths from a few nanometers to a few millimeters[7]. Soot containing CNT did not alter lung function and did not induce any measurable inflammation in the bronchial space in exposed guinea pigs. In mice instilled with SWNTs, exposure to high doses (5 mg/kg) resulted in mortality in approximately 15% of instilled mice within 24 hours of dosing. This mortality is due to mechanical obstruction of the upper respiratory tract by the droplet and not to the inherent lung toxicity of the instilled SWNT particles. SWNT can inhibit human cell growth by inducing cell apoptosis and reducing cell adhesion. Recently, SWNT and DWNT have been shown to activate the human serum complement system through both the classical and alternative pathways. Complement activation by carbon nanotubes leads to the generation of pro inflammatory peptides and may promote adverse effects such as inflammation and granuloma formation[8]. A unique method of visualizing tumor cells using the natural biocompatible polymer chitosan SWCNTs were treated using chitosan (CHIT) and fluorescein isothyocyanate (FITC) in this study. Because most cancer cells express folic acid receptors, this was further conjugated with folic acid (FA) to create the functional FITC-CHIT-SWCNT-FA conjugation. These unique functionalized SWCNTs were discovered to be soluble and stable in phosphate buffered saline, as well as easily transportable inside human cervical cancer HeLa cells. FITC-CHIT-SWCNT-FA, which combines the intrinsic features of CNTs with the adaptability of chitosan and folic acid, can be used as a promising device for medication targeting tumor cells as well as imaging[9].

2.2 LIPOSOMES

Liposomes are spherical vesicles composed of a phospholipid bilayer with hydrophilic and hydrophobic properties. Due to their amphipathic nature, lipophilic drugs can be entrapped in the phospholipid bilayer or adsorbed

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on the liposome surface, while hydrophilic drugs can be further encapsulated within the aqueous interior of the vesicles and their phospholipid. Due to the lipid bilayer structure, liposomes have excellent biocompatibility and biodegradability[10]. An invivo invitro study shows that Liposomes Poly Lactic-co-Glycolic Acid-cisplatin-Avastin (L-PLGA-Cis-Avastin®) targeted nanoparticles also showed increased cellular internalization and accumulation in xenograft tumors after systemic administration. Additionally, L-PLGA-Cis-Avastin® may inhibit xenograft tumor growth. Taken together, this modified nanoparticle system has the potential to improve the therapeutic efficacy of cisplatin and reduce the toxicity of cisplatin through molecular targeting. This nanoparticle system may serve as a promising, specific targeting method in the treatment of cervical cancer. This study shows that liposome nanoparticles reduce the toxicity of cisplatin[11].

2.3 GOLD NANOPARTICLES

Gold nanoparticles (GNPs) are becoming increasingly popular in biomedical research due to their optical and thermal properties. They have been successfully used as contrast agents for diagnosis and cancer treatment. An advantageous property of GNPs in biomedical applications is that they can be synthesized in specific sizes and shapes. Additionally, the inert nature of GNPs provides high chemical and physical stability. Due to the small size of the GNPs, the surface area-to-volume ratio of the formulation is high. This property improves the loading and stability of drugs or other bioconjugated moieties. Drug solubility and pharmacokinetic parameters were improved [12]in a recent in vivo study on nude mice, which showed that silica-coated gold nanoparticles ($Au@SiO_2$) conjugate with antibodies against scavenger receptor class B type I (SR-BI) and have the potential to visually track and treat cervical cancer. The fluorescein isothiocyanate (FITC)-labeled $Au@SiO_2$-SR-BI antibody was synthesized. The expression and location of SR-BI protein in cervical cancer cells were detected by Western blot and immunofluorescence assay, respectively. The effect of nanoparticles on tumor formation in nude mice was determined. This indicates that photothermal therapy with SR-BI-conjugated FITC-$Au@SiO_2$ is an effective method to combat cervical cancer cells. Antibody-conjugated $Au@SiO_2$ nanoparticles may have therapeutic potential for cervical cancer [13].

2.4 IRON OXIDE NANOPARTICLE

The current study shows that the(3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide) Assay(MTT assay) demonstrated high cytotoxicity of curcumin-loaded folic acid-modified hyperbranched polyglycerol @Iron oxide(HPG@Fe3O4) nanoparticles toward HeLa cells and decreased survival of cancer cells at 24, 48, and 72 h. The addition of Folic Acid (FA) to polyhydroxylated HPG@Fe3O4 nanoparticles increased the cellular uptake of the nanoparticles and increased the therapeutic potential of the nanocarriers. FA@HPG@Fe3O4 nanoparticles can be conjugated and released with curcumin and other drug candidates for cervical cancer treatment[14]. Iron oxide nanoparticles significantly promote immune cell activation and cytokine production, leading to strong humoral and cellular immune responses. These results suggest that this nanoparticle-based delivery system has great potential to be used as a general platform for cancer vaccines[15].

2.5 HUMAN ALBUMIN BASED NANOPARTICLE

Human serum albumin is the most abundant transport protein in plasma and has recently been widely used to form nanoparticles for cancer drug delivery. The main reasons for choosing albumin protein as a cargo for drug delivery are its excellent biocompatibility, biodegradability, and nonimmunogenicity. Furthermore, the albumin structure, which contains three homologous domains consisting of a single polypeptide (585 amino acids), contains various hydrophobic substances through noncovalent interactions. Albumin exhibits active tumor-targeting functions through interaction with Albumin binding glycoprotein (gp60) and Secreted Protein and rich in Cysteine (SPARC) proteins, which are abundant in tumor-associated endothelial cells and the tumormicroenvironment [16].The human albumin-based nanoparticle-releasing chemotherapeutic drug paclitaxel (PTX) is the first nanomedicine approved by the Food and Drug Administration (FDA) for clinical use in the treatment of metastatic breast cancer. This nanoparticle, Abraxane (ABI-007, nab-paclitaxel), has much milder side effects, such as acute hypersensitivity reactions, anemia, and cardiovascular events that are often caused by free PTX. This is an excellent example of how nanotechnology is a promising approach to cancer

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treatment. Abraxane is being tested in phase I and phase II clinical trials for cervical cancer [17].

2.6 CURCUMIN(CUR):

Curcumin is a phytochemical obtained from the turmeric plant. It is often used to treat various types of diseases, such as cancer. Nevertheless, its effectiveness is limited due to rapid metabolism, low bioavailability, low water solubility, and systemic excretion[18]. In cervical cancer cell lines, Nano CUR efficiently slows cell growth, induces apoptosis, and stops the cell cycle. Nano-CUR therapy influenced entities related to carcinogenesis, such as Micro Ribo nucleic acid(miRNAs), transcription factors, and proteins. Furthermore, Nano-CUR effectively reduced tumor burden in a pre-clinical orthotopic mouse model of cervical cancer by reducing oncogenic Micro Ribo-Nucleic acid-21 (miRNA-21), suppressing nuclear beta-catenin, and inhibiting expression of E6/E7 HPV oncoproteins, which includes the smoking compound benzo[a]pyrene (BaP), which causes E6/E7 and Interleukin-6(IL-6)expression. These promising preclinical results show that Nano-CUR could be a viable treatment option for cervical cancer[19]. Curcumin (Cur) has shown promising anti-cancer activity but is susceptible to chemical instability (e.g., photodegradation), hydrophobicity, poor absorption, poor bioavailability, a short plasma half-life, and various body tissues. Its clinical implementation is limited due to its low distribution. To alleviate these drawbacks, various types of nanocarriers, such as liposomes, Solid lipid nanoparticles (SLNs), polymeric micelles, polymeric nanoparticles, niosomes, dendrimers, and inorganic NPs, have been used as delivery devices for Cur. Despite all these developments, some aspects of Cur nanomedicine remain controversial, such as poor manufacturing reproducibility and poor in vitro-in vivo correlation [20].

III. CONCLUSION:

Nanotechnology holds transformative potential for the treatment of cervical cancer by enabling targeted, efficient drug delivery systems that improve therapeutic outcomes while minimizing side effects. Various types of nanoparticles, including carbon nanotubes, liposomes, gold nanoparticles, and curcumin-loaded nanoparticles, have shown significant promise in enhancing drug stability, solubility, and tumor targeting. These advancements overcome many limitations associated with traditional therapies, such as chemotherapy and radiation, and offer new avenues for personalized, less invasive treatment options.

While challenges in reproducibility, in vivo efficacy, and clinical translation remain, the growing body of research in nanoparticle-based therapies underscores their potential to revolutionize cervical cancer treatment. With continued development and refinement, nanomedicine could significantly improve the effectiveness of current therapies, enhance patient outcomes, and reduce treatment-related toxicity. As we move forward, integrating nanotechnology with conventional cancer treatment regimens, along with ongoing clinical trials and research, will be crucial in realizing the full potential of these innovative therapies for cervical cancer.

IV. FUTURE PERSPECTIVES IN NANOTECHNOLOGY-BASED THERAPIES FOR CERVICAL CANCER

Nanotechnology holds immense promise for the future of cervical cancer treatment, offering the potential for more precise, efficient, and personalized therapies. As advancements in nanomedicine continue to evolve, the future of cervical cancer care is poised for significant transformation.

4.1 Enhanced Targeted Therapy:

Nanoparticles designed to target specific molecular markers associated with cervical cancer cells are likely to become more refined. These therapies would enable higher concentrations of therapeutic agents at the tumor site, improving efficacy while minimizing side effects. Over time, nanoparticles such as carbon nanotubes, gold nanoparticles, and liposomes will be engineered for enhanced targeting capabilities, reducing off-target effects and potentially eliminating the need for systemic chemotherapy. This progress could lead to a more personalized approach to cervical cancer treatment, where therapies are tailored to the unique characteristics of each patient's tumor.

4.2 Multi-ModalTreatment Approaches:

Nanotechnology's ability to combine diagnostic, therapeutic, and monitoring functions within a single nanoparticle platform presents a future where cervical cancer treatment is not just more effective but also more comprehensive. Nanoparticles could be designed to simultaneously deliver chemotherapy, radiation, or gene therapy

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while also enabling real-time monitoring of treatment responses. This integration of multiple therapeutic modalities into one system could revolutionize the way cervical cancer is managed, making treatment more dynamic and adaptable.

4.3 Overcoming Current Treatment Limitations:

The limitations of current cervical cancer treatments, such as chemotherapy and radiation therapy, include high toxicity, poor bioavailability of drugs, and resistance development. Nanotechnology promises to mitigate these issues by improving drug solubility, enhancing tissue penetration, and reducing systemic toxicity. For instance, nanocarriers could help overcome the poor bioavailability of curcumin and other naturally derived agents, which are currently limited by their chemical instability and low solubility. Future innovations will likely focus on refining these nanoparticle formulations to maximize therapeutic efficacy while minimizing adverse effects.

4.4 Advancement in Immunotherapy:

Nanotechnology also holds potential in the field of immunotherapy for cervical cancer. The use of nanoparticles to stimulate the immune system and enhance immune responses could complement traditional treatments. Nanoparticles that carry cancer vaccines, adjuvants, or immunostimulatory agents may help to prime the immune system, allowing for better detection and destruction of cervical cancer cells. With the ability to fine-tune immune responses, nanotechnology may offer new avenues for treating advanced or recurrent cervical cancer that is resistant to conventional therapies.

4.5 Clinical Translation and Regulatory Approvals:

Despite the promising preclinical results, the successful translation of nanotechnology from laboratory research to clinical practice remains a significant challenge. Issues related to reproducibility, regulatory approval, and large-scale production need to be addressed for widespread clinical application. The next decade will likely witness accelerated clinical trials and collaborations between academic researchers, pharmaceutical companies, and regulatory bodies to bring nanotechnology-based therapies to the forefront of cervical cancer treatment.

4.6 Personalized Nanomedicine:

As genomic and molecular research continues to uncover the unique signatures of individual cancers, nanotechnology can be leveraged to design therapies that are precisely tailored to a patient's tumor. Personalized nanomedicine approaches, where nanoparticles are specifically engineered based on the molecular characteristics of a patient's cancer, will likely become a cornerstone of future treatment regimens. This precision medicine approach could improve treatment outcomes, reduce the risk of relapse, and significantly enhance overall survival rates.

In conclusion, the future of cervical cancer treatment is bright, with nanotechnology paving the way for more effective, targeted, and personalized therapies. While challenges remain, the rapid pace of innovation in nanoparticle-based drug delivery systems and immunotherapies provides hope for improved treatment options. By overcoming current limitations and advancing clinical applications, nanotechnology has the potential to revolutionize cervical cancer care and improve the quality of life for patients worldwide.

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