

Plant-Derived Nanoparticles in Cervical Cancer: From Green Synthesis to Targeted Nanotherapy

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Abstract: *Cervical cancer continues to pose a significant global health challenge, particularly in resource-limited regions where early diagnosis and treatment facilities are inadequate. Conventional treatment strategies such as chemotherapy and radiotherapy are often limited by adverse side effects, non-specific targeting, and the emergence of drug resistance. In this context, plant-mediated nanoparticles have gained considerable attention as a safer and more sustainable alternative.*

These nanoparticles are synthesized using plant extracts rich in bioactive compounds that function as natural reducing and stabilizing agents, eliminating the need for toxic chemicals. The present review explores the potential of plant-derived nanoparticles in cervical cancer management, including their applications in targeted drug delivery, diagnostic imaging, and direct anticancer activity. Various nanoparticles such as silver, gold, and zinc oxide have demonstrated notable cytotoxic effects against cervical cancer cell lines by inducing oxidative stress, promoting apoptosis, and disrupting cellular proliferation pathways.

Although encouraging results have been reported in preclinical studies, challenges related to large-scale production, reproducibility, and clinical translation remain. Nevertheless, plant-based nanoparticles offer a promising and eco-friendly platform for the development of advanced cancer therapeutics.

Keywords: Cervical cancer, Green synthesis, Nanoparticles, HeLa cells, SiHa cells, Anticancer activity, HPV

I. INTRODUCTION

Cervical cancer ranks among the most common malignancies affecting women worldwide and remains a leading cause of cancer-related mortality, particularly in developing nations. The high incidence in these regions is largely attributed to inadequate screening programs, limited awareness, restricted access to HPV vaccination, and delayed diagnosis. Despite being largely preventable, the disease continues to impose a substantial public health burden. Current therapeutic approaches, including surgical intervention, chemotherapy, and radiotherapy, are widely used depending on disease progression. However, commonly used chemotherapeutic agents such as cisplatin and paclitaxel often suffer from limitations including poor selectivity, systemic toxicity, and the development of resistance. Similarly, radiotherapy may lead to unintended damage to surrounding healthy tissues, resulting in long-term complications. These drawbacks highlight the urgent need for alternative treatment strategies that are both effective and less toxic. Nanotechnology has emerged as a powerful tool in oncology, offering innovative solutions for drug delivery and disease management. Due to their nanoscale size and modifiable surface properties, nanoparticles can enhance drug bioavailability and enable targeted delivery to tumor tissues through mechanisms such as the enhanced permeability and retention effect. In recent years, green synthesis of nanoparticles using plant extracts has gained increasing importance. This approach avoids the use of hazardous chemicals and relies on naturally occurring phytochemicals such as flavonoids, alkaloids, and phenolic compounds, which facilitate nanoparticle formation and stabilization. In addition to their role in synthesis, these biomolecules contribute to the biological activity of nanoparticles.



Plant-derived nanoparticles, particularly metallic and metal oxide types, have demonstrated significant anticancer effects in cervical cancer models. Studies have shown their ability to induce programmed cell death, generate reactive oxygen species, and inhibit tumor growth in cell lines such as HeLa and SiHa. Furthermore, these nanoparticles can be engineered as carriers for drugs and genetic material, opening new avenues for advanced therapeutic strategies.

II. LITERATURE REVIEW

Zinc Oxide Nanoparticles (ZnO NPs): ZnO nanoparticles synthesized using *Solanum nigrum* exhibited strong anticancer activity against HeLa cells via apoptosis induction. Characterization techniques such as UV-Vis, SEM, TEM, XRD, and FTIR confirmed nanoparticle formation. Cytotoxicity assays (MTT, DAPI staining) revealed dose-dependent cell death, along with increased expression of p53 and caspases and suppression of β -catenin signaling. Similarly, ZnO nanoparticles synthesized using *Gracilaria edulis* demonstrated cytotoxic effects against SiHa cells with an IC₅₀ value of 35 μ g/mL. The mechanism involved ROS-mediated mitochondrial apoptosis, confirmed through staining assays and flow cytometry.

Gold Nanoparticles (AuNPs): Gold nanoparticles synthesized from *Catharanthus roseus* showed potent anticancer activity against HeLa cells. Characterization confirmed particle sizes of 25–35 nm. These nanoparticles induced ROS-mediated mitochondrial apoptosis, regulated Bax/Bcl-2 protein expression, and activated caspase pathways. The reported IC₅₀ value was as low as 5 μ g/mL, indicating high therapeutic potential.

Silver Nanoparticles (AgNPs): Silver nanoparticles synthesized using *Catharanthus roseus*, *Nepeta deflersiana*, and *Ginkgo biloba* extracts demonstrated significant anticancer effects.

- *Catharanthus roseus*-derived AgNPs showed strong cytotoxicity and anti-metastatic activity in HeLa229 cells.
- *Nepeta deflersiana* AgNPs induced ROS generation, lipid peroxidation, mitochondrial dysfunction, and apoptosis.
- *Ginkgo biloba* AgNPs activated the mitochondrial apoptotic pathway via cytochrome c release and caspase activation.

These studies highlight the selective toxicity of AgNPs toward cancer cells while sparing normal cells.

Mechanism:

Plant-based nanoparticles exhibit anticancer activity through multiple interconnected biological pathways. One of the primary mechanisms involves the generation of reactive oxygen species, which leads to oxidative stress and subsequent mitochondrial dysfunction. This process ultimately triggers apoptosis through activation of caspase enzymes.

Additionally, these nanoparticles can interfere with normal cell cycle progression, causing arrest at specific phases and thereby inhibiting uncontrolled cell division. DNA damage and disruption of transcriptional processes further contribute to cancer cell death. Some nanoparticles also demonstrate the ability to inhibit angiogenesis, thereby restricting tumor growth by limiting blood supply. Moreover, their anti-metastatic properties help prevent the spread of cancer cells to distant organs.

Applications in Cervical Cancer Therapy:

Plant-based nanoparticles have diverse applications:

Targeted Drug Delivery: Improved solubility, stability, and tumor-specific delivery

Theranostics: Combined diagnostic and therapeutic applications

Photodynamic Therapy: Enhanced ROS generation using photosensitizers

Gene Delivery: Efficient transport of siRNA, miRNA, and CRISPR systems

Combination Therapy: Co-delivery of drugs and phytochemicals for synergistic effects



III. CONCLUSION

Plant-based nanoparticles have emerged as a promising alternative in the field of cancer therapeutics, particularly for cervical cancer. Their environmentally friendly synthesis, combined with enhanced biocompatibility and reduced toxicity, makes them attractive candidates for biomedical applications. These nanoparticles exhibit significant anticancer activity through various mechanisms, including oxidative stress induction, apoptosis, and inhibition of tumor progression. Furthermore, their role as drug delivery vehicles enhances the effectiveness of conventional therapies while minimizing adverse effects. Despite these advantages, several challenges must be addressed before clinical implementation, including standardization of synthesis methods, large-scale production, and comprehensive safety evaluation. Continued research integrating nanotechnology, plant science, and clinical studies will be crucial for translating these findings into practical medical applications.

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