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Review on Nanogold and Nano silver for cervical Cancer Therapy

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ABSTRACT

Cervical cancer is one of the primary causes of female death, with a mortality rate in developing areas surpassing 200,000 per year. Despite a decrease in cervical cancer cases in affluent countries over the last decade, the prevalence in developing countries continues to climb at an alarming rate. The rise in cervical cancer incidence is ascribed to a lack of financial resources and the disease's inherent risk factors. Reduced drug potency, non-specificity, undesirable side effects, and the development of multiple drug resistance (MDR) limit traditional anticancer therapy, resulting in a decline in long-term anticancer therapeutic efficacy. The use of nanoparticles (NPs) in cancer therapies has spawned a new field of study known as cancer nanomedicine. NPs, in contrast to standard anti-cancer medications, take a targeted strategy that avoids side effects. We discussed the role of gold and silver NPs (AgNPs) in cancer nanomedicine in this communication. Bionanotechnology has played a critical role in creating a novel medicine, gold nanoparticles (AuNPs), for cancer treatment. In this study, we discovered that photosynthesized Catharanthus roseus (CR) AuNPs trigger mitochondrial-mediated apoptotic signalling pathways via reactive oxygen species (ROS) induced cytotoxicity in the cervical cancer cell line (HeLa) using an in vitro model. Silver nanoparticles have a significant role in current nanotechnology. Their antibacterial properties have also been thoroughly reported. Green nanoparticle production has various advantages over chemical synthesis. In this study, silver nanoparticles mediated by Thuja occidentalis leaf extract were produced without needing a stabilising agent and examined for anticancer and antimicrobial properties. Silver nanoparticles mediated by Thuja occidentalis leaf extract were generated in ambient conditions. They showed a narrow size distribution within the range of 10–15 nm, with an average particle size of 12.7 nm. At concentrations of 6.25–50 g/mL, these nanoparticles showed anti-cancer efficacy against human breast (MCF 7, MDA MB 231), cervical cancer (HeLa), and mouth epidermoid carcinoma (KB) cell lines.

1. Introduction

Cancer is a state in which the body's cells grow out of control. Even if cancer spreads to other parts of the body, it is named after the segment of the body where it begins for eternity. Cervical cancer is a type of cancer that starts in the cervix (Figure: 1).

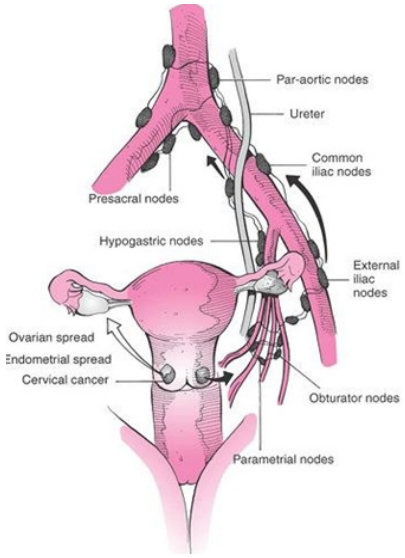

Figure: 1. Cancer that begins in the cervix

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The cervix connects the vaginal canal (birth canal) to the uterus' upper section. Whilst a woman is pregnant, the uterus (or womb) is where the baby develops. Cervical cancer is an ailment that affects women. It is most common in women over the age of 30. An enduring infection causes cervical cancer with particular human papillomavirus (HPV) (Baniste *et al*., 2017). The human papillomavirus (HPV) is a virus that is multiplied from one person to another for the duration of sexual activity (Figure: 2).

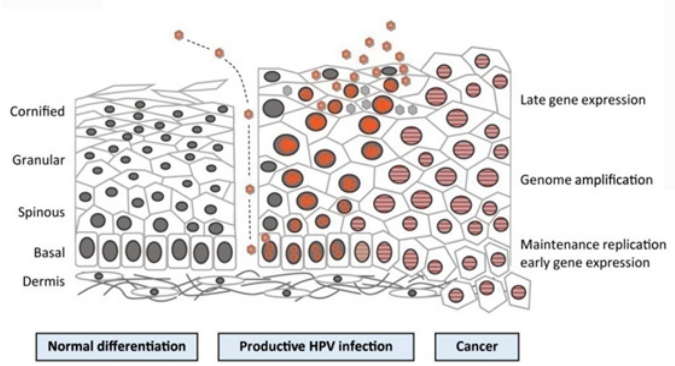

Figure: 2. Human papillomavirus (HPV) life cycle and Cancer

HPV will communicate a disease to at least half of sexually active adults at some point in their lives, but only a tiny percentage of women will develop cervical cancer (Sung et al., 2021). Cervical cancer can be prevented using screening tests and the HPV vaccine. Cervical cancer is primarily treated when detected early and is connected with a long survival time and a high quality of life.

Risk factors of cervical cancer

Human papillomavirus (HPV), a common virus spread from one person to another during intercourse, is responsible for nearly all cervical malignancies. HPV comes in a variety of forms. Some HPV kinds can induce alterations to a woman's cervix, eventually leading to cervical cancer, while others can produce genital or skin warts.HPV is so widespread that almost everyone contracts it at some point in their lives. Because HPV has typically no symptoms, you won't know if you have it. HPV will go away on its own for most women; but if it does not, there is a potential that it will develop cervical cancer over time. Having HIV (the virus that causes AIDS) or any illness that makes it difficult for your body to fight off health problems can raise your chance of cervical cancer (Stelzle et al., 2020). Smoking, taking birth control pills for a long time (5–10 years), having three or more children, and having several sexual partners are all risk factors.

Types of Treatment

Cervical cancer is treatable in several ways. It varies according to the type of cervical cancer and how far it has spread. Treatment options include surgery, chemotherapy, and radiation therapy. Doctors remove cancerous tissue during an operation. To shrink or kill cancer cells, certain drugs are utilised. The drugs can be pills, medicines injected into your veins, or a combination of both. High-energy rays (similar to X-rays) are used to kill cancer cells. Gynecologic oncologists are doctors who focus on cancers of the female reproductive system. Surgeons are medical doctors who perform operations. Medical oncologists are doctors who treat cancer using medicine (Lei et al., 2020). Oncologists who employ radiation to treat cancer are known as radiation oncologists.

Anti-cervical cancer activity of Nano Silver

Sinigrin was used as a reducing and stabilising agent in the production of AgNPs. Various analytical techniques were used to characterise the produced AgNPs. A series of cellular and biochemical assays were used to assess the anticancer effects of combined treatment with CPT and AgNPs. Real-time reverse transcription-polymerase chain reaction was used to evaluate the expression of pro-and antiapoptotic genes. According to the results of this investigation, the combined therapy of CPT and AgNPs significantly reduced the vitality and proliferation of HeLa cells. Furthermore, compared to a single therapy, the combined impact considerably increases oxidative stress markers while decreasing antioxidative stress markers. Moreover, the combination treatment increases the expression of proapoptotic genes while reducing the expression of anti-apoptotic genes.

Because of their unique physical, chemical, optical, and biological features, silver nanoparticles (AgNPs) are commonly utilised metal nanoparticles in the health care industry. It has antibacterial, antiviral, antifungal, and anticancer properties. Camptothecin (CPT) and its derivatives are topoisomerase inhibitors and strong anticancer medicines that can be used to treat a variety of malignancies. Despite this, the combined effects of CPT and AgNPs on apoptosis in human cervical cancer cells (HeLa) remain unknown. As a result, we looked at the synergistic effect of CPT and AgNPs on human cervical cancer cells.

Surprisingly, the combined treatment affects several cellular signalling molecules important in cell survival, cytotoxicity, and death. Overall, these findings imply that CPT and AgNPs cause cell death by changing the permeability of the mitochondrial membrane and activating caspases 9, 6, and 3. Increased ROS production and antioxidant depletion appear to be linked to synergistic cytotoxicity and apoptosis. In comparison to monotherapy, a combination of CPT and AgNPs may positively benefit the treatment of cervical cancer. Nanoparticle-mediated cancer therapy can improve cancer therapeutic efficiency by combining nanoparticles with anticancer drugs in tumour control while also reducing unwanted side effects by increasing pharmacokinetics and drug payload deposition in tumours. AgNPs have been shown to have anti-cancer properties. In contrast, DNA-topoisomerase I inhibitors like CPT analogues have been shown to have harmful effects on cancer cells by promoting the activation of apoptotic caspases and the generation of reactive oxygen species (ROS), which increases anticancer activity. To investigate the possibility of combined action of CPT and AgNPs in HeLa cells, the cells were first treated with various concentrations of CPT and AgNPs, with the findings showing that both CPT and AgNPs cause cell death dose-dependently.

By boosting ROS production and LDH leakage and modifying mitochondrial membrane potential and activation of caspase 9, 6, and 3, the combination of CPT and AgNPs significantly

limits cell growth and promotes cytotoxicity and apoptosis. It also raises prooxidants like MDA and protein carbonyl content while lowering levels of antioxidants, including GSH, SOD, CAT, and GPx. Proapoptotic genes including p53, p21, Cyt C, Bid, Bax, and Bak, and antiapoptotic genes like Bcl-2 and Bcl-xL, are upregulated by the combination treatment. Finally, the combination of CPT and AgNPs modifies the expression of Akt1, RAF, MEK, Erk1/2, JNK, P38, NF-B, and Cyclin D, which are involved in cell survival, viability, proliferation, cytotoxicity, and apoptosis (Gardea-Torresdey et al., 2003; Makarov et al., 2014; Haumesser -2016; Thanh-2014; Thanh et al., 2014; Polte 2015). The findings of this study imply that combining CPT and AgNPs at lower doses could potentially cause cytotoxicity and apoptosis without causing any unwanted harmful effects, thereby increasing the efficacy of two separate cancer therapy agents. As a result, combining nanoparticles with anticancer medicine appears to be a viable cancer research strategy. In practice, when compared to single-agent chemotherapy, combination chemotherapy produces a better response and longer survival.

Anti cervical cancer activity of Nano Gold

Researchers have created gold nanoparticles that can stop human cervical cancer cells from growing. They made the nanoparticles with an extract from a medicinal plant that has been used to treat cancer patients in the past.

One of the most frequent malignancies in humans is cervical cancer. The sexually transmitted human papillomavirus (HPV) infection raises the risk of invasive cervical cancer. About 365 million Indian women over the age of 15 are at risk of having cervical cancer. More than 100,000 new cases of cervical cancer are detected each year, with 74,000 Indian women dying as a result. Chemotherapy, for example, is an effective treatment that has significant side effects.

The researchers used the essence of the medicinal plant to make gold nanoparticles in order to produce a simple and cost-effective treatment for cervical cancer. The extract aided in the creation of crystalline gold nanoparticles with sizes ranging from 5 to 35 nanometers. The anticancer capabilities of these nanoparticles were subsequently explored by exposing them to cultivated human cervical cancer cells. against cervical cancer cells, the nanoparticles showed effective anticancer effects. They stopped cancer cells from growing by interrupting their cell cycle and destroying their DNA. The cancer cells were treated with nanoparticles, which activated enzymes that caused mass suicide. The researchers say that the gold nanoparticles made using the plant extract can be developed as a drug candidate for human cervical cancer therapy.

Gold nanoparticles (AuNPs) have been widely explored and are well-known for their medical applications. Chemical and physical synthesis methods are a way to make AuNPs. In any case, the hunt for other more ecologically friendly and cost-effective large-scale technologies, such as environmentally friendly biological processes known as green synthesis, has been gaining interest by worldwide researchers. The international focus on green nanotechnology research has resulted in various nanomaterials being used in environmentally and physiologically acceptable applications. Several advantages over conventional physical and chemical synthesis (simple, one-step approach to synthesize, cost-effectiveness, energy efficiency, and biocompatibility) have drawn scientists' attention to exploring the green synthesis of AuNPs by exploiting plants' secondary metabolites. Biogenic approaches, mainly the plant-based synthesis of metal nanoparticles, have been chosen as the ideal strategy due to their environmental and in vivo safety and ease of synthesis. In this review, we reviewed the use of green synthesized AuNPs in cancer treatment by utilizing phytochemicals found in plant extracts. This article reviews plant-based methods for producing AuNPs, characterization methods of synthesized AuNPs, and discusses their physiochemical properties. This study also examines recent breakthroughs and achievements in using green synthesized AuNPs in cancer treatment and different mechanisms of action, such as reactive oxygen species (ROS), mediated mitochondrial dysfunction and caspase activation, leading to apoptosis, etc., for their anticancer and cytotoxic effects (Camargo et al., 2015; Viswanatha et al., 2007; Voorhees -1985; Tadros 2013; Clark-2013 and Shedbalkar et al., 2015). Understanding the mechanisms underlying AuNPs therapeutic efficacy will aid in developing personalized medicines and treatments for cancer as a potential cancer therapeutic strategy.

Conclusion

In the 21st century, the biogenesis of nanomedicine has a great deal of potential for treating cancer by developing efficient anticancer nanomedicine and drug delivery systems that deliver potent drugs effectively to specific targeted areas. Looking at the enormous significance of AuNPs over the past few years and the safety and biocompatibility of green synthesis methods, it is envisaged that green synthesized AuNPs will eventually be beneficial in cancer therapy and diagnostic area. Plant-based AuNPs are likely to be highly advantageous in the fight against cancer due to their biocompatibility and pronounced anticancer therapeutic and diagnostic efficacy. These AuNPs may pave the way for developing a new generation of anticancer medicines in this fashion. Because of its pharmaceutical applications, the AuNPs industry has already evolved into a massive economy and is expected to increase more worldwide. Plant-based AuNPs will provide a considerable portion of this percentage if significant innovations and research are performed. Plant-based synthesis can provide a convenient and cost-effective outlet for AuNPs. Extensive research should be focused on designing and engineering the synthesis of plant-based AuNPs to meet the expectations commonly placed on chemically synthesized AuNPs. The green synthesis of AuNPs is still in its early stages. However, the in vivo study of AuNPs in various animals, along with three-dimensional spheroids and organoids models, has received little attention in the published literature. More research on this is needed, which will boost confidence in translational to clinical studies for the effective and safe utilization of AuNPs in cancer patients. To achieve this, the mass-scale manufacture of cost-effective and efficient AuNPs functionalized with moieties such as anticancer drugs and targeting ligands is required. Thus, certain efforts were needed to enhance nanoparticles synthesis at a large scale, successful clinical trial, resulting in nanoparticles with potential therapeutic applications, such as personalized

cancer therapy.

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