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REVIEW ARTICLE

Nanoparticle's efficacy in the suppression of heavy metals that affect breast cancer progression

Yasir Nawaz*[1], Saba Munir[2], Fouzia Tanvir[3], Asma Umar[4], Muhammad Ali[5]

[*1] PhD scholar, Department of Zoology, Faculty of Life Sciences, University of Okara, Okara, Pakistan

[2] PhD scholar, Department of Zoology, Faculty of Life Sciences, University of Okara, Okara, Pakistan

[3] Assistant Professor, Department of Zoology, Faculty of Life Sciences, University of Okara, Okara, Pakistan

[4] Senior Demonstrator, Department of Biochemistry, Allama Iqbal Medical College, Lahore, Pakistan

[5] Student, Department of Medical Laboratory Technician, Abasyn University, Islamabad, Pakistan

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Correspondence

** Yasir Nawaz*

royyasirnawaz@gmail.com

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ABSTRACT

The study aimed to assess the literature to explore the efficacy of different nanoparticles that play a role in suppressing various heavy metals that cause breast cancer. Breast cancer is a prevalent reason of death among females around the world. Heavy metals, including arsenic, beryllium, cadmium, nickel, hexavalent chromium, and much more, play a role in the expansion of various types of cancer, mainly breast cancer. Nanomedicine has unbelievable potential for developing cancer treatment and diagnosis by inventive biocompatible nanocomposites for treatment. Gold nanoparticle's role as an effective treatment is quickly increasing. Silver exhibited significant interactivity among various nanoparticles due to its distinctive characteristics, such as conductivity, stability, catalytic properties, and antibacterial attributes. These can also be used for antimicrobial activities for many microorganisms such as bacteria, fungi, protozoans, and, recently, viruses. The data from various studies was retrieved. The studies on heavy metals and nanoparticles and their role were retrieved and added to this study. This will help people understand the influential role of nanomedicine in suppressing breast cancer. It is concluded that extensive efforts have been devoted to addressing breast cancer by utilizing various nanoparticles, including gold and silver nanoparticles. Silver nanoparticles, gold nanoparticles, and Myr-AuNPs (Gold nanoparticles) demonstrate promise as potent anticancer agents for breast cancer. However, further research is needed to combat the current state of breast cancer effectively.

Keywords: *Breast cancer, Heavy metals, Nanoparticles, Nanomedicine, Gold, Silver.*

Introduction

Breast cancer

Breast cancer is a widespread and important reason for mortality among females around the world, with about 23% of total new cases and 14% of deaths in 2008. Nearly half of these occur in developed countries.[1] According to the latest GLOBOCAN 2018 data from the International Agency for Research on Cancer (IARC), gathered from 185 countries, there were 2.3 million new cases of breast cancer, constituting 11.7% of all cancer cases. The reported mortality rate for breast cancer was 6.9%.[2, 3] In 2019, 76.4% of women aged 50 to 74 indicated that they had undergone a mammogram within the preceding two years.[4] In 2020, breast cancer represented 24.5% of the 19.3 million new cancer cases around the world. Within this, 16.8% occurred in Sub-Saharan Africa (SSA). Additionally, breast cancer constituted 15% of the 9.9 million global cancer-related deaths, with 12.1% of these deaths occurring in Sub-Saharan Africa.[5] Despite experiencing a comparable incidence of breast cancer, Black women face a 40% higher mortality rate compared to their White counterparts.[6]

Many genes, enzymes, and molecules protect cancer cells against chemotherapy.[7] Owing to its pronounced traits of high metastasis, uncontrolled proliferation, immune evasion, and elevated mortality, current approaches for cancer management encompass surgical intervention, radiation therapy, and the administration of chemotherapeutic drugs.[8] Finally, these pathways were selected for drug treatment, playing a role in suppressing cancer cell propagation.[9]

Role of Heavy metals in breast cancer

Exposure to environmental pollutants such as cadmium, chromium, nickel, and arsenic falls into Group 1 of the International Agency for Research on Cancer's classification of carcinogens. Additionally, lead and mercury are reported as presumed human cancer-causing agents.[10] Many heavy metals play a role in the expansion of various types of cancer (i.e., arsenic, beryllium, cadmium, nickel, hexavalent chromium, and many more). Many studies reported the role of cadmium in cancer development.[11-19]

An epidemiological study unveiled a twofold increase in the risk of Breast Cancer (BC) among women with creatinine-adjusted urine cadmium levels exceeding 0.58 µg/g compared to those with levels less than 0.26 µg/g.[20] Elevated concentrations of cadmium in both breast cancer tissue and the urine of cancer patients, considering cumulative exposure from various sources, including smoking and diet, suggest a potential association between cadmium and breast cancer.

However, it's essential to acknowledge that this conclusion is somewhat tempered by specific methodological issues, such as age differences between the compared groups and a relatively small number of subjects.[21] Evidence shows that the path of contact and the chemical state of the cadmium is vital to developing tumor by contact with environmental pollutants.[22] Cadmium-induced carcinogenesis can be elucidated through various mechanisms: aberrant gene expression, inhibition of DNA damage repair, induction of oxidative stress, and suppression of apoptosis. Foremost among these factors is oxidative stress, primarily due to its role in the induction of abnormal gene expression, inhibition of DNA damage repair, and promotion of apoptosis in response to cadmium exposure.[23]

Previously, the occurrence of heavy metals as a possibly toxic accumulation to inorganic pesticide mixture was discussed. They stated that many metals like cadmium, cobalt, copper, and zinc are at high levels as a mixture in pesticide preparation. High lead, nickel, iron, and manganese levels were detected in other measures.[24]

Nanotechnology

Nanotechnology is a multidisciplinary area currently very favorable in treating cancer.[25] Nanomedicine has unbelievable potential for developing cancer treatment and diagnosis by inventive biocompatible nanocomposites for treatment, which shows a very appropriate method of nanoparticles.[26] In recent years, there has been an unparalleled surge in the utilization of nanocarriers, specifically within the size spectrum ranging from 10 to 100 nm, emerging as a novel therapeutic approach in cancer treatment. The US FDA has approved two therapeutic nanocarriers, liposomes and albumin nanoparticles, for clinical application. Moreover, an illustrative instance of an enhanced permeability and retention (EPR)-guided nano vector application in breast cancer chemotherapy is exemplified by liposomal doxorubicin and albumin-bound paclitaxel (Abraxane).

Current research priorities focus on target-specific drug therapy and early diagnosis methods for various pathologies, with nanotechnology emerging as a pivotal component in addressing these challenges.[27, 28] The data from various studies was retrieved. The studies on heavy metals and nanoparticles and their role were retrieved and added to this study. The previously reported studies were obtained from different sites and well-reputed journals to explore the study thoroughly. Various databases, including Google Scholar, were employed to acquire relevant data. The focus was on retrieving previous studies that investigated the impact of heavy metals and their treatment using nanotechnology.

Specifically, the study aimed to gather data on the effects of heavy metals on breast cancer and the utilization of nanoparticles in its treatment. Data that did not pertain to these specific aspects were excluded from the study.

Nanoparticles to suppress breast tumors:

Recently, a particular focus has been on utilizing nanomaterials as an efficient method for delivering drugs in cancer treatment. Ongoing investigations are dedicated to optimizing this approach to mitigate the adverse effects of conventional methods. Notably, various types of nanoparticles are commonly employed in research for drug delivery in breast cancer (BC) treatment. These include liposomes, mesoporous silica nanoparticles, viral nanoparticles, and polymer-, metal-, or carbon-based nanoparticles. Different drug loading techniques, such as encapsulation, covalent or electrostatic binding, and adsorption, are employed based on the specific characteristics of the nanoparticles.

Nanoparticles are selected for particular areas by surface alterations, which provide precise biochemical contacts with receptors found on targeted cells.[26-29] Another significant role of nanoparticles is the capability to deliver treatments to the targeted areas, crossing many biological blocks like blood-brain barriers.[30-33] The expansion of nanoparticle technique as imaging contrast chemicals also make the manufacture of multifunctional particles capable of selected tumor tomography and distribution of beneficial drugs.[34] The formation of nanoparticles by plants gets attention, principally because of its simplistic method and does not need any process like maintenance of microbial cultures and various cleansing stages.[35]

A simple and environmentally friendly bottom-up synthesis method was employed, utilizing Murraya Koenigii leaf extract as a reducing and stabilizing agent. This process resulted in the production of silver nanoparticles under ambient conditions and gold nanoparticles at 373K. The nanoparticles were thoroughly characterized through UV–vis, transmission electron microscopy (TEM), X-ray diffraction (XRD), and FTIR analyses. This approach allows for the creation of well-dispersed silver nanoparticles, approximately 10nm in size, and gold nanoparticles, about 20nm in size. Silver nanoparticles with a size of about 10nm, exhibiting a symmetric surface plasmon resonance (SPR) band centred at 411nm, were achieved within 5 minutes of adding the leaf extract to the solution of $AgNO_3$ at room temperature.

Nearly spherical gold nanoparticles with a size of approximately 20nm, featuring an SPR at 532nm, were obtained by introducing the leaf extract to the boiling solution of HAuCl4. The crystalline nature of the nanoparticles was confirmed through high-resolution TEM images, selected area electron diffraction (SAED), and XRD patterns. FTIR spectra revealed that the biomolecules responsible for capping differed between gold and silver nanoparticles. A comparative analysis with the author's earlier reports on biosynthesis is also provided.[35] The role of heavy metals in the tumor development and the utilization of gold and silver nanoparticles to suppress their effect (Figure 1).

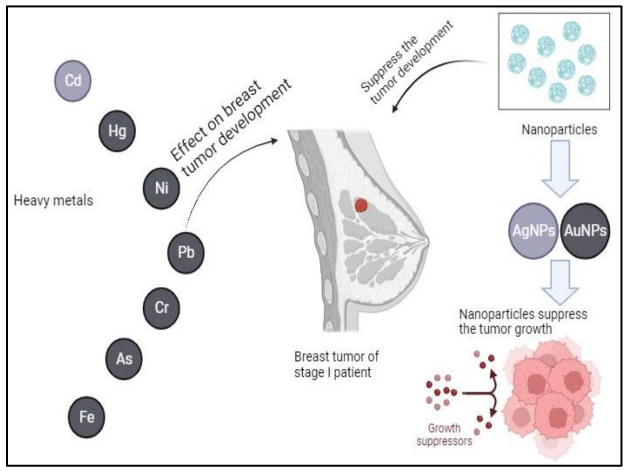

Figure 1: Heavy metals effect and their suppression by nanoparticles

Gold nanoparticles

The importance of gold nanoparticles (AuNP) as a drug delivery system (DDS) quickly increases.[36, 37] Gold nanoparticles exhibit high selectivity against cancerous cells, primarily attributed to their enhanced permeability and retention (EPR) effects.[38] Gold nanoparticles (AuNPs) can be designed in various configurations to sense stimuli, including molecular binding events or changes in ionic concentration. These engineered AuNPs can promptly respond by releasing cargo into cells or tissues, undergoing degradation, or even facilitating the chemical modification of drugs in both in vitro and in vivo settings. Nano-based materials not only hold the potential for integrating multiple therapeutic functions into a single platform but can also be directed to specific tissues.

This enables their reach to sub-cellular compartments or malignancies at different stages, enhancing their precision and effectiveness.[39] Their applications make them very capable of treatment. Precise production of different-sized particles (i.e., 1 to 150 nm) with partial size dispersity has been recognized,[40] and using ligand place-exchange responses,[41] a monolayer performing different functions can be invented. This structural diversity enables particle surfaces to contain many targeted agents.[42-44]

Upon exposure to infrared (IR) radiations, biological systems undergo a sequence of processes categorized into three phases: physical, chemical, and biological, each characterized by varying time scales.[45] In the initial nanoseconds of exposure, during the physical phase, IR interacts with biomolecules, leading to ionization or excitation and the generation of free radicals. DNA is a primary target Among various cellular components, influencing radiobiological effects. If possessing sufficient energy, ejected electrons travel further, colliding with subsequent atoms and initiating a cascade of ionization events. Transitioning into the chemical phase, these highly reactive radicals undergo rapid reactions, either permanently fixing the damage or scavenging reactions to restore cellular charge equilibrium. In the final biological phase, cellular processes are activated to repair radiation-induced damage.

The success or failure of these repair mechanisms determines the cell's fate, with unsuccessful repair eventually leading to cell death over a span ranging from seconds to days or even years. Hydrophobic medicines can be laden on gold Nanoparticles (NPs) by non-covalent relations, which requires no structural change to the medicine for drug release.[46] Also, covalent coupling to the gold NP by cleavable associations can be used to carry prodrugs to cells, and medicine can then be released by exterior[47] or interior[48] response. Regardless of the technique used, the tunability of the gold NP single layer is critical for interior or exterior release processes. Nanotechnology is considered an essential part of treatment design and distribution,[49] and among numerous NPs, gold NPs are highly discriminating for cancer cells generally due to their improved penetrability and retaining effects.[38, 50]

Using the potential poisonousness of particles, NP preparations are used for better imaging of lumps due to their improved acceptance and attention in cancer cells.[51,52] Chemical structure knowledge of NPs allows the binding and transportation of anticancer remedies straight to the lump. The use of AuNPs has also been principally helpful in improving the exposure of tumor-containing cells.[52-54] It is clear that there are beneficial uses for heavy metals like gold to detect tumors in the cell, yet care is required when using other transitional metals.

Silver NPs

Among different NPs, silver nanoparticles (AgNPs) were very interactive in their unique characteristics, like conductivity, stability, catalytic and antibacterial character. Silver and silver-containing materials are used for antimicrobial activities for many microorganisms, such as bacteria, fungi, protozoans, and viruses.[55] The development of Multiple drug resistance (MDR) and the severe disadvantages of many remedies currently cause cancer to become very dangerous and lead to death around the world.

Curcumin, a natural diphenolic compound derived from turmeric (Curcuma longa), has demonstrated its capability to modulate intracellular signalling pathways governing cancer cell growth, inflammation, invasion, and apoptosis, highlighting its anticancer potential. This review focuses on designing and developing various delivery systems to achieve sustained and effective curcumin delivery, including nanoparticles, self-assemblies, nanogels, liposomes, and complex formulations. Additionally, we delve into the anticancer applications and clinical benefits associated with nano-curcumin formulations. While exploring the field, we highlight a limited number of innovative multifunctional and composite nanosystem strategies that provide simultaneous therapy and imaging characteristics. Furthermore, we summarize the challenges inherent in developing curcumin delivery platforms and present current solutions to enhance curcumin bioavailability and maximize its anticancer potential for therapeutic applications.

There is an urgent need to develop treatment strategies for early analysis and treatment with fewer side effects.[56] Current studies have focused on nano oncology that leads nanoscale particles and beneficial drugs for early judgement and its handling.[57] The practical applications of Gold and Silver Nanoparticles (Table 1).

Table 1: Applications of gold and silver nanoparticles

Sr.	Gold Nanoparticles	Silver Nanoparticles
1	Cancer detection and imaging	Production of reactive oxygen species and oxidative stress, DNA damage, cell cycle arrest
2	Detect biomarkers in the diagnosis of heart diseases	Helps in the induction of tumor cell death by apoptosis
3	Detect cancer types	Inhibit cell proliferation
4	Detect infectious agents	Acts as antimicrobial activity against a wide range of microorganisms like bacteria, fungi, protozoa and viruses
5	Immunoassays	Helpful in anticancer therapy
6	Deliver drugs to specific sites	Applied in the promotion of wound repair and bone healing, or as the
7	Helps in making imaging	vaccine adjuvant
8	Improve anticancer drug bioavailability	Acts as anti-diabetic agent
9	Photodynamic therapy and photothermal therapy	Acts as biosensors

Conclusion

In this study, we explored the efficacy of various nanoparticles, including gold NPs, silver NPs, and Myr-AuNPs, in combatting breast cancer. Much work is done to combat breast cancer by different nanoparticles, i.e., gold NPs, silver NPs and many more. To conclude, silver NPs, gold NPs, and Myr-AuNPs are helpful for BC as a potent anticancer medicine. More research is required to combat the present condition of breast cancer.

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