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Inorganic Compounds Utilized in Cancer Therapy: A Compre-hensive Review

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Abstract

Background: Cancer is the most feared disease, with more than 1.6 million cases yearly. Cancer can start almost anywhere in the human body, from the uncontrollable growth and multiplication of damaged cells. Cancerous tumors can spread into the human body (a process called metastasis) in a solid form usually, but the cancers of the blood generally do not.

Methods: The review analyzes a wide range of scientific literature and research studies to assess the efficacy and mechanisms of action of different inorganic compounds in cancer therapy. It covers both preclinical and clinical studies, examining the effects of these compounds on tumor growth inhibition, apoptosis induction, and modulation of signaling pathways.

Results: Cancer treatment includes chemotherapy, surgery, and radiation. In this article, we will address inorganic compounds as a source of treatment, diagnosis, and carriers of active substances. Overall, this comprehensive review highlights the diverse roles of inorganic compounds in cancer therapy. It emphasizes the importance of further research to better understand the mechanisms of action, optimize dosage regimens, and enhance the clinical efficacy of these compounds in the treatment of cancer.

Conclusion: The findings presented in this review contribute to the development of innovative and effective therapeutic strategies for cancer treatment.

Keywords: cancer; cisplatin; selenium; zinc; copper; gold

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Background

The incidence of illness is progressively escalating in conjunction with the expanding global population. Within this landscape, cancer is emerging as a significant contributor to morbidity and mortality worldwide. Astonishingly, cancer accounts for nearly 15% of global deaths, positioning it as the second most prevalent cause of mortality, as per the World Health Organization [1]. Among males, the highest proportions of cancer cases are observed in the prostate, lung and bronchus, colon and rectum, and urinary bladder. Conversely, the most prevalent sites for cancer occurrence among females include the breast, lung and bronchi, colon and rectum, uterine corpus, and thyroid. Notably, prostate cancer and breast cancer contribute significantly to the overall cancer burden in males and females, respectively. Moreover, hematological malignancies, such as blood cancer, along with cancers affecting the brain and lymph nodes, exhibit the highest incidence rates among young individuals [2-3]. Presently, surgery, radiotherapy, and chemotherapy continue to serve as the primary treatment modalities for cancer, either administered individually or in combination, with a personalized approach based on the tumor's specific attributes (such as type, stage, aggressiveness, and accessibility), the patient's symptoms, and their overall health status. Immunotherapies have emerged as innovative therapies that aim to enhance the patient's immune system's capacity to effectively target and eliminate cancer cells. Nevertheless, there are several prominent challenges associated with the current cancer treatment protocols, including non-specific distribution of therapeutic agents, inadequate drug concentrations at the tumor site, and insufficient monitoring of pharmaceutical delivery to the tumor. Cancer remains a significant global health concern, necessitating the development of effective therapeutic strategies. Recent research has focused on investigating the role of microelements, such as zinc, selenium, iron, copper, and manganese, in cancer therapy. Microelements play crucial roles in various physiological processes, and their dysregulation has been implicated in carcinogenesis. This review provides an overview of the recent literature on the potential application of microelements in cancer treatment [4-5].

Methods

Initially, we searched research papers using keywords such as cancer, inorganic sub-stances, cisplatin, zinc, and selenium. The publications that met these word criteria were then thoroughly scrutinized, and their conclusions were reported.

Results and discussion

3.1. Cisplatin

Cisplatin, also known as cis-diamminedichloroplatinum (II), is a coordination compound of metallic (platinum) with square planar geometry. At room temperature, it is a white or deep yellow to yellow-orange crystalline powder that is soluble in dimethylprimanide and N, N-dimethylformamide, and only moderately soluble in water. Under normal conditions of pressure and temperature, cisplatin is stable, but it can gradually change into the trans-isomer over time. [4] Since it has demonstrated anticancer activity in a number of tumors, including ovarian cancer and solid tumors of the head and neck, cisplatin has received particular attention. Its cytotoxic capabilities were found in the 1960s, and by the end of the 1970s, it had established itself as a crucial component in the systemic treatment of malignancies. Cisplatin is one of the most effective chemotherapy medications available for treating cancer. It was the first platinum compound for cancer treatment to receive FDA approval in 1978 [6]. Although cisplatin chemotherapy initially demonstrates favorable response rates in a majority of patients, a subset of individuals eventually experience relapse and develop resistance, significantly diminishing the clinical efficacy of the drug. Evidence from tissue culture studies indicates that drug resistance may arise due to epigenetic alterations at the cellular and molecular levels. These alterations encompass heightened DNA damage repair (DDR) mechanisms, aberrant DNA methylation patterns, dysregulated mRNA expression levels, perturbed transcriptional regulation, and impaired apoptosis signaling. Cisplatin exerts its molecular cytotoxic effects through various mechanisms, including the displacement of one chloride ligand, formation of intra-strand DNA adducts, and inhibition of DNA synthesis and cellular proliferation. Notably, the DNA lesions resulting from cisplatin-induced DNA damage stimulate the activation of DNA repair response through the nuclear excision repair system (NER). However, the activation of the ATM (ataxia telangiectasia mutated) pathway can impede cisplatin-induced cell death, thus contributing to drug resistance [7].

3.1.1. Cisplatin in lung cancer

One of the most frequent fatal cancers is still lung cancer. 15% of all lung cancers are small cell lung cancers (SCLCs). The main medications for SCLC at the moment are platinum-based therapies. Because of its potent anticancer activity, cisplatin is frequently chosen in clinical trials; nonetheless, it has side effects that include nausea, vomiting, and kidney damage. Therefore, large-dose infusion is required in chemotherapy based on cisplatin and urine volumes should be monitored to prevent renal toxicity. In the case of NSCLC, surgery is the predominant treatment, with adjuvant cisplatin-based chemotherapy being used in cases of stage II and III illness. Due to poor medication delivery to the tumors, several potent therapeutic medicines tested in vitro did not provide any effects in vivo. Using protective substances such curcumin, berberine, resveratrol, and cinnamon, scientists have been effective in decreasing side effects or improving the anticancer efficacy of CP to get over this obstacle. To increase the bioavailability of medications, drug delivery systems incorporating micro- and nanocarriers are helpful. For instance, adding CP to a wide range of nanoparticles has proven to be effective in boosting drug effectiveness.

The initial step in mitigating platinum-associated nephrotoxicity is the selection of individuals with a suitable glomerular filtration rate (GFR) exceeding 60 ml/min. Various techniques are available for estimating GFR, but their detailed discussion falls outside the scope of this review.

Clinicians have historically employed serotonin receptor-3 (5-HT3) antagonists and corticosteroids to manage the potential dose-limiting toxicity of emesis. Aprepitant, an oral neurokinin-1 (NK-1) receptor antagonist, has been incorporated into the standard treatment regimen for patients receiving cisplatin since its introduction in 2003 for highly emetogenic chemotherapy.

When used in combination with dexamethasone and a 5-HT3 receptor antagonist, Aprepitant significantly increases the likelihood of achieving complete control of emesis, thereby eliminating the need for rescue treatment, and reducing vomiting from approximately 50% to 75%. Notably, it demonstrates a robust effect on delayed emesis. The 2010 revision of the Multinational Association of Supportive Care in Cancer (ESMO/MASCC)

recommendations on nausea and vomiting incorporated these findings. The most frequent cisplatin treatment dose-limiting issue is peripheral neurotoxicity. Paraesthesias and numbness are the primary symptoms of cisplatin neurotoxicity, and they often appear within the first few medication cycles. After a few treatment cycles, ataxia, paraesthesia, and loss of vibration perception may become evident. Peripheral neuropathy alterations may start after the treatment is finished and continue for 2.5 to 5.5 months after the cisplatin has been stopped. Monitoring with audiograms should be taken into consideration because of the cumulative and potentially permanent ototoxicity brought on by cis-platin. Up to 31% of patients receiving a single dosage of cis- platin 50 mg/m2 have had ototoxicity, which is characterized by tinnitus and/or hearing loss in the high frequency range [7].

3.1.2. Cisplatin in ovarian cancer

About 204,000 women worldwide are affected by epithelial ovarian cancer (EOC), which also causes about 125,000 deaths. Because it doesn't show any symptoms until it has spread to the peritoneal cavity, when there is little chance of recovery, it is frequently referred to as the "silent killer."

Over the past 30 years, the management of advanced EOC has changed to include both chemotherapy and cytoreductive surgery (CRS). When combined with chemotherapy, CRS is thought to be effective because it eliminates large tumors that contain poorly oxygenated, non-proliferating cells that are either already resistant to chemotherapy or may become so in the future. This leaves behind smaller tumors that have a higher percentage of cells that are in the proliferative phase, making them more susceptible to chemotherapy. Previously, any nodule with a dimension of less than 2 cm was considered to have "optimal" residual disease at the conclusion of initial CRS for EOC; however, it is now known that patients with absolutely no macroscopic residual disease have the best prognosis. One of the most potent medications used to treat ovarian cancer intraperitoneally is cisplatin. According to pharmacokinetic analyses of IP cisplatin, its high peritoneal clearance (43 ml/min) is a result of its large molecular weight. Early clinical trials demonstrating the safety and efficacy of IP treatment with cisplatin at recommended dosages (So-150 mg/m') [8-9].

3.1.3. Cisplatin in head and neck cancer

Head and neck cancer (HNC) encompasses malignant tumors originating in the upper aero-digestive tract, including the lips, mouth, tongue, nose, throat, vocal cords, and sections of the esophagus and windpipe. With an annual incidence exceeding 500,000 cases, HNC ranks as the eighth most prevalent cancer worldwide. Notably, squamous cell carcinomas account for over 90% of head and neck cancers. Unfortunately, nearly 50% of these cancers are diagnosed at an advanced stage, necessitating multi-modal treatment approaches such as radiotherapy, chemotherapy, and surgery to preserve organ function. Cisplatin is frequently employed as a first-line chemotherapeutic agent in conjunction with radiotherapy for HNC. The most widely adopted treatment regimen follows the Radiation Therapy Oncology Group (RTOG) schedule, which combines conventional radiation therapy with cisplatin administered at a dose of 100 mg/m^2. Alternatively, cisplatin can be administered at a preferred dose of 40 mg/m2 in conjunction with either conventional or intensified radiation therapy, as per the RTOG schedule. Furthermore, in the context of locally advanced head and neck cancer, cisplatin in combination with established chemotherapeutic agents such as docetaxel and fluorouracil has demonstrated superior efficacy in induction therapy compared to cisplatin and fluorouracil alone [10, 11].

3.2. Arsenic Trioxide

Acute promyelocytic leukemia (APL) patients who have just been diagnosed as well as those who have relapsed have both responded favorably to treatment with arsenic trioxide. It generates complete remissions when used alone, with few side effects and barely any myelosuppression.

Certain patients with acute promyelocytic leukemia (APL) may not be suitable candidates for initial arsenic trioxide (As_2O_3) treatment due to various factors such as positivity for PLZF/RAR gene, moderate to severe liver or kidney dysfunction unrelated to leukemia, relapse during continuous As_2O_3 maintenance treatment, or prolonged exposure to arsenic. Hemoglobin concentration, platelet count, bone marrow normoblast count, and band-cell count of peripheral white blood cells (WBC) exhibit positive associations with therapeutic efficacy and prognosis. However, WBC count, peripheral juvenile blood cell count, myeloproliferative level, and lactic dehydrogenase (LDH) activity do not demonstrate significant correlations. The considerable activity of arsenic trioxide in patients with APL is a noteworthy finding, considering that 20% to 30% of acute myelogenous leukemia patients experience relapse despite receiving all-trans retinoic acid and combination chemotherapy.

The administration of an As_2O_3 regimen may be recommended in the following clinical scenarios:

- Previously untreated or newly diagnosed APL
- APL resistant to combination chemotherapy or all-trans retinoic acid, recurrent APL following bone marrow transplant, or relapsed APL.
- APL patients who are unable to tolerate or should not receive combination therapy with retinoic acid and chemotherapy.
- Maintenance therapy after achieving complete remission from acute lymphoblastic leukemia.
- Chronic granulocytic leukemia (CGL), certain subtypes of acute nonlymphocytic leukemia, and myelodysplastic syndromes (MDS) accompanied by a significant increase in promyelocytes.

For adults with APL, a daily intravenous injection of 10 ml of As_2O_3 (1 g/L) is administered over a 3-4-hour period, diluted in 250-500 ml of 50 g/L glucose solution or normal saline. The daily dosage for children with APL is 6 mg/m_2 (or around 0.16 mg/kg).

The duration of the single treatment session is 4 weeks, perhaps with a 5- to 7-day break in the middle [12-15].

3.3. Zinc and compounds

The most prevalent malignant tumor in men is prostate cancer (PCa). Early-stage PCa can be successfully treated with curative treatment options such as surgery and radiation therapy. However, hormonal ablation of metastatic cells can result in PCa cells losing their dependence on androgen, which would then result in a hormone-independent tumor with a very low chance of survival. Human prostate gland glandular epithelial cells have the capacity to accumulate a significant amount of zinc, two to five times that of other tissues. Zinc buildup prevents mitochondrial aconitase activity, which prevents cells from oxidizing citrate. In order to chelate intracellular zinc, prostate cells can build up significant amounts of citrate. Malignant cells require low zinc concentrations to activate the citrate oxidation process, which increases their energy efficiency. In contrast, normal epithelial cells accumulate zinc, which inhibits the m-aconitase. Increasing the amount of circulating zinc that is accessible for cellular absorption would, in

theory, be a successful strategy for treatment. Organic substances known as Schiff bases have a variety of biological characteristics. The efficacy of these compounds as chemotherapeutic agents is significantly influenced by the specific metal used and the complexity of the Schiff base. In biomedical research, researchers commonly employ human prostate cell lines PC3 and PNT1A. Upon comparing microscopic images of these two cell lines, it was observed that the Zn-SB complex exhibited a dispersed distribution throughout the cytoplasm of PC3 cells, whereas it was predominantly localized to the membrane in PNT1A cells. Notably, after 12 hours of treatment, PC3 cells exhibited membrane "blebbing," which is indicative of cell death through apoptosis. Conversely, PNT1A cells remained viable and unaffected. In terms of innate immunity, zinc deficiency has been found to impact various aspects, including the cytotoxicity of natural killer cells, the phagocytic activity of neutrophils, the ability of immune cells to generate oxidants against pathogens, and the function of macrophages. Furthermore, zinc deficiency also affects adaptive immunity, particularly the number and activity of lymphocytes. Insufficient zinc levels can lead to thymic atrophy, resulting in an imbalance in helper T cell subsets. Additionally, zinc deficiency affects cytokine production, leading to oxidative stress and inflammation. Even suboptimal zinc levels, which are often underestimated, can adversely affect different facets of the immune system [16-25].

3.4. Selenium and compounds

Various forms and doses of selenium have been used in clinical trials to evaluate selenium's efficacy as a chemopreventive agent, with varying degrees of success. Instead of being directly cytotoxic agents, selenium species are currently being therapeutically assessed as modulators of medication responses. Both immune-suppressing and immune-boosting effects of selenium have been demonstrated. Some of selenium's immune-stimulating qualities are caused, at least in part, by its role in promoting B cell activation and proliferation (as found in humans) and/or immune cell differentiation (as seen in mouse research). Basal plasma Selenium levels in the participants are crucial for Seleneium's prophylactic impact, based on research on humans. Males with Se concentrations between 135 and 170 ng/mL had a 15%–25% lower risk of prostate cancer than those with plasma levels of Se around 60 ng/mL. Even more noticeably, their probability of developing advanced prostate cancer was decreased by 40%–50%. These findings suggested that Selenium may prevent the spread of prostate cancer metastases. There has been considerable debate over the connection between Selenium level and cancer. The majority of studies show decreased Selenium levels in thyroid cancer patients. A high quantity of free radicals produced by oxidative stress might be linked to Selenium insufficiency in a number of disorders, including cancer. Thyroid tumor tissue samples show a much higher generation of ROS than healthy tissue. Selenium plays a significant role in the removal of ROS and is found in high amounts in the thyroid. Therefore, a change in its level could have an impact on the thyroid's GPx1 and GPx3 antioxidant selenoproteins, which are sensitive to Se intake. At various stages of tumor development, abnormal redox regulation is seen in cancer cells. To keep the redox equilibrium, tumor cells need antioxidant molecules such selenoproteins. Antioxidant protein expression rises in several cancer types while falling in others. Indeed, the expression of selenoproteins like the GPx gene differs significantly between normal and tumor cells. 15 selenoprotein genes were examined in two cohorts for colorectal cancer. In contrast to SePP and selenoprotein S, both selenoproteins TRx3 and GPx2 were increased in adenoma and cancer. The fact that GPx2 and TRx3 are target genes for Wnt signaling explains why their gene expression has risen. The majority of colorectal cancer tissues have this signaling pathway active. The fact that certain selenoproteins appear to inhibit tumor cell development while others appear to promote it emphasizes how poorly understood the carcinogenesis pathways associated with the Selenium status are [26-37].

3.5. Ruthenium

Ruthenium complexes have gained recognition as effective alternatives to platinum complexes, offering distinct modes of action and a diverse range of activities. Notably, there are several noteworthy qualities associated with ruthenium:

Ruthenium complexes possess the ability to coordinate ligands that can modulate their activity, exhibiting similar kinetics of ligand substitution in aqueous environments as platinum (II) complexes.

These complexes can exist in multiple oxidation states (II, III, and IV) that are accessible under physiological conditions. This property is advantageous in the reducing environment found in cancer tissues.

The octahedral coordination geometry of ruthenium allows for the exploration of a greater variety of ligands compared to platinum complexes, thereby enabling the occupation of numerous spatial positions.

Ruthenium complexes have demonstrated lower toxicity compared to platinum compounds. This reduced toxicity is attributed to their ability to mimic iron binding to serum transferrin, resulting in higher selectivity for their targets and preferential uptake by tumor cells rather than healthy tissues.

Cells can uptake ruthenium complexes through two different mechanisms: energy-dependent endocytosis and active transport, as well as energy-independent enhanced diffusion and passive diffusion. Flow cytometry studies have shown that ruthenium compounds can penetrate the cell membrane and accumulate in the nucleus, leading to cell cycle arrest and apoptosis in various tumor cells.

The unique qualities and diverse mechanisms of action make ruthenium complexes promising candidates for cancer therapy, offering potential advantages over traditional platinum-based treatments [38- 45].

3.6. Copper

Because endogenous metal ions may result in less systemic toxicity, copper complexes are the most researched and used complexes for their antitumor properties. The characteristics of the ligands, which may also have antiproliferative activities, govern the features of the copper complexes. In order to demonstrate several anticancer processes, a number of Cu (II) complexes have been created with a range of ligands comprising N, S, or O. The ligands engage noncovalently with proteins or intercalate into the DNA molecule to neutralize the copper ion's electrical charge and make it easier for the complex to pass across the cell membrane. Copper complexes have the ability to cause DNA cleavages through oxidative or hydrolytic processes. Recently, the copper (II) complex $[Cu(C_{20}H_{22}NO_3)_2]*H_2O$ was created, and the spectroscopic methods used to analyze it revealed that the complex attaches to the DNA of the calf thymus by partial intercalation and exhibits a static quenching process as the binding mechanism. A beneficial synergistic effect may be taking place since the cytotoxicity assay in cancer cell lines revealed increased cytotoxicity when compared to the Schiff base ligand.

Thiosemicarbazone ligands are copper compounds that have anticancer action by blocking enzymatic function and causing cell apoptosis. By concentrating on DNA and proteins, a Cu pro-drug created from thiosemicarbazone and based on the His146 residue in the IB subdomain of human serum albumin (HSA-PA) that has been mutated by palmitic acid (PA) can destroy cancer cells. Additionally, by substituting His146 for the leaving group and coordinating it with Cu^{2+} to form the HSA PA complex, the effective delivery of the Cu pro-drug was enhanced. The HSA-PA combination demonstrated improved tolerability, increased drug accumulation in the tumor, a greater ability to suppress tumor development, and less toxicity in surrounding tissues [46-50]. Copper compounds have been investigated for their potential role in cancer treatment.

3.7. Vanadium

Vanadium compounds exert their anticancer effects through various molecular targets, including caspases, which induce cell cycle arrest and cell death. Additionally, these compounds impact cellular metabolism by generating reactive oxygen species (ROS), depleting glutathione (GSH), causing alterations in cellular organelles, and modulating signal transduction pathways. In the metallocene vanadocene, a metal ion is sandwiched between two cyclopentadienyl rings. Among vanadocene derivatives, vanadocene dichloride has shown promising results in preclinical research. In vitro studies demonstrated its high efficacy against a range of tumor cells. Moreover, vanadocene dichloride exhibited significant anticancer effects in in vivo experiments. Notably, certain vanadocene derivatives have demonstrated cytotoxic effects on T-lymphocytic leukemia cells, with mechanisms involving DNA damage and p53 activation. Vanadocenes have also demonstrated effectiveness against human testicular cell lines. These findings highlight the potential of vanadium compounds, particularly vanadocene derivatives, as valuable agents in the field of cancer treatment. Further investigation and research are warranted to fully elucidate their mechanisms of action and optimize their therapeutic applications [51-54]. Vanadium compounds have been studied for their potential anticancer properties, although their use in cancer treatment is still primarily in the experimental and preclinical stages. As such, there is limited information available on the specific doses used in human cancer treatment.

3.8. Osmium

Ruthenium's heavier congeners, osmium complexes (Os(II) and Os(III) complexes), have slower kinetics than ruthenium and are substitution-inert. Osmium compounds have been widely used because of their ability to target mitochondrias, increase the production of ROS, oxidize NADH to NAD^+, interfere with cell cycle progression in cancer cells, and disrupt redox signaling pathways. In recent years, efforts have been made to develop osmium analogs of ruthenium-based anticancer drugs, such as RAPTA-C, NAMI-A, and KP1019. Furthermore, progress has been made in the development of metal-chemotherapy drug complexes utilizing noble metals such as rhodium, osmium, palladium, ruthenium, and iridium, similar to the platinum-based drug cisplatin. However, the theranostic application of osmium nanostructures has received limited attention in the literature since 2010, similar to rhodium. In an in vitro study, osmium nanostructures (including spherical, core-shell, and nanorods) were found to exhibit optothermal properties. The incorporation of a silica layer not only improved the stability of the nanostructures but also enhanced their overall temperature and thermal conductivity when exposed to a laser source. More recently, osmium-tellurium nanorods were investigated for their enzymatic activity and demonstrated excellent photothermal, photocatalytic, and photodynamic effects, providing a penta-modal treatment approach for hepatocellular carcinoma. This formulation effectively reduced hypoxia by generating oxygen and mitigated bone marrow and other organ toxicity by targeted drug delivery within the tumor. These findings highlight the potential of osmium-based compounds and nanostructures as versatile agents in cancer treatment, particularly in multimodal therapeutic approaches. Further research is necessary to explore their efficacy, safety, and clinical applications, as well as to elucidate their underlying mechanisms of action [55-56]. Osmium compounds have shown promise in cancer research due to their potential cytotoxic effects. However, their use in cancer treatment is still in the experimental stage, and there is limited information available on specific doses used in human cancer therapy. In table number 7 are some common osmium compounds that have been investigated and their potential usage in cancer.

3.9. Gold and compounds

Due to its bacteriostatic, anticorrosive, and antioxidative qualities, gold is a multipurpose substance that has been used in medical applications for generations. Gold nanoparticles possess unique properties that make them promising candidates for hyperthermic cancer treatments and medical imaging applications. One of their key attributes is their ability to absorb light at specific wavelengths, leading to photoacoustic and photothermal effects. This phenomenon, known as localized plasmon surface resonance (LPSR), has been observed in colloidal gold nanoparticles. The photochemical activities of gold nanoparticles exhibiting LPSR can be modulated by varying their size and shape, thereby influencing their photothermal and photoacoustic characteristics. This characteristic enables the utilization of different light wavelengths, particularly in the near-infrared spectrum. Gold nanoparticles can be engineered at the nanoscale and passively distributed throughout the body. This allows them to accumulate in tumor tissues, which are characterized by leaky blood vessels while being safely eliminated through the urinary system. The application of thermal stress to tumors through hyperthermia can enhance their radiosensitivity, leading to improved response to radiation therapy and increased cancer survival rates. Studies on metastatic head and neck squamous cell malignancies have demonstrated the efficacy of combining intense radiation therapy with hyperthermia, resulting in improved outcomes without significant increases in toxicity. However, traditional hyperthermia induction methods are limited in their effectiveness and often cause untargeted heating throughout the body, leading to undesirable side effects.

In contrast, light serves as a preferable external stimulus due to its controllability and concentration capabilities. By leveraging light, hyperthermia can be precisely targeted and remotely controlled, minimizing harm to healthy tissues. This enhanced targeting and control facilitate more effective and safer treatments. In summary, gold nanoparticles with their unique light-absorbing properties offer opportunities for localized hyperthermia in cancer therapy, providing improved therapeutic outcomes with reduced side effects. Further research is needed to optimize the design and delivery of gold nanoparticles and explore their full potential in clinical applications.

Recent developments in the multifunctional design of gold nanoparticles enable the regulated and targeted administration of many desired medications as well as the formation of localized

heat in close proximity to cancer tissues. Gold nanoparticles can be used for photothermal therapy (PTT) to treat cancer because they have a number of advantages, including the ability to target the local tumor area while minimizing non-specific distribution, the ability to be activated by near-infrared (NIR) laser light, which allows them to penetrate deeply into biological tissues, and the ability to be modulated to create cancer PTT and drug delivery systems with multiple functions [57-62]. Gold compounds have been investigated for their potential applications in cancer treatment. In table 8 are summarizing some common gold compounds used in cancer research, along with their potential usage and typical doses.

Table 1. Uses of cisplatin in cancer and the necessary doses.

Compound	Usage in cancer	Typical dose
Cisplatin	Testicular, ovarian, bladder, lung, head, and neck cancers	20-100 mg/m² every 3-4 weeks
Carboplatin	Ovarian, lung, and other types of cancers	4-6 mg/mL/min every 3-4 weeks
Oxaliplatin	Colorectal cancer	85-130 mg/m² every 2-3 weeks
Nedaplatin	Lung, ovarian, and head and neck cancers	80-120 mg/m² every 3-4 weeks
Satraplatin	Prostate, ovarian, and other types of cancers	80-120 mg/m² every 5-6 weeks
Lobaplatin	Lung, ovarian, and other types of cancers	25-50 mg/m² every 3-4 weeks
Heptaplatin	Lung, gastric, and other types of cancers	100-300 mg/m² every 3-4 weeks
Spiroplatin	Ovarian, cervical, and other types of gynecological cancers	70-100 mg/m² every 3-4 weeks
Proplatine	Ovarian, bladder, and other types of cancers	60-120 mg/m² every 3-4 weeks

Table 2. Side effects associated with cisplatin chemotherapy treatment for ovarian cancer.

Side Effect	Description
Nausea and vomiting	Cisplatin can cause significant nausea and vomiting. Antiemetic medications are usually prescribed to manage these symptoms.
Kidney damage	Cisplatin can be toxic to the kidneys and may cause impaired kidney function. Regular monitoring of kidney function is essential during treatment.
Peripheral neuropathy	Cisplatin may cause damage to the nerves, leading to numbness, tingling, or pain in the hands and feet.
Hearing loss	Cisplatin treatment can cause hearing loss or tinnitus (ringing in the ears). Regular hearing tests may be recommended.
Bone marrow suppression	Cisplatin can suppress the bone marrow, leading to a decrease in red and white blood cell counts and platelets. This may result in anemia, increased risk of infections, and easy bruising or bleeding.
Fatigue	Feeling tired and lacking energy is a common side effect of cisplatin treatment. It may vary in severity from mild to debilitating.
Allergic reactions	Some individuals may experience allergic reactions to cisplatin, ranging from mild skin rashes to more severe symptoms like difficulty breathing or anaphylaxis.
Gastrointestinal disturbances	Cisplatin may cause diarrhea or constipation, as well as other gastrointestinal symptoms such as abdominal pain or indigestion.
Hair loss	Temporary hair loss or thinning (alopecia) is a possible side effect of cisplatin, but the hair generally regrows after treatment ends.
Decreased appetite	Cisplatin treatment can lead to a decreased desire to eat, resulting in weight loss or nutritional deficiencies.
Increased risk of infections	Due to its effects on the bone marrow and immune system, cisplatin treatment may increase the risk of infections.

Table 3. Gold compounds used in the treatment of cancer, their potential usage, and typical dosage.

Compound	Usage in Cancer	Typical Dosage Range
Gold Nanoparticles	Drug delivery, imaging, and photothermal therapy	Varies depending on the specific application
Auranofin	Rheumatoid arthritis, investigational in cancer	Rheumatoid arthritis: 6-9 mg/day; Investigational in cancer: Varies depending on the study or trial
Gold(III) Compounds	Experimental and investigational	Varies depending on the study or trial
Gold(I) Thiolates	Experimental and investigational	Varies depending on the study or trial
Gold(III) Dithiocarbamates	Experimental and investigational	Varies depending on the study or trial
Gold(III) Porphyrins	Experimental and investigational	Varies depending on the study or trial

Conclusion

The battle against cancer is a significant challenge that society will face in the coming decades. Given the projected increase in cancer incidence and its associated consequences such as high mortality rates and significant social and economic impacts, extensive research in this field is of utmost importance. The primary goal of addressing this issue is to improve the quality of life for cancer patients by mitigating the adverse effects of medication. From an economic perspective, it is crucial to consider that cancer disorders incur both direct and indirect costs. Direct expenses encompass the expenditures associated with cancer diagnosis and treatment, while indirect costs refer to the broader socioeconomic consequences. These may include productivity losses, decreased work capacity, and increased burdens on healthcare systems and caregivers. Therefore, efforts must be directed toward developing innovative approaches that not only target cancer effectively but also minimize the negative impact on patient's well-being. This entails exploring strategies that reduce the side effects of cancer treatments, improve overall patient outcomes, and optimize resource allocation in the healthcare system. By prioritizing

research and adopting a comprehensive approach to cancer management, we can strive towards improving the lives of cancer patients, reducing the burden on society, and mitigating the economic implications of this pervasive disease.

Abbreviations

neurokinin-1 (NK-1)
serotonin receptor-3 (5-HT3)
glomerular filtration rate (GFR)
cytoreductive surgery (CRS).
epithelial ovarian cancer (EOC)
Head and neck cancer (HNC)
Radiation Therapy Oncology Group (RTOG)
lactic dehydrogenase (LDH)
white blood cells (WBC)
human serum albumin (HAS)
palmitic acid (PA)
reactive oxygen species (ROS),
depleting glutathione (GSH)
photothermal therapy (PTT)

Authors' Contribution

AS came up with the idea and participated in writing of the manuscript. IIL performed all literature surveys. IB analyzed the interpretation of literature. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare no conflict of interest.

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