J Nanostruct 15(1): 190-199, Winter 2025

RESEARCH PAPER

Recent Updates on Chemotherapy of Pt Complexes and Pt Nano-Composites for Breast Cancer Therapy: A Mini-Review

Bobojonov Otabek Khakimboy Ugli [1], Ghufran Lutfi Ismaeel [2], Safaa Mustafa Hameed [3], Ali Fawzi Al-Hussainy [4] *, Baydaa Abd [5], Hadil Hussain Hamza [6], Sarah Salah Jalal [7], Reem Mohsin Khalaf [8], Jalalova Vazira Zamirovna [9], Jurayeva Dilafruz Jamurodovna [10], Tovbaeva Mukaddam Safarovna [10], Meliboev Rozali Abdusattor ogli [11], Korshubaeva Rano Khazratkulovna [12]

[1] *Department of Fruits and Vegetables, Urganch State University, Uzbekistan*

[2] *Department of Pharmacology, College of Pharmacy, University of Al-Ameed, Karbala, Iraq*

[3] *Department of Optics, College of Health and Medical Technology, Sawa University, Almuthana, Iraq*

[4] *College of Pharmacy, Ahl Al Bayt University, Kerbala, Iraq*

[5] *Al-Manara College for Medical Sciences, Amarah, Iraq*

[6] *Department of Medical Laboratories Technology, Al-Nisour University College, Baghdad, Iraq*

[7] *College of Pharmacy, National University of Science and Technology, Dhi Qar, Iraq*

[8] *Mazaya University College, Iraq*

[9] *Department Clinic Pharmacology, Bukhara State Medical Institute, Uzbekistan*

[10] *International School of Finance Technology and Science, Uzbekistan*

[11] *Department of Hospital and Faculty Surgery, Fergana Medical Institute of Public Health, Uzbekistan*

[12] *Uzbekistan-Finland Pedagogical Institute, Uzbekistan*

ARTICLE INFO

Article History:
Received 22 September 2024
Accepted 26 December 2024
Published 01 January 2025

Keywords:
Breast cancer
Chemotherapy
Nanochemotherapy
Nanocomposites
Pt complexes

ABSTRACT

Breast cancer continues to be one of the most widespread cancers globally, underscoring the need for the ongoing development of treatment strategies to enhance patient outcomes. This review examines the significance of platinum (Pt) complexes and platinum nanocomposites in the chemotherapy of breast cancer, emphasizing their distinct mechanisms of action and potential to improve treatment effectiveness. Conventional chemotherapeutic agents frequently encounter issues such as systemic toxicity and the emergence of drug resistance, challenges that platinum-based compounds, particularly cisplatin and its analogs, seek to mitigate. Recent progress in nanotechnology has facilitated the creation of targeted delivery systems that enhance the bioavailability and localization of platinum compounds at tumor sites, thereby minimizing off-target effects. This review evaluates various studies that investigate the synthesis, characterization, and anticancer mechanisms of platinum nanoparticles (PtNPs) and their composites, including their interactions with breast cancer cell lines and their potential role as radiosensitizers. Furthermore, we explore the combination of platinum-based therapies with immune checkpoint inhibitors and other innovative treatments to address resistance mechanisms, especially in aggressive subtypes such as triple-negative breast cancer (TNBC). The role of personalized medicine, informed by genetic and molecular profiling of tumors, is also discussed in relation to the selection of suitable platinum therapies. By clarifying the current state and future prospects of platinum complexes in breast cancer treatment, this review aims to contribute to ongoing research initiatives and stimulate novel strategies to enhance therapeutic effectiveness and improve patient quality of life.

How to cite this article
Khakimboy Ugli B., Ismaeel G., Hameed S. et al. Recent Updates on Chemotherapy of Pt Complexes and Pt Nano-Composites for Breast Cancer Therapy: A Mini-Review. J Nanostruct, 2025; 15(1):190-199. DOI: 10.22052/JNS.2025.01.018

* *Corresponding Author Email: otabekbobojonov74@gmail.com*

INTRODUCTION

The advancement of chemotherapy has profoundly altered the landscape of breast cancer treatment, leading to improved therapeutic outcomes and enhanced efficacy [1-4]. Although conventional chemotherapeutic agents have proven effective against a range of cancers, they are often accompanied by significant systemic toxicity and the emergence of drug resistance, which pose substantial challenges [5, 6]. Recently, the integration of metal complexes into chemotherapy has surfaced as a promising approach to augment the effectiveness of anticancer treatments [7-10]. These metal complexes especially Pt-complexes, distinguished by their unique physicochemical characteristics and multifunctional properties, have the potential to interact with biological targets in innovative manners, thereby addressing some of the limitations associated with traditional agents [10-14]. This review examines the convergence of chemotherapy and Pt complexes, with a particular focus on platinum complexes nanocomposites, and investigates the mechanisms through which these metal-based compounds exert their anticancer properties. We will analyze Pt complexes, and their roles in enhancing the efficacy of standard chemotherapy regimens, increasing selectivity for cancer cells, and reducing adverse effects. Additionally, this article seeks to highlight recent progress in the design, synthesis, and clinical application of these complexes, offering a thorough overview of the current state and future prospects for the incorporation of metal complexes into chemotherapeutic strategies. In addition, Fig. 1 shows different types of chemotherapy drugs for breast cancer treatment.

Breast cancer continues to be one of the most widespread and formidable malignancies worldwide, impacting millions of women annually [15, 16]. Despite significant progress in early detection and therapeutic approaches, the intricate biology of breast cancer, marked by its various subtypes and differing therapeutic responses, poses ongoing challenges for effective treatment. Among the diverse treatment strategies, platinum-based agents, particularly cisplatin and its derivatives, have garnered significant interest due to their distinct mechanisms of action and potential efficacy against multiple breast cancer subtypes, notably triple-negative breast cancer (TNBC), which frequently exhibits resistance to conventional therapies [17-20]. The cytotoxic effects of platinum complexes are primarily mediated through the induction of DNA cross-links, which ultimately trigger apoptosis in rapidly proliferating cancer cells [21, 22]. Recent investigations have concentrated on improving the effectiveness of platinum compounds while addressing issues such as systemic toxicity, the emergence of drug resistance, and restricted therapeutic windows. Researchers have been examining the potential of these complexes in conjunction with other chemotherapeutic drugs, targeted therapies, and innovative delivery systems to enhance treatment outcomes for patients with breast cancer.

This review intends to present a thorough examination of the role of platinum complexes in breast cancer therapy, emphasizing their mechanisms of action, clinical effectiveness, and the status of ongoing clinical trials. Furthermore, we will explore advancements in the development of novel platinum analogs and their prospective roles in personalized medicine. By clarifying the complex interplay between platinum complexes and breast cancer, this article aspires to inform and motivate further research aimed at improving the efficacy of existing treatment modalities and ultimately enhancing patient outcomes.

LITERATURE REVIEW

In 2024, Li et al. aimed to elucidate the anticancer mechanisms of platinum nanoparticles (PtNPs) that are coated with polyethylene glycol (PEG) and conjugated with Rutin (Rutin-PEG-PtNPs) within a breast cancer cell line [23]. The synthesis of PtNPs was achieved using an extract from Dendrobium officinale, followed by PEG coating and Rutin conjugation. Characterization of these nanoparticles was performed utilizing Fourier-transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD), dynamic light scattering (DLS), and transmission electron microscopy (TEM). The study assessed the viability of breast cancer cells (MCF-7) and normal breast cells (MCF-10A) post-treatment with PEG-PtNPs and Rutin-PEG-PtNPs through the MTT assay. Additionally, the activities of superoxide dismutase (SOD) and catalase (CAT), along with malondialdehyde (MDA) levels and lactate dehydrogenase (LDH) leakage, were evaluated in the treated cells. The expression levels of genes such as p53, Bax, Bcl-2, caspase-8, and caspase-9, as well as the cytokines

NF-κB and IL-6, were analyzed using quantitative polymerase chain reaction (qPCR) and enzyme-linked immunosorbent assay (ELISA). The findings indicated that the nanoparticles were sized between 30 to 60 nm. Notably, Rutin-PEG-PtNPs exhibited enhanced cytotoxicity towards breast cancer cells (IC_{50}: 45.5 µg/mL) compared to normal breast cells (IC50: 69.4 µg/mL). The expression of p53, Bax, caspase-8, and caspase-9 was significantly upregulated by factors of 1.96, 1.84, 1.31, and 2.79, respectively, while Bcl-2 expression was diminished in cells treated with Rutin-PEG-PtNPs. Furthermore, SOD and CAT activities were found to decrease, whereas LDH leakage and MDA levels increased following treatment with Rutin-PEG-PtNPs. The levels of NF-κB and IL-6 in the treated cell cultures were reduced by 22.6% and 17.0%, respectively. Overall, Rutin-PEG-PtNPs demonstrated significant potential as an.

In 2023, Aghaei et al. developed and characterized platinum-functionalized oxygenated single-walled carbon nanotubes (O-SWCNTs-Pt) that were subsequently coated with folic acid (FA) and bovine serum albumin (BSA), resulting in the composite O-SWCNTs-Pt-BSA-FA [24]. This novel nano-sensitizer was employed to enhance the therapeutic effectiveness of X-ray radiation in an in vitro mouse model of breast cancer (4T1). The characterization of the nano-sensitizer was conducted using various analytical techniques, including TEM, selected area electron diffraction (SAED), dynamic light scattering (DLS), zeta potential measurements, XRD, UV-Vis, and FTIR spectroscopy. The assessment of cell viability was performed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, evaluating the effects of the nanocarriers O-SWCNTs-BSA, O-SWCNTs-Pt-BSA, Pt-BSA-FA, and O-SWCNTs-Pt-BSA-FA at concentrations of 10, 30, and 90 µg/mL, both in the presence and absence of X-ray exposure at doses of 4 and 8 Gy. The findings indicated that the application of O-SWCNTs-BSA, O-SWCNTs-Pt-BSA, Pt-BSA-FA, and O-SWCNTs-Pt-BSA-FA combined with 8 Gy at a concentration of 90 µg/mL resulted in survival reductions of 75.31%, 65.32%, 67.35%, and 60.35%, respectively. The O-SWCNTs-Pt-BSA-FA exhibited a hydrodynamic diameter of 88.57 nm and a surface charge of −29 mV, suggesting notable stability. In comparison to O-SWCNTs-BSA, O-SWCNTs-Pt-BSA, and Pt-BSA-FA, it demonstrated significantly enhanced cytotoxicity against the 4T1 cell line. Additionally,

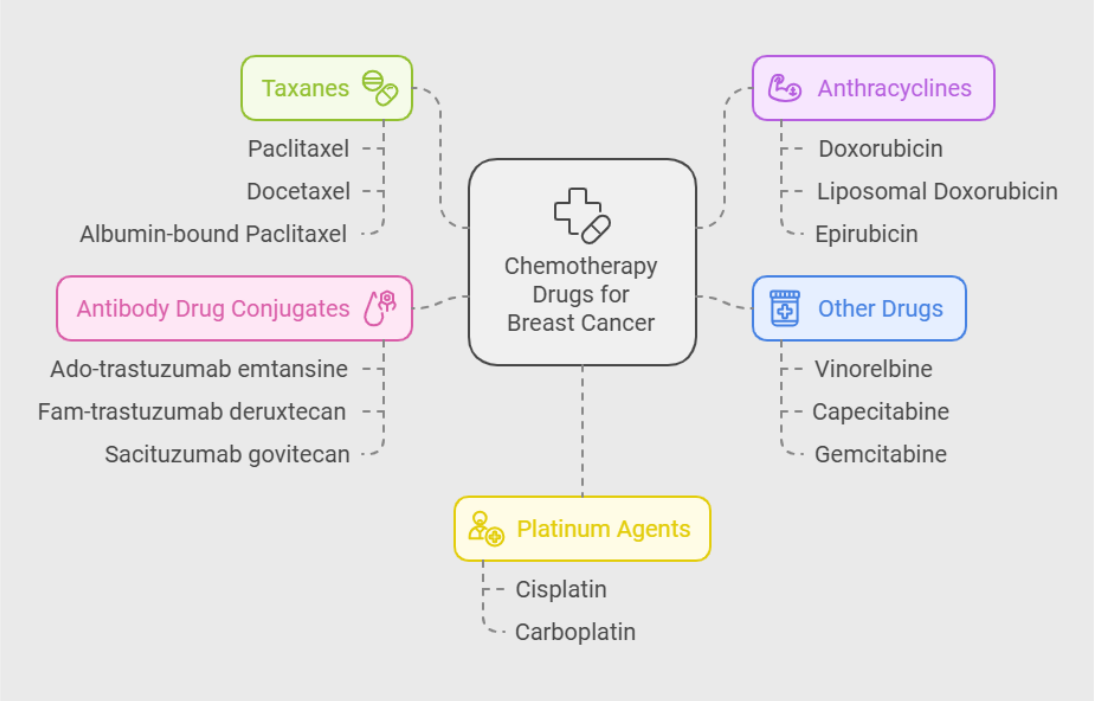

Fig. 1. Types of chemotherapy drugs for breast cancer.

it is important to highlight that single-walled carbon nanotubes (SWCNTs) possess the potential to function as a controlled release and delivery system for platinum nanoparticles (PtNPs) due to their distinctive properties and ability.

In 2022, Zhang et al. conducted a study aimed at synthesizing and evaluating platinum nanoparticles (Pt NPs) coated with bovine serum albumin (BSA), referred to as Pt@BSA NPs [25]. These nanoparticles are proposed as a potential radiosensitizer to enhance the efficacy of X-ray therapy in radiotherapy applications. Due to their high atomic number, Pt NPs may serve as a viable alternative to gold nanoparticles in this context. Additionally, BSA not only stabilizes the nanoparticles but also provides a protective environment for them, preventing their premature release from the reticuloendothelial system during circulation in the bloodstream. The physical and chemical characteristics of Pt@BSA NPs were analyzed using various techniques, including TEM, UV-Vis, FTIR, SEM, and DLS. The biocompatibility of these nanoparticles was assessed through a hemolysis test. Subsequently, the nanoparticles were applied at varying concentrations to 4 T1 cells, and their effectiveness was evaluated both in the presence and absence of X-ray exposure. The TEM images revealed an average diameter of 6.64 ± 1.3 nm, while DLS measurements indicated a hydrodynamic size of 29.4 nm. Furthermore, the nanoparticles exhibited a negative surface charge of −29.3 mV. Notably, breast cancer cells demonstrated increased toxicity when exposed to both the nanoparticles and X-rays simultaneously.

In 2021, Manzoor et al. conducted a study in which platinum nanoparticles were synthesized through the interaction of platinum ions with the leaf extract of Psidium guajava [26]. The structural characteristics of these nanoparticles were analyzed using a variety of characterization methods. The confirmation of platinum nanoparticle formation was indicated by the absence of the absorbance peak at 261 nm in the UV-visible spectrum. Additionally, GC-MS and FT-IR analyses identified functional groups that facilitated the bioreduction of metal ions and the stabilization of the platinum nanoparticles. DLS imaging techniques further validated the production of stable, monodispersed platinum nanoparticles, which exhibited a zeta potential of -23.4 mV. Morphological assessments via HR-TEM and SEM revealed the presence of spherical platinum nanoparticles with an average diameter of 113.2 nm. XRD analysis confirmed the crystalline structure of the biosynthesized platinum nanoparticles, which exhibited a face-centered cubic arrangement. EDAX results indicated a 100% platinum content by weight, affirming the sample's purity. The cytotoxicity of the biosynthesized platinum nanoparticles was evaluated in a breast cancer cell line (MCF-7) using a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, yielding an IC50 value of 167.2 mg/ml. Furthermore, a wound healing assay demonstrated that treatment with platinum nanoparticles exerted an anti-migratory effect on MCF-7 cells. Flow cytometry analysis with propidium iodide (PI) staining revealed that treatment with platinum nanoparticles inhibited cell proliferation, resulting in significant cell cycle arrest at the G0/G1 phase and a marked reduction in cell distribution within the S and G2/M phases. The antibacterial efficacy of bio-synthesized platinum nanoparticles was assessed against four pathogenic bacterial strains: Bacillus cereus (Gram-positive), Pseudomonas aeruginosa (Gram-negative), Klebsiella pneumoniae (Gram-negative), and Escherichia coli (Gram-negative). The results indicated that the biosynthesized platinum nanoparticles exhibited a dose-dependent inhibitory effect on the pathogenic bacteria, demonstrating a notably greater impact on Gram-negative bacteria in comparison to Gram-positive bacteria. This combination of environmentally friendly synthesis and the inherent antibacterial and anti-proliferative properties of these biogenic nanoparticles positions them as promising candidates for applications in nanomedicine.

In 2021, Hullo et al. explored the potential of platinum nanoparticles (PtNPs) as radiosensitizers in two distinct breast cancer cell lines, T47D and MDA-MB-231, which exhibited varying levels of radiation sensitivity [27]. The study found that PtNPs were internalized by both cell lines and localized within lysosomes and multivesicular bodies. However, analyses of various cellular responses—including clonogenicity, survival rates, mortality, cell-cycle distribution, oxidative stress, and DNA double-strand breaks—did not demonstrate any significant enhancement effect when cells were pre-treated with PtNPs prior to irradiation, in contrast to radiation treatment alone. This finding diverges from earlier research conducted under similar conditions on cervical cancer HeLa cells, indicating that the effectiveness

of radio-enhancement is highly dependent on the specific cell type. Simulations of the initial ionization processes, which considered the characteristics of irradiation and realistic physical parameters within the biological samples, suggested that PtNPs could only marginally increase dose deposition (by 3%) in their immediate vicinity. Certain features that might contribute to the biological effects were not included in the simulation, suggesting that both chemical and biological factors could account for the observed discrepancies. Notably, the study revealed that in the breast cancer cell lines examined, PtNPs displayed ambivalent redox properties, possessing antioxidant capabilities that could mitigate the potential radio-enhancement effect. This research underscores the notion that the effectiveness of PtNPs in enhancing radiation effects is significantly influenced by cell type, with no observable effect in the T47D and MDA-MB-231 breast cancer cell lines. Consequently, further investigations utilizing additional relevant biological models are warranted to assess such combined therapeutic strategies, particularly given that numerous clinical trials have already validated the efficacy of integrating nanoagents with radiotherapy across various tumor types.

In 2021, Wawrowicz et al. conducted a study that represents the initial phase of research into the utilization of core-shell (Au@Pt) nanoparticles for electron Auger therapy targeting HER2+ (human epidermal growth factor receptor 2) breast cancer and hepatocellular carcinoma [28]. The synthesis of gold nanoparticles (30 nm) with a platinum shell was achieved with a high efficiency exceeding 80%. These nanoparticles were subsequently assessed through in vitro experiments focusing on binding affinity, internalization, and cytotoxicity. To elucidate the mechanisms underlying platinum-induced cytotoxicity in HepG2 cells, the concentration of platinum within isolated cell nuclei and cytoplasm was measured using inductively coupled plasma mass spectrometry (ICP-MS). The absence of platinum in the cell nuclei indicates that the cytotoxic effects may be linked to the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS). Further investigations on the SKOV-3 cell line, utilizing a synthesized targeting bioconjugate (Au@Pt-PEG-trastuzumab), demonstrated a strong affinity of this formulation for HER2+ cells, along with its internalization and localization in the perinuclear region, as well as partial presence within the nucleus. In contrast, the binding to HER2-negative MDA-MB-231 cells was minimal, and Au@Pt-PEG-trastuzumab did not penetrate these cells. The findings are encouraging and support the need for further exploration of Auger electron therapy employing radiopharmaceuticals based on ^{193m}Pt and ^{195m}Pt.

In 2021, a sandwich-type sensitive voltammetric immunosensor was developed for the detection of the breast cancer biomarker, human epidermal growth factor receptor 2 (HER2) by Yola [29]. This electrochemical immunosensor utilized a composite of gold nanoparticles decorated on a copper-organic framework (AuNPs/Cu-MOF) and a quaternary chalcogenide composed of platinum-doped graphitic carbon nitride (g-C3N4). The quaternary chalcogenide, specifically the Cu_2ZnSnS_4 nanoparticle (CZTS NP) combined with platinum-doped g-C_3N_4 (designated as CZTS NPs/Pt/g-C_3N_4), was synthesized. The AuNPs/Cu-MOF composite was successfully created through an amidation reaction involving AuNPs functionalized with amino groups and Cu-MOFs containing carboxylic acid groups. Following the conjugation of the HER2 antibody and HER2 antigen to the AuNPs/Cu-MOF sensor platform, the CZTS NPs/Pt/g-C_3N_4 composite was synthesized using a one-pot hydrothermal method. After a 30-minute immunoreaction, the HER2 immunosensor was characterized using various techniques, including TEM, SEM, XRD, XPS, FTIR, cyclic voltammetry (CV), and electrochemical impedance spectroscopy (EIS). The resulting immunosensor demonstrated remarkable sensitivity, achieving a detection limit of 3.00 fg mL^{-1}, along with notable attributes such as high selectivity, stability, reproducibility, and reusability.

In 2020, Puja et al. conducted a study focused on the synthesis of polymeric platinum nanoparticles utilizing polyvinyl pyrrolidone (PVP) as a stabilizing agent [30]. The high-throughput characterization revealed that these nanoparticles exhibited superior surface morphology and favorable dispersibility in aqueous environments. Notably, HR-TEM analyses demonstrated that the polymeric platinum nanoparticles were predominantly spherical in shape, with sizes ranging from 2 to 10 nm. Additionally, the anticancer efficacy of these nanoparticles was assessed against human MCF-7 breast cancer cell lines. The findings indicated that the polymeric platinum nanoparticles effectively inhibited cancer cell proliferation in a

dose-dependent manner, with a half-maximum inhibitory concentration (IC_{50}) of 96.36 µg ml^{-1}. Moreover, fluorescence-based staining techniques provided evidence of altered cell death patterns, suggesting the presence of late apoptotic bodies, nuclear fragmentation, changes in mitochondrial membrane potential, and increased reactive oxygen species generation. Collectively, these results imply that polymeric platinum nanoparticles possess significant anticancer properties and hold potential as future chemotherapeutic agents. Furthermore, the implications of this research may extend to various other cancer types.

In 2020, Barbanente et al. proposed an innovative approach for the treatment of early-stage bone metastases, which entails the localized co-delivery of various chemotherapeutic agents to enhance therapeutic efficacy and address the limitations associated with conventional chemotherapy [31]. This study presents findings that selenite-doped hydroxyapatite nanoparticles, which are loaded with a hydroxyapatite-binding anti-tumor platinum complex (PtPP-HASe), effectively inhibit the proliferation of cancer cells while preserving the proliferation of bone marrow stem cells. The PtPP-HASe nanoparticles exhibited a nanocrystalline structure, with selenium (Se) and platinum (Pt) concentrations varying from 0-10 wt.% and 1.5-3 wt.%, respectively. The release kinetics of Se and Pt from these nanoparticles indicated a cumulative release of approximately 10 wt.% and 66 wt.% after a period of 7 days, respectively. At a Pt/Se ratio of 8, the released Pt and Se species significantly decreased the cell counts of human prostate (PC3) and human breast cancer cells (MDA-MB-231) by more than a factor of 10, while exerting minimal effects on co-cultured human bone marrow stem cells (hBMSc). These novel nanoparticles exhibit a high degree of anticancer selectivity, presenting significant potential for the development of new biomaterials with effective and targeted chemotherapeutic properties against cancer cells.

In 2019, Momeni et al. reported that the reaction between potassium tetrachloroplatinate(II) and dimethylsulfide, in conjunction with a mixture of HBr and KBr, yields trans-[PtBr2(SMe2)2] [32]. Furthermore, the complex [$PtBr_2(Me_2bpy)$] (where Me_2bpy denotes 4,4'-dimethyl-2,2'-bipyridine) was synthesized through the interaction of trans-[$PtBr_2(SMe_2)_2$] with Me2bpy. The crystal structure of the yellow variant of [$PtBr_2(bu_2bpy)$] (with bu2bpy representing 4,4'-di-tert-butyl-2,2'-bipyridine) was elucidated using X-ray crystallography. The analysis of the single-crystal structure of the complex [$PtBr_2(bu_2bpy)$] indicates that the platinum center exhibits a square planar configuration, characterized by a twofold rotational axis passing through the platinum atoms. Investigations into the thermal properties of a series of diimine platinum(II) complexes, [$PtX_2(bu_2bpy)$] (where X = Cl, Br, I), demonstrate an increase in thermal stability in the order: [$PtI_2(bu_2bpy)$] < [$PtCl_2(bu_2bpy)$] < [$PtBr_2(bu_2bpy)$]. The complexes [$PtBr_2(bpy)$] (bpy = 2,2'-bipyridine), [$PtBr_2(Me_2bpy)$], and [$PtX_2(bu_2bpy)$] (X = Cl, Br, I) were evaluated for their cytotoxic effects against two human breast cancer cell lines, MCF-7 and MDA-MB-468, revealing that [$PtCl_2(bu_2bpy)$] exhibited the most pronounced cytotoxicity towards both cell lines, underscoring the significant influence of the halide and diimine ligands. Additionally, semi-spherical platinum (0) nanoparticles (NPCs) were synthesized through the straightforward calcination of [$PtX_2(bu_2bpy)$] (X = Cl, Br, I) at 800 °C in an air atmosphere.

In 2019, Xiong et al. developed an optimal docking system utilizing nanoparticles (NPs) that consisted of a laurate-functionalized Pt(IV) prodrug (Pt(lau)), human serum albumin (HSA), and lecithin [33]. This system was designed through computational modeling, synthesized via nanoprecipitation, and subsequently validated using fluorescence spectroscopy. Given the tendency of macrophages to be preferentially attracted to breast cancer, exosomes secreted by murine RAW 264.7 cells, referred to as Rex, and were isolated for the encapsulation of the NPs. This advanced delivery system, termed NPs/Rex, exhibited the requisite physicochemical characteristics, improved colloidal stability, and a redox-responsive release mechanism. Studies on cytodynamics demonstrated that NPs/Rex were internalized through various pathways, circumvented entrapment by cellular bilayers, and effectively platinized nucleic acids following bioreduction within the cytosol. The intracellular activation of Pt(lau) was substantiated by the characteristic effects of cisplatin on cell proliferation and cell cycle dynamics after treatment with NPs/Rex. In vivo studies revealed that the bioinspired Rex coating conferred prolonged circulation time in the bloodstream, targeted organ specificity, and enhanced biocompatibility, alongside robust

platinum (Pt) chemotherapy efficacy against breast cancer cells in orthotopic fat pad tumors and metastatic lung nodules. Consequently, this promising nanoplatform may offer significant insights into the derivatization and advancement of Pt-based anticancer therapeutics currently utilized in clinical settings.

In 2018, Rokade et al. presented the inaugural findings regarding the anticancer properties of phytogenic platinum nanoparticles (PtNPs) and palladium nanoparticles (PdNPs) derived from the extract of the medicinal plant Gloriosa superba tuber (GSTE) [34]. The synthesis of these nanoparticles was achieved within a five-hour period at a temperature of 100°C, as evidenced by the appearance of dark brown and black colors corresponding to PtNPs and PdNPs, respectively, alongside an increase in peak intensity observed in the UV-visible spectra. HRTEM revealed that the nanoparticles were monodispersed and spherical, with sizes measuring less than 10 nm. The elemental composition was confirmed through EDS, while DLS was utilized to assess the hydrodynamic size of the particles. The anticancer efficacy against MCF-7 (human breast adenocarcinoma) cell lines was determined using MTT assays, flow cytometry, and confocal microscopy. The PtNPs and PdNPs exhibited anticancer activities of 49.65±1.99% and 36.26±0.91%, respectively. The predominant mechanism of action was identified as the induction of apoptosis, which was elucidated by the externalization of phosphatidylserine and the occurrence of membrane blebbing. These results underscore the potential of phytogenic methods for the synthesis of nanoscale platinum and palladium compounds in the treatment and management of breast cancer.

In 2016, Koohi-Moftakhari-Esfahani et al. successfully developed cisplatin-loaded polybutylcyanoacrylate (PBCA) nanoparticles (NPs) and assessed their efficacy and toxicity using an orthotopic breast cancer model [35]. The preparation of cisplatin-loaded PBCA NPs was achieved through a miniemulsion polymerization method. Characterization of the nanoparticles was conducted utilizing photon correlation spectroscopy, inductively coupled plasma optical emission spectrometry (ICP-OES), and spectrophotometry techniques. The cytotoxicity of the nanodrug was evaluated using the MTT assay. To determine the efficacy of the cisplatin-loaded PBCA NPs, an orthotopic breast tumor model was employed. The results indicated a significant reduction in cell viability of the nanodrug, showing a 75% decrease compared to the standard drug within the first 24 hours. In vivo experiments revealed that a greater number of mice treated with cisplatin bound to PBCA NPs (8 mice) compared to those receiving the standard drug (5 mice). Additionally, when considering body weight loss as an indicator of toxicity, the group receiving the nanodrug exhibited significantly less weight loss (20%) compared to the drug-receiving group (26%).

In 2014, Li et al. conducted a study that focused on the development of polysaccharide nanoparticles specifically designed for tumor-targeted delivery and controlled release of cisplatin, utilizing luteinizing hormone-releasing hormone (LHRH) as a targeting mechanism [36]. This innovative nanoparticle delivery system exhibited several distinctive characteristics: (1) the degradation products of the carrier, namely dextran and succinic acid, have received approval from the United States Food and Drug Administration for parenteral applications, suggesting a favorable safety profile and significant potential for practical use; (2) the processes for drug loading and LHRH conjugation were executed efficiently in an aqueous environment, eliminating the need for organic solvents and thereby adhering to principles of green chemistry; and (3) the design strategy prioritized drug encapsulation prior to the modification with targeting ligands, ensuring that the targeting molecules were effectively attached to the nanoparticle surfaces. When compared to free cisplatin, both non-targeted and targeted nanoparticles demonstrated sustained drug release, extended circulation time in the bloodstream, and diminished systemic toxicity. Notably, the LHRH-targeted nanoparticles exhibited markedly higher cellular uptake in MCF-7 tumor cells in vitro and improved accumulation in MCF-7 xenograft tumors in vivo, relative to their non-targeted equivalents. The systemic administration of these targeted nanoparticles containing cisplatin through intravenous injection resulted in enhanced tumor suppression in MCF-7 tumor-bearing mice, outperforming both the non-targeted nanoparticles and free cisplatin. Overall, the LHRH-mediated polysaccharide nanoparticles represent a promising advancement in nanomedicine for the targeted delivery of cisplatin to tumors.

FUTURE DIRECTIONS

The prospective role of platinum complexes and platinum nanocomposites in breast cancer chemotherapy is highly promising, particularly through the adoption of innovative therapeutic approaches designed to increase effectiveness while reducing toxicity [37-41]. Current research emphasizes the creation of targeted delivery systems that leverage nanotechnology to enhance the bioavailability and precise localization of platinum compounds at tumor sites, which may mitigate off-target effects and improve therapeutic efficacy [42, 43]. Furthermore, the investigation of combination therapies that incorporate platinum-based agents alongside immune checkpoint inhibitors and other novel targeted treatments has the potential to address resistance mechanisms and enhance the management of difficult subtypes, such as triple-negative breast cancer (TNBC) [44, 45]. Progress in personalized medicine, facilitated by the identification of specific genetic and molecular markers associated with breast cancer, may guide the selection of suitable platinum therapies tailored to the individual tumor characteristics of patients [46-50]. In addition, ongoing research into the mechanisms of action and resistance pathways related to platinum complexes will aid in the development of new platinum-based drugs and formulations, including second and third-generation compounds that may demonstrate superior efficacy. Collectively, these advancements are set to significantly alter the landscape of breast cancer chemotherapy, providing renewed hope for improved survival rates and enhanced quality of life for patients.

CONCLUSION

In conclusion, the integration of platinum complexes and platinum nanocomposites into breast cancer chemotherapy represents a significant advancement in the quest for more effective and targeted cancer treatments. This review has highlighted the multifaceted roles of platinum-based agents, particularly cisplatin and its derivatives, in addressing the challenges posed by traditional chemotherapy, including systemic toxicity and the emergence of drug resistance. The unique mechanisms of action of platinum complexes, primarily through the formation of DNA cross-links leading to apoptosis, underscore their potential as powerful anticancer agents. Recent developments in nanotechnology have further enhanced the therapeutic landscape by enabling the design of platinum nanocomposites that improve drug delivery and bioavailability. These innovations facilitate targeted localization of platinum compounds at tumor sites, thereby minimizing off-target effects and enhancing treatment efficacy. The exploration of combination therapies, particularly those that integrate platinum-based agents with immune checkpoint inhibitors and other novel therapeutic modalities, offers promising avenues to overcome resistance mechanisms, especially in aggressive breast cancer subtypes such as triple-negative breast cancer (TNBC). Moreover, the progress in personalized medicine, driven by the identification of specific genetic and molecular markers associated with breast cancer, allows for tailored treatment strategies that optimize the use of platinum therapies based on individual tumor characteristics. Ongoing research into the mechanisms of action and resistance pathways related to platinum complexes is crucial for the development of new platinum-based drugs and formulations, including second and third-generation compounds that may exhibit enhanced efficacy and reduced toxicity. The findings discussed in this review indicate that platinum complexes and their nanocomposites hold significant promise for improving therapeutic outcomes in breast cancer treatment. As research continues to evolve, the potential for these innovative therapies to transform the current treatment landscape is substantial. Future studies should focus on clinical trials to validate the efficacy and safety of these novel approaches, ultimately aiming to enhance survival rates and quality of life for breast cancer patients. The ongoing commitment to understanding the intricate interactions between platinum-based therapies and cancer biology will be essential in shaping the future of breast cancer chemotherapy, paving the way for more effective and personalized treatment options.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

REFERENCES

1. Ikeda T, Jinno H, Matsui A, Masamura S, Kitajima M. The role of neoadjuvant chemotherapy for breast cancer treatment. Breast Cancer. 2002;9(1):8-14.

2. Mayer EL, Burstein HJ. Chemotherapy for Metastatic Breast Cancer. Hematol Oncol Clin North Am. 2007;21(2):257-272.
3. Kashiwagi S, Yashiro M, Takashima T, Aomatsu N, Ikeda K, Ogawa Y, et al. Advantages of adjuvant chemotherapy for patients with triple-negative breast cancer at Stage II: usefulness of prognostic markers E-cadherin and Ki67. Breast cancer research : BCR. 2011;13(6):R122-R122.
4. Sapunar F, Smith IE. Neoadjuvant chemotherapy for breast cancer. Ann Med. 2000;32(1):43-50.
5. Buchholz TA, Hunt KK, Whitman GJ, Sahin AA, Hortobagyi GN. Neoadjuvant chemotherapy for breast carcinoma. Cancer. 2003;98(6):1150-1160.
6. Bianchini G, Balko JM, Mayer IA, Sanders ME, Gianni L. Triple-negative breast cancer: challenges and opportunities of a heterogeneous disease. Nature reviews Clinical oncology. 2016;13(11):674-690.
7. Li XL, Wang MF, Zeng LZ, Li GK, Zhao RY, Liu FD, et al. Bithiophene-Functionalized Infrared Two-Photon Absorption Metal Complexes as Single-Molecule Platforms for Synergistic Photodynamic, Photothermal, and Chemotherapy. Angew Chem Int Ed. 2024;63(27).
8. Fang R, Li Y, Jin J, Yang F, Chen J, Zhang J. Development of Anticancer Ferric Complex Based on Human Serum Albumin Nanoparticles That Generate Oxygen in Cells to Overcome Hypoxia-Induced Resistance in Metal Chemotherapy. J Med Chem. 2024;67(2):1184-1196.
9. Li Y, Huang F, Stang PJ, Yin S. Supramolecular Coordination Complexes for Synergistic Cancer Therapy. Acc Chem Res. 2024;57(8):1174-1187.
10. Ni K, Montesdeoca N, Karges J. Highly cytotoxic Cu(ii) terpyridine complexes as chemotherapeutic agents. Dalton Transactions. 2024;53(19):8223-8228.
11. Adhikari S, Nath P, Das A, Datta A, Baildya N, Duttaroy AK, et al. A review on metal complexes and its anti-cancer activities: Recent updates from in vivo studies. Biomedicine and Pharmacotherapy. 2024;171:116211.
12. Qader SM, Azhin hamad m, Muhammed AM, Omer RA, Abdulkareem EI, Rashid RF. Potential of organometallic complexes in medicinal chemistry. Reviews in Inorganic Chemistry. 2024.
13. Wang M, Li G, Jiang G, Cai J, Zhong W, Huang R, et al. Dual-targeting tumor cells hybrids derived from Pt(IV) species and NF-κB inhibitors enables cancer therapy through mitochondrial dysfunction and ER stress and overcomes cisplatin resistance. Eur J Med Chem. 2024;266:116095.
14. Bogojeski J, Soldatović T, Petrović B. Mechanisms of the reactions of structurally similar platinum(II), palladium(II) and gold(III) complexes: a minireview dedicated to the research of Prof. Dr. Živadin D. Bugarčić. J Coord Chem. 2023;77(7-8):619-637.
15. Obidiro O, Battogtokh G, Akala EO. Triple Negative Breast Cancer Treatment Options and Limitations: Future Outlook. Pharmaceutics. 2023;15(7):1796.
16. Thapa R, Ali H, Afzal O, Ahmad Bhat A, Hassan Almalki W, Alzarea Sami I, et al. Correction to: Unlocking the potential of mesoporous silica nanoparticles in breast cancer treatment. J Nanopart Res. 2023;25(9).
17. Wu L, Qu L, Yang C, Xu Y, Zhang L, Yang S, et al. Advance in the application of MOF composites for breast cancer biomarkers sensing detection. Materials Today Chemistry. 2024;38:102107.
18. Patil SM, Karade VC, Kim JH, Chougale AD, Patil PB. Electrochemical Detection of a Breast Cancer Biomarker with an Amine-Functionalized Nanocomposite Pt–Fe_3O_4–MWCNTs–NH_2 as a Signal-Amplifying Label. ACS Applied Materials & Interfaces. 2024;16(20):25601-25609.
19. Zhang F, Feng L, Jia C, Wu Y, Liu J, Shuai X, et al. Mixed-valence Pt(0)/Pt^{2+} nanoassemblies as high-Z radiosensitizers and metallo-immune regulators for potent radiotherapy of breast cancer. Nano Today. 2023;48:101708.
20. Li W, Xiao Y, Guo G, Peng J, Zhu N, Chen Z, et al. Cuprous oxide nanocomposites with photothermal (PTT) and chemical dynamics (CDT) effects induce cuproptosis in breast cancer using the strategy of increasing inflow and reducing outflow. Nano Today. 2024;56:102223.
21. Lin D, Piao J, Wang Y, Chen Y, Shi S, Cao J, et al. Cancer cell membrane biomimetic composites of cisplatin prodrug for targeted eradication of circulating tumor cells in whole blood. Composites Communications. 2024;47:101882.
22. Arumugam M, Murugesan B, Chinnalagu Dk, Cai Y, Ponnurengam Malliappan S, Balasekar P, et al. Multifunctional silk fibroin and cellulose acetate composite nanofibers incorporated with palladium and platinum nanoparticles for enhanced wound healing: Comprehensive characterization and in vivo assessment. Colloids Surf Physicochem Eng Aspects. 2024;684:133153.
23. Li Y, Guo J, Gong X, Zhang H, Ma K, Sui Y, et al. Inhibitory effects of platinum nanoparticles coated with polyethylene glycol and conjugated with Rutin on the MCF-7 breast cancer cell line. Arabian Journal of Chemistry. 2024;17(3):105567.
24. Aghaei A, Shaterian M, Danafar H, Likozar B, Šuligoj A, Gyergyek S. Synthesis of single-walled carbon nanotubes functionalized with platinum nanoparticles to sense breast cancer cells in 4T1 model to X-ray radiation. Microchimica Acta. 2023;190(5).
25. Zhang Y, Zheng D, Talaei S, Abasi M. Albumin stabilized Pt nanoparticles as radiosensitizer for sensitization of breast cancer cells under X-ray radiation therapy. Inorg Chem Commun. 2022;140:109423.
26. Manzoor S, Bashir DJ, Imtiyaz K, Rizvi MMA, Ahamad I, Fatma T, et al. Biofabricated platinum nanoparticles: therapeutic evaluation as a potential nanodrug against breast cancer cells and drug-resistant bacteria. RSC advances. 2021;11(40):24900-24916.
27. Hullo M, Grall R, Perrot Y, Mathé C, Ménard V, Yang X, et al. Radiation Enhancer Effect of Platinum Nanoparticles in Breast Cancer Cell Lines: In Vitro and In Silico Analyses. Int J Mol Sci. 2021;22(9):4436.
28. Wawrowicz K, Majkowska-Pilip A, Gaweł D, Chajduk E, Pieńkowski T, Bilewicz A. Au@Pt Core-Shell Nanoparticle Bioconjugates for the Therapy of HER2+ Breast Cancer and Hepatocellular Carcinoma. Model Studies on the Applicability of (193m)Pt and (195m)Pt Radionuclides in Auger Electron Therapy. Molecules (Basel, Switzerland). 2021;26(7):2051.
29. Yola ML. Sensitive sandwich-type voltammetric immunosensor for breast cancer biomarker HER2 detection based on gold nanoparticles decorated Cu-MOF and Cu_2ZnSnS_4 NPs/Pt/g-C_3N_4 composite. Microchimica Acta. 2021;188(3).
30. Puja P, Vinita NM, Devan U, Velangani AJ, Srinivasan P, Yuvakkumar R, et al. Fluorescence microscopy-based analysis of apoptosis induced by platinum nanoparticles against breast cancer cells. Appl Organomet Chem. 2020;34(9).
31. Barbanente A, Nadar RA, Esposti LD, Palazzo B, Iafisco M,

van den Beucken JJJP, et al. Platinum-loaded, selenium-doped hydroxyapatite nanoparticles selectively reduce proliferation of prostate and breast cancer cells co-cultured in the presence of stem cells. Journal of Materials Chemistry B. 2020;8(14):2792-2804.
32. Momeni BZ, Fathi N, Janczak J, Shahsavari Z. Dihaloplatinum(II) complexes having diimine ligands: crystal structure, thermal properties, cytotoxicity effects against breast cancer cells and application as a precursor towards nanoparticles. J Coord Chem. 2019;72(4):619-632.
33. Xiong F, Ling X, Chen X, Chen J, Tan J, Cao W, et al. Pursuing Specific Chemotherapy of Orthotopic Breast Cancer with Lung Metastasis from Docking Nanoparticles Driven by Bioinspired Exosomes. Nano Lett. 2019;19(5):3256-3266.
34. Rokade SS, Joshi KA, Mahajan K, Patil S, Tomar G, Dubal DS, et al. Gloriosa superba Mediated Synthesis of Platinum and Palladium Nanoparticles for Induction of Apoptosis in Breast Cancer. Bioinorg Chem Appl. 2018;2018:4924186-4924186.
35. Koohi Moftakhari Esfahani M, Alavi SE, Shahbazian S, Ebrahimi Shahmabadi H. Drug Delivery of Cisplatin to Breast Cancer by Polybutylcyanoacrylate Nanoparticles. Adv Polym Tech. 2016;37(3):674-678.
36. Li M, Tang Z, Zhang Y, Lv S, Yu H, Zhang D, et al. LHRH-peptide conjugated dextran nanoparticles for targeted delivery of cisplatin to breast cancer. Journal of Materials Chemistry B. 2014;2(22):3490.
37. Patel P, Vedarethinam V, Korsah MA, Danquah MK, Jeevanandam J. Exploring the Potential of Nanoparticles in the Treatment of Breast Cancer: Current Applications and Future Directions. Applied Sciences. 2024;14(5):1809.
38. Arshad R, Kiani MH, Rahdar A, Sargazi S, Barani M, Shojaei S, et al. Nano-Based Theranostic Platforms for Breast Cancer: A Review of Latest Advancements. Bioengineering (Basel, Switzerland). 2022;9(7):320.
39. Xiong Y, Rao Y, Hu J, Luo Z, Chen C. Nanoparticle-Based Photothermal Therapy for Breast Cancer Noninvasive Treatment. Adv Mater. 2023.
40. Kumar PPP, Lim D-K. Gold-Polymer Nanocomposites for Future Therapeutic and Tissue Engineering Applications. Pharmaceutics. 2021;14(1):70.
41. Joshi A, Vishnu G K A, Sakorikar T, Kamal AM, Vaidya JS, Pandya HJ. Recent advances in biosensing approaches for point-of-care breast cancer diagnostics: challenges and future prospects. Nanoscale advances. 2021;3(19):5542-5564.
42. Nag S, Mitra O, Tripathi G, Adur I, Mohanto S, Nama M, et al. Nanomaterials-assisted photothermal therapy for breast cancer: State-of-the-art advances and future perspectives. Photodiagnosis Photodyn Ther. 2024;45:103959.
43. Zhou Y, Gong J, Deng X, Shen L, Wu S, Fan H, et al. Curcumin and nanodelivery systems: New directions for targeted therapy and diagnosis of breast cancer. Biomedicine & Pharmacotherapy. 2024;180:117404.
44. Bhushan A, Gonsalves A, Menon JU. Current State of Breast Cancer Diagnosis, Treatment, and Theranostics. Pharmaceutics. 2021;13(5):723.
45. Cui G, Wu J, Lin J, Liu W, Chen P, Yu M, et al. Graphene-based nanomaterials for breast cancer treatment: promising therapeutic strategies. Journal of nanobiotechnology. 2021;19(1):211-211.
46. Wang Y, Sun S, Zhang Z, Shi D. Nanomaterials for Cancer Precision Medicine. Adv Mater. 2018;30(17).
47. Andoh V, Ocansey DKW, Naveed H, Wang N, Chen L, Chen K, et al. The Advancing Role of Nanocomposites in Cancer Diagnosis and Treatment. International journal of nanomedicine. 2024;19:6099-6126.
48. Gao X, Caruso BR, Li W. Advanced Hydrogels in Breast Cancer Therapy. Gels (Basel, Switzerland). 2024;10(7):479.
49. Singh S, Miglione A, Raucci A, Numan A, Cinti S. Towards sense and sensitivity-based electrochemical biosensors for liquid biopsy-based breast cancer detection. TrAC, Trends Anal Chem. 2023;163:117050.
50. Jafari A, Al-Ostaz A, Nouranian S. Biomedical Potential of Cellulose: Current Trends and Future Directions. Polym Adv Technol. 2024;35(12).