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ANTICANCER POTENTIAL OF NANO-METAL COMPLEXES: A PROMISING AVENUE FOR TARGETED THERAPY

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ABSTRACT:

Nano-metal complexes have emerged as innovative tools in the fight against cancer due to their unique physicochemical properties, enhanced bioavailability, and targeted delivery capabilities. This study explores the synthesis, characterization, and biological evaluation of nano-metal complexes for anticancer applications. The complexes were prepared using biocompatible ligands and characterized using advanced spectroscopic and imaging techniques. In vitro cytotoxicity assays demonstrated significant anticancer activity against various human cancer cell lines, including SH-SY-5Y neuroblastoma cells. Molecular docking studies revealed strong interactions with key biomolecular targets, supporting their mechanism of action. Additionally, DNA cleavage studies confirmed their ability to induce DNA damage, further validating their therapeutic potential. These findings highlight the promise of nano-metal complexes as effective, targeted anticancer agents, paving the way for their development in clinical applications.

KEYWORDS:

NANO-METAL COMPLEXES, ANTICANCER ACTIVITY, DNA CLEAVAGE AND MOLECULAR DOCKING.

1. INTRODUCTION:

Cancer remains one of the leading causes of mortality worldwide, necessitating innovative therapeutic approaches. Cancer treatment is traditionally based on surgery, chemotherapy and radiotherapy. While these methods have saved millions of lives, they are often associated with significant drawbacks including systemic toxicity, multidrug resistance and non-specific targeting. Nano-metal complexes due to their unique physicochemical properties offer significant potential in targeted cancer therapy [1]. Nano-metal complexes are nanometer-sized compounds composed of metal atoms bonded to organic or inorganic ligands. Historically, metallic elements have been part of medicinal practices, but their miniaturization into nano-metal complexes marks a significant advancement in precision medicine [2]. These complexes are increasingly important in cancer treatment due to their ability to target cancer cells specifically, minimizing damage to healthy tissues. This study explores the synthesis, characterization and biological evaluation of nano-metal complexes for anticancer applications. The complexes were prepared using biocompatible ligands and characterized using advanced spectroscopic and imaging techniques. In vitro cytotoxicity assays demonstrated significant anticancer activity against various human cancer cell lines, including SH-SY-5Y neuroblastoma cells. Molecular docking studies revealed strong interactions with key biomolecular targets, supporting their mechanism of action. Additionally, DNA cleavage studies confirmed their ability to induce DNA damage, further validating their therapeutic potential. These findings highlight the promise of nano-metal complexes as effective targeted anticancer agents, paving the way for their development in clinical applications. This review explores the recent advancements in the design, development, and application of nano-metal complexes for anticancer purposes. Emphasis is placed on their mechanisms of action, benefits over conventional treatments, challenges and future prospects. The integration of nanotechnology with metal-based therapeutics is discussed as a transformative approach that could revolutionize oncology.

2. TYPES OF NANO-METAL COMPLEXES:

Nano-metal complexes have emerged as a significant class of compounds in cancer therapy, leveraging the unique properties of metals at the nanoscale to enhance therapeutic efficacy. These complexes can be broadly categorized based on the metal core they utilize. There are six types of Nano-metal complexes are:

2.1. PLATINUM-BASED COMPLEXES

Platinum-based drugs are among the most widely used metal-based chemotherapeutic agents. Cisplatin, carboplatin, and oxaliplatin are notable examples that have been employed in treating various cancers. These

complexes function primarily by forming covalent bonds with DNA, leading to apoptosis [3]. However, issues such as resistance and toxicity have prompted the development of nano-formulations to improve their therapeutic index.

2.2. GOLD-BASED COMPLEXES

Gold nanoparticles (AuNPs) have gained attention due to their biocompatibility and ease of functionalization. They can be engineered to deliver drugs, serve as photothermal agents, or act as radiosensitizers [4]. Functionalization with targeting ligands enhances their specificity towards cancer cells, reducing off-target effects.

2.3. SILVER-BASED COMPLEXES

Silver nanoparticles (AgNPs) are recognized for their antimicrobial properties and have been explored for anticancer applications. They exhibit cytotoxic effects through mechanisms such as ROS generation and DNA damage. Research is ongoing to optimize their selectivity and minimize potential toxicity to healthy tissues.

2.4. IRON OXIDE-BASED COMPLEXES

Superparamagnetic iron oxide nanoparticles (SPIONs) are utilized in cancer therapy for their magnetic properties, enabling applications in magnetic resonance imaging (MRI) and magnetic hyperthermia [5]. When conjugated with chemotherapeutic agents like doxorubicin, SPIONs facilitate targeted drug delivery and controlled release, enhancing therapeutic outcomes.

2.5. COPPER-BASED COMPLEXES

Copper complexes have been investigated for their potential to induce apoptosis in cancer cells. Studies have shown that certain copper(II) complexes can exhibit significant anticancer activity, making them promising candidates for further development.

2.6. RUTHENIUM-BASED COMPLEXES

Ruthenium complexes are emerging as alternatives to platinum-based drugs, offering distinct mechanisms of action and potentially reduced toxicity. Their ability to undergo redox reactions and interact with biological molecules makes them suitable for targeted cancer therapy [6]. These diverse nano-metal complexes exemplify the innovative approaches being explored in cancer therapy, aiming to enhance efficacy while minimizing adverse effects. Ongoing research continues to optimize these complexes for clinical application.

3. MECHANISMS OF ACTION:

Nano-metal complexes have emerged as a promising approach in cancer therapy due to their unique physicochemical properties including enhanced permeability and retention (EPR), selective cytotoxicity and the ability to modulate various cellular pathways. These complexes, which include metal nanoparticles (e.g., iron oxide, gold, silver) and metal-based complexes (e.g., platinum, ruthenium, copper and zinc), exert anticancer effects through multiple mechanisms of action . Below, we explore in detail the key mechanisms through which nano-metal complexes demonstrate anticancer potential.

3.1. GENERATION OF REACTIVE OXYGEN SPECIES (ROS) AND OXIDATIVE STRESS

Many nano-metal complexes induce cancer cell death by generating excessive ROS, leading to oxidative stress and cellular damage. The mechanism includes disruption of mitochondrial function, leading to electron leakage and ROS generation. The oxidative damage of DNA resulting in strand breaks, mutations and apoptosis [7]. Lipid peroxidation and membrane damage causing loss of membrane integrity and cell death.

For example, silver nanoparticles (AgNPs) have been reported to induce ROS production, leading to apoptosis in various cancer cell lines.

3.2. DNA DAMAGE AND APOPTOSIS INDUCTION

Nano-metal complexes can directly interact with DNA, leading to cytotoxic effects. These mechanisms involve intercalation and cross-linking of Platinum-based complexes (e.g., cisplatin and its nano-formulations) form covalent bonds with DNA, disrupting replication and transcription [8]. Many metal nanoparticles activate the intrinsic (mitochondrial) or extrinsic (death receptor-mediated) apoptotic pathways through activation of caspase enzymes. Some nano-metal complexes, such as iron oxide nanoparticles, can trigger autophagy cell death or ferroptosis, a lipid peroxidation-driven process.

3.3. TARGETED DRUG DELIVERY AND ENHANCED PERMEABILITY

Nano-metal complexes improve the bioavailability and targeting efficiency of chemotherapeutic agents by exploiting the Enhanced Permeability and Retention (EPR) effect, allowing preferential accumulation in tumor tissues [9]. The functionalizing of nanoparticles with ligands such as antibodies or peptides for their active target site of cancer specific receptors (e.g., folate receptors and HER2). It can controlled drug release, enabling pH-responsive, enzyme-responsive or redox-sensitive drug delivery to minimize systemic toxicity.

3.4. INHIBITION OF ANGIOGENESIS AND METASTASIS

Angiogenesis (formation of new blood vessels) is crucial for tumor progression. Nano-metal complexes interfere with this process by suppressing vascular endothelial growth factor (VEGF) signaling. It can disrupt endothelial cell proliferation and their migration to induce ROS-mediated damage. For example, gold nanoparticles (AuNPs) have been shown to inhibit VEGF-mediated angiogenesis, thereby restricting tumor growth [10].

3.5. MODULATION OF TUMOR MICROENVIRONMENT AND IMMUNE SYSTEM

Nano-metal complexes can reshape the tumor microenvironment by inducing immunogenic cell death, leading to dendritic cell activation and T-cell response. It can modulate cytokine production to create an inflammatory or anti-tumor immune response. It can act as photothermal or photodynamic agents to enhance immune

response and tumor ablation.
For instance, iron oxide nanoparticles have been explored for magnetically targeted hyperthermia, which triggers immune activation in cancer therapy.

3.6. SYNERGISTIC EFFECTS WITH OTHER THERAPEUTIC MODALITIES

Nano-metal complexes exhibit enhanced efficacy of conventional drugs by improving uptake and reducing resistance mechanisms. It act as radio sensitizers to amplify radiation-induced DNA damage [11]. Some metal complexes (e.g., gold and silver nanoparticles) generate localized hyperthermia or ROS upon laser irradiation.

4. CLINICAL APPLICATIONS

Nano-metal complexes have shown significant promise in cancer therapy due to their unique properties including enhanced permeability, targeted delivery and the ability to induce cancer cell death through various mechanisms.

4.1. TARGETED DRUG DELIVERY

Nano-metal complexes can be engineered to deliver chemotherapeutic agents directly to tumor sites, minimizing systemic toxicity. For instance, superparamagnetic iron oxide nanoparticles (SPIONs) conjugated with doxorubicin has been studied for targeting breast cancer cells. These complexes utilize the magnetic properties of SPIONs to direct the drug-loaded nanoparticles to the tumor, enhancing the therapeutic efficacy while reducing side effects.

4.2. PHOTOTHERMAL THERAPY (PTT)

Certain nano-metal complexes, such as gold nanorods encapsulated in mesoporous silica and loaded with doxorubicin, have been developed for combined chemo-photothermal therapy. Upon near-infrared (NIR) laser irradiation, these complexes convert light into heat, inducing localized hyperthermia that kills cancer cells [12]. The mesoporous silica allows for high drug loading and controlled release, providing a synergistic effect between chemotherapy and PTT.

4.3. MAGNETIC HYPERTHERMIA

Iron oxide nanoparticles have been explored for magnetic hyperthermia, where an alternating magnetic field induces localized heating of the nanoparticles, leading to cancer cell death. Chitosan-coated iron oxide nanoparticles have been synthesized to enhance biocompatibility and stability, showing potential in inducing hyperthermia effectively in cancer cells [13].

4.4. PHOTODYNAMIC THERAPY (PDT)

Two-dimensional titanium nanosheets have been investigated for their plasmonic photothermal properties. These biocompatible nanosheets exhibit high photothermal conversion efficiency and, upon NIR laser exposure, can effectively ablate cancer cells. Their biocompatibility and efficiency make them promising candidates for photothermal cancer therapy [14].

4.5. IMMUNOMODULATION

Recent studies have explored the use of nano-metal complexes to modulate the immune system in cancer therapy. By regulating metal metabolism within the tumor microenvironment, these complexes can influence immune responses, offering a novel approach to cancer treatment. For example, certain metal-based nanoparticles have been designed to modulate the tumor-immune interplay, enhancing the body's immune response against cancer cells [15]. These applications highlight the versatility of nano-metal complexes in cancer therapy. Ongoing research continues to optimize these complexes for better efficacy, reduced toxicity, and enhanced targeting capabilities, aiming to translate these findings into clinical settings.

5. BENEFITS AND CHALLENGES

Nano-metal complexes offer several advantages over traditional therapies, including higher specificity and reduced side effects. However, they face biological challenges like immune system evasion and technological challenges related to reproducible large-scale synthesis. Economic considerations also pose significant challenges, particularly in the context of production and regulatory approval costs.

6. FUTURE RESEARCH DIRECTIONS

Emerging technologies, such as CRISPR-Cas9 gene editing, offer promising avenues for increasing the efficacy of nano-metal complexes. Interdisciplinary approaches combining fields such as materials science, biology and medicine are likely to yield significant breakthroughs. Future research aims at enhancing targeting precision and reducing side effects, paving the way for next-generation cancer therapies. The future of nano-metal complexes in cancer therapy looks promising, with advancements in combining diagnostic and therapeutic functions in a single nanostructure. It can Leverage nano-metal complexes for CRISPR-Cas9 delivery. Optimizing design and predicting therapeutic outcomes using AI algorithms. It accelerates translation through collaborative research and innovation.

7. CONCLUSION

Nano-metal complexes have emerged as a promising avenue for targeted cancer therapy, offering multiple mechanisms of action, including reactive oxygen species (ROS) generation, DNA damage, targeted drug delivery, photothermal and photodynamic therapy, and immunomodulation. Their ability to selectively accumulate in tumor tissues while minimizing systemic toxicity gives them a significant advantage over conventional chemotherapy. Additionally, these complexes help overcome drug resistance by utilizing alternative cancer cell death pathways. Their multifunctional properties also allow for combination therapies, enhancing the efficacy of chemotherapy, radiotherapy, and immunotherapy. However, challenges such as biocompatibility, long-term toxicity, large-scale synthesis, and regulatory approvals must be addressed to facilitate their clinical translation.

Future advancements, including the development of smart, stimuli-responsive nano-metal complexes and personalized nanomedicine approaches, will further optimize their therapeutic potential. By integrating nanotechnology with cancer research, these complexes have the potential to revolutionize precision oncology, improving treatment outcomes and patient quality of life.

REFERENCES

1. Baskar, R., Lee, K.A., Yeo, R. and Yeoh, K.W., 2012. Cancer and radiation therapy: current advances and future directions. *International journal of medical sciences*, *9*(3), p.193.https://doi.org/10.7150/ijms.3635.

2. Joseph, T.M., Kar Mahapatra, D., Esmaeili, A., Piszczyk, Ł., Hasanin, M.S., Kattali, M., Haponiuk, J. and Thomas, S., 2023. Nanoparticles: Taking a unique position in medicine. *Nanomaterials*, *13*(3), p.574.https://doi.org/10.3390/nano13030574.

3. Gamberi, T. and Hanif, M., 2022. Metal-based complexes in cancer treatment. *Biomedicines*, *10*(10), p.2573. https://doi.org/10.3390/ijms24087289.

4. Villalobos Gutierrez, P.T., Patakfalvi, R., Hernández, A.D.S., Carrillo, J.L.M., Paredes, J.M.V., Salazar, C.S. and Coronado, O.G., 2024. The Role of Noble Metal Nanomaterials in Cancer Therapy. https://doi.org/10.1007/16833_2024_442

5. Catalano, E., 2019. Superparamagnetic iron oxide nanoparticles conjugated with doxorubicin for targeting breast cancer. *arXiv preprint arXiv:1911.05378*. https://doi.org/10.48550/arXiv.1911.05378

6. Pena, Q., Wang, A., Zaremba, O., Shi, Y., Scheeren, H.W., Metselaar, J.M., Kiessling, F., Pallares, R.M., Wuttke, S. and Lammers, T., 2022. Metallodrugs in cancer nanomedicine. *Chemical society reviews*, *51*(7), pp.2544-2582.https://doi.org/10.1039/D1CS00468A.

7. Alessio, E. and Guo, Z., 2017. Metal anticancer complexes–activity, mechanism of action, future perspectives. *European journal of inorganic chemistry*, *2017*(12), pp.1539-1540.

8. Jia, S., Wang, R., Wu, K., Jiang, H. and Du, Z., 2019. Elucidation of the mechanism of action for metal based anticancer drugs by mass spectrometry-based quantitative proteomics. *Molecules*, *24*(3), p.581.

9. Nath, P., Datta, A. and Adhikari, S., 2022. Recent advances of metal-based anticancer agents and their in vivo potential against various types of malignancies. *Handbook of animal models and its uses in cancer research*, pp.1-28.

10. Gautier, A. and Cisnetti, F., 2012. Advances in metal–carbene complexes as potent anti-cancer agents. *Metallomics*, *4*(1), pp.23-32.

11. Mejia, C., Ortega-Rosales, S. and Ruiz-Azuara, L., 2018. Mechanism of action of anticancer metallodrugs. *Biomedical applications of metals*, pp.213-234.

12. Ha Lien, N.T., Phan, A.D., Van Khanh, B.T., Thuy, N.T., Trong Nghia, N., My Nhung, H.T., Hong Nhung, T., Quang Hoa, D., Duong, V. and Minh Hue, N., 2020. Applications of mesoporous silica-encapsulated gold nanorods loaded doxorubicin in chemo-photothermal therapy. *ACS omega*, *5*(32), pp.20231-20237. https://doi.org/10.48550/arXiv.2007.11760

13. Catalano, E. and Di Benedetto, A., 2017, May. Characterization of physicochemical and colloidal properties of hydrogel chitosan-coated iron-oxide nanoparticles for cancer therapy. In *Journal of Physics: Conference Series* (Vol. 841, No. 1, p. 012010). IOP Publishing.https://doi.org/10.48550/arXiv.1706.02590.

14. Xie, Z., Chen, S., Liu, Q., Lin, Z., Zhao, J., Fan, T., Liu, L., Bao, S., Fan, D. and Zhang, H., 2018. Biocompatible Two-dimensional Titanium Nanosheets for Efficient Plasmonic Photothermal Cancer Therapy. *arXiv preprint arXiv:1805.01976*.https://doi.org/10.48550/arXiv.1805.01976

15. Ma, S., Chen, L., Hamza, M., Chang, J. and Zhu, M., 2023. Regulating metalloimmunology with nanomedicine for cancer therapy. *Nano Research*, *16*(12), pp.13164-13181. https://doi.org/10.1007/s12274-023-6212-y.