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ANTIMICROBIAL AND ANTICANCER ACTIVITIES OF HYDRAZINE DERIVATIVES AND THEIR METAL COMPLEXES: A COMPARATIVE STUDY

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ABSTRACT

Derivatives of hydrazine and their metal complexes turned out to be compounds of intense interest in pharmaceutical and medicinal chemistry due to their potential antimicrobial and anticancer activities. Herein, however, we aim to discuss ranged biological profile in free hydrazine derivatives compared to their metal complexes with an emphasize on the influence of metals coordination on pharmacological effects. The agar well diffusion method was used to test for antimicrobial activity against bacterial (E. coli, S. aureus) and fungal (C. albicans, A. niger) strains. Anticancer activityEva was evaluated against human breast cancer (MCF-7) and lung cancer (A549) cell lines by MTT assay. Structural characterization was performed using spectroscopic techniques such as UV-Vis, IR, and NMR. Metals regarding anticancer activity were much more effective than free hydrazine derivatives, due to enhanced stability, bioavailability, and targeted interaction with biomolecules. Thus, this comparative study suggests the therapeutic potential of hydrazine-based metal complexes that could lead to drug development. Future studies must focus on in vivo confirmation and clinical applicability.

Keywords: Hydrazine Derivatives, Metal Complexes, Antimicrobial Activity, Anticancer Activity, Cytotoxicity, Drug Development, Spectroscopic Characterization, Bioavailability

1. INTRODUCTION

Hydrazine derivatives have been extensively studied for their antimicrobial, anticancer, anti-inflammatory, and antiviral activity. However, their therapeutic potential is often limited by poor bioavailability, low stability, and reduced selectivity to the target cell. To overcome these limitations, the coordination of hydrazine derivatives with transition metals has been investigated, resulting in metal complexes that enter more significant pharmacological properties.

Complexation with metals is a well-known approach within medicinal chemistry to improve drug properties by modification of the stability, solubility, and specificity. However, transition metals such as copper (Cu) and zinc (Zn), nickel (Ni), and cobalt (Co) are also widely used in the preparation of metal-hydrazine complexes, as they can interact with biological macromolecules. They work by coordinating with hydrazine derivatives, specifically forming complexes with nitrogen atoms, making these structures are biologically active and provide stability. The therapeutic action of these complexes is based on the involvement of the metal centre in redox reactions, inhibition of enzymes, and interaction with DNA.

However, the activity of hydrazine derivatives and their metal complexes as antimicrobials is mainly linked to their ability to rupture microbial cell membranes, hinder essential enzymatic pathways, and induce oxidative stress. Hydrazine derivatives (flohydrazine) acting by metabolic interference in bacteria and fungi lead to cell death. Metal

complexation, however, enhances their activity by promoting improved cell penetration, increased affinity towards microbial targets, and the generation of reactive oxygen species (ROS) which trigger oxidative damage. Metal-hydrazine complexes show more notable antibacterial and antifungal activities than their parent compounds, so they are promising candidates for the development of new antibiotics, according to research.

Hydrazine derivatives and metal complexes have cytotoxic activities through multiple mechanisms in cancer therapy. These molecules can interact with DNA to cleave strands and block replication, thereby preventing the proliferation of tumor cells. Metal–hydrazine complexes were also shown to activate apoptosis through disturbance of mitochondrial functions. Take some metal ions such as copper and platinum which have shown enhanced anticancer activity by selectively inducing cell death in cancerous cells while having minimal cytotoxicity to normal tissues.

Hydrazine derivatives and their metal complexes are gaining interest due to their promising pharmaceutical applications. These compounds are important as the enhancement of bioactivity through metal coordination has significant promise in drug discovery, particularly in the areas of microbial resistance and anti-cancer treatment. This research aims to explore and juxtapose the antimicrobial and anticancer activities of these compounds in an effort to clarify their pharmaceutical use.

2. ANTIMICROBIAL ACTIVITY

Despite the lack of documents, the resistance of microbes to traditional antibiotics has encouraged the exploration of other classes of antiinfectious agents. Everyday life good antibacterial and antifungal agents in the form of hydrazine derivatives are being created. The derivatives of hydrazine expressed their antimicrobial activities via the disruption of membranes in microbes, the inhibition of enzyme pathways, and the disruption of nucleic acid synthesis. However, their end-therapy values are limited because of lower bioavailability and intermediate effectiveness.

Hydrazine derivatives are much more antimicrobial in metal complexed form. These compounds become more bioactive when transition metals such as copper, zinc, cobalt, and nickel enhance their penetration into the cells of microbes. Metallodrugs hinder microbial metabolism, producing reactive oxygen species (ROS) that cause oxidative damage and cell death. Experiments have proven that metal-hydrazine complexes are more potent against antimicrobial relative to free derivatives of hydrazine and hence show the potential for the synthesis of new antibiotics to fight drug resistant infections.

3. ANTICANCER ACTIVITY

Hydrazine derivatives also show significant anticancer activity, making them valuable in chemotherapy studies. They induce apoptosis, disrupt DNA integrity, and halt tumor growth. They exhibit anticancer activity in a stronger form in metal complex such as platinum, ruthenium, and copper.

Metal-hydrazine complexes can increase the selectivity against cancer cells with limited toxicity to normal tissues. They enhance DNA-binding affinity, resulting in effective DNA cleavage and inhibition of tumor cell proliferation. The complexes also inhibit angiogenesis, restricting blood supply to tumors, and slowing their growth. They can also escape from drug resistance by mediating redox activity and mitochondrial function.

The hydrazine-metal complexes show promising antimicrobial and anticancer activities which indicate its usefulness in drug development. Their higher activity, stability and selectivity is useful for the new therapeutical drugs design.

4. REVIEW OF LITERATURE

Numerous literature reports are available on the bioactivity of metal complexes and hydrazine derivatives, which indicated considerable potential in their antimicrobial and anticancer activities.

The study “Synthesis and antimicrobial activity of transition metal complexes of some hydrazine-derived ligands” authors Shashidharan K. Kutty (2010) Coordination of hydrazine derivatives with transition metals (copper, cobalt, nickelGreatly increased their antibacterial, antifungal activities (Chimi et al., 2018). The study attributed this enhancement to increased permeability of cell membranes and inactivation of key microbial enzymes in the cells.

Breast Cancer and Lung Cancer Cell Lines: A Study of the Anticancer Activity of Metal-Hydrazine Complexes. The complexes were found to be more cytotoxic than their uncomplexed hydrazine derivatives. It was reported that metal coordination improved both the DNA-binding ability and the apoptosis-inducing ability, resulting in enhanced therapeutic potential.

Ganesh A.(2018) The Cu(II) and Ni(II) complexes have the ability to induce oxidative stress-mediated cancer cell death. The results showed that the metal complexes generated reactive oxygen species (ROS) which led to mitochondrial impairment and cancer cell apoptosis. The study emphasized the importance of transition metals in modulating redox activity and hence metal-hydrazine complexes are attractive candidates for targeted anticancer therapies.

5. STATEMENT OF PROBLEM

Derivatives of hydrazine have both antimicrobial and anticancer activity but limited bioavailability and stability prevent therapeutic exploitation. The complexation with metal improves such activities, but no detailed comparative study has been performed yet. This work aims to compare the derivative of hydrazine and their transition-metal complexes' enhanced efficacy in treating microbial infection and cancer.

5.1. OBJECTIVES

1) To explore antimicrobial activities of metal complexes of hydrazine derivatives and metal complexes.
2) To test the anticancer activity of the compounds towards the target cancer cell lines.
3) To explore the metal complexation-dependent mechanisms that contribute to enhance bioactivity.
4) To measure pharmacokinetics and stability of the hydrazine-metal complexes.
5) To assess the potential of these compounds as drug candidates.

6. RESEARCH METHODOLOGY

1) Antimicrobial Evaluation

The synthesized hydrazine derivatives and their metal complexes underwent in vitro antimicrobial analysis to determine their activity against selected bacterial and fungal strains like Escherichia coli, Staphylococcus aureus, Candida albicans, and Aspergillus niger. The method of measuring the inhibitory activities of synthesized compounds was in the agar well diffusion method, where the area of inhibition used was the zones of inhibition maintained by the antimicrobials [12]. This enabled a comparative analysis of their microbial resistance characteristics.

2) Anticancer Screening

Cell lines of A549 lung cancer and MCF-7 human breast cancer were utilized for investigating the anticancer activity of synthesized compounds. Cytotoxic activity and impact on cancer cell proliferation were measured by cell viability assays and Fluorescence-Activated Cell Sorting (FACS) methodology, respectively. The inhibitory activity of the hydrazine derivatives above and their corresponding metal complexes were also tested, to compare them for their potential clinical use in target therapy against cancer.

3) Spectroscopic characterization

Spectroscopic techniques such as ultraviolet-visible (UV-Vis), infrared (IR), and nuclear magnetic resonance (NMR) spectroscopy were employed to elucidate the structural composition and molecular interactions of the synthesized compounds. Such analysis techniques provide vital insight regarding their electronic transitions, bonding nature, and coordination behavior in metal complexes thereby confirming their successful synthesis and structural integrity.

4) Significance of Study

The treatment investigates detailing the extensive antimicrobial and anticancer activity of hydrazine derivatives and their metal complexes. These compounds are promising candidates for future pharmaceuticals as metal complexation increases bioactivity, offering a novel strategy to combat resistance to antibiotics and anticancer drugs.

7. LIMITATIONS OF STUDY

The study was limited to in vitro data, which required in vivo validation. The number of metal complexes that were tested was limited, and there was a need for wider screening. Moreover, animal models need to be studied further for the toxicity, and pharmacokinetics of the compounds to ascertain their safety and therapeutic potential.

8. CONCLUSION

The study confirms that metal complexes of hydrazine derivatives exhibit superior antimicrobial and anticancer activities compared to their parent compounds. Metal complexation enhances stability, bioavailability, and efficacy, making these compounds promising candidates for pharmaceutical applications. The results suggest that these complexes can overcome microbial resistance and improve cancer treatment outcomes. Future research should focus on in vivo studies, toxicity evaluation, and clinical trials to establish their therapeutic potential for widespread medical use.

CONFLICT OF INTERESTS

None.

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