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ROLE OF TRANSITION METAL COMPLEXEX IN CHEMOTHERAPY AND IMMUNOTHERAPY

Author's Name: [1]Dr Mamta Rani Kaushik , [2]Vimlesh Sharma

Affiliation: [1]*Assistant Professor, Department of Chemistry, K.R.P.G. College, Mathura, India*

[2]*Assistant Professor, Department of Chemistry, Patel Shri Teekaram Degree College, Hardoi , India*

E-Mail: drmkaushik07@gmail.com

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Abstract

For decades, transition coordination compounds have gained more and more attentions in the design of new metal Compound including innate immunity. By suppressing tumors and activating immune system homeostatic mechanisms. Chemotherapy may help overcome this tumor- induced immune tolerance. As such, chemotherapy may therefore support improved results from novel immune –modulating therapies. Immunotherapies, and in combining them with chemotherapy to achieve additive or synergistic clinical activity. Two major ways that chemotherapy promotes tumor immunity are by inducing immunogenic cell death as part of its intended therapeutic effect ,and by disrupting strategies that tumors use to evade immune recognition. This second strategy in particular is dependent on the Drug, its dose, and the schedule of chemotherapy administration in relation to antigen exposure or releastalse. In this cancer immunology at the crossroads article we focus on cancer vaccines and immune checkpoint blockade as a forum for reviewing preclinical and clinical data demonstrating the interplay between immunotherapy and chemotherapy. In the past, metal-based compounds were widely used In the treatment of disease conditions, but the lack of clear distinction between the therapeutic and toxic doses was a major challenge.

Keywords: *Chemothereapy,Immunotherapy,Metal Macrocyclic Complexes.*

INTRODUCTION

The discovery of cisplatin by Barnett Rosenberg in 1960,a milestone in history of metal-based compounds used in the treatment of cancers was witnesses. Therapeutic potential of metal-based compounds date back to ancient time.1Metals and metal compounds have been used in medicine for several thousands of years. The ten most active meals, arsenic, antimony, bismuth, gold, vanadium, iron, rhodium, titanium, gallium and platinum. The medicinal used and applications of metals and metals complexes are of increasing clinical and commercial importance. Metal ions in biological system and coordination chemistry. The field of inorganic chemistry. In medicine may usefully be divided into two main categories; firstly ligands as drugs which target meat ions in some form, whether free or protein-bound; and secondary, metal based drugs and imaging agents where the central metal ion is usually the key feature of the mechanism of action, among these platforms for controlled drugs delivery, macro cyclic compounds have attracted increasing interest with Remarkable developments in Nano medicine. Their physiochemical properties endow macro cyclic compounds with unique capabilities for nucleic acids and drugs delivery in a wide range of fields, rigid macro cyclic structures in certain essential properties, such as membrane permeability, metabolic stability and overall pharmacokinetics, all these structural properties and various functions improve The stability, biocompatibility, the drug –loading capacity and tissular permeation of the drug delivery systems, as well as the effectiveness and safety in immune-chemo therapy.

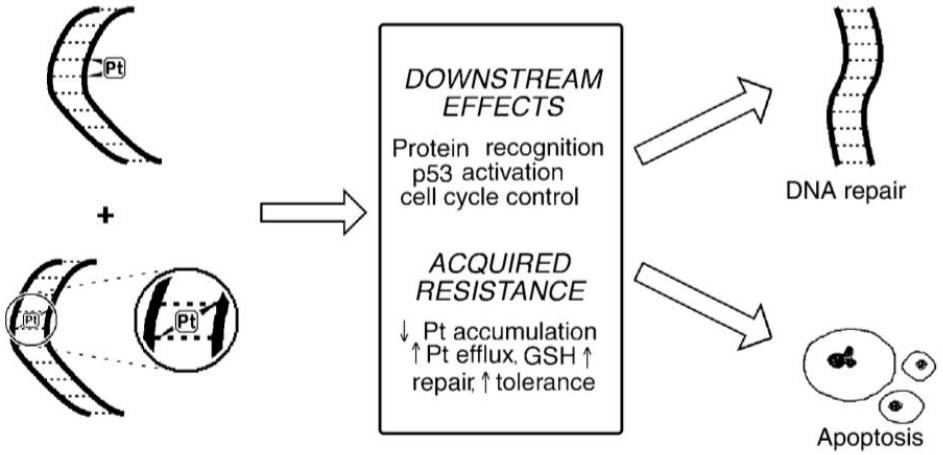
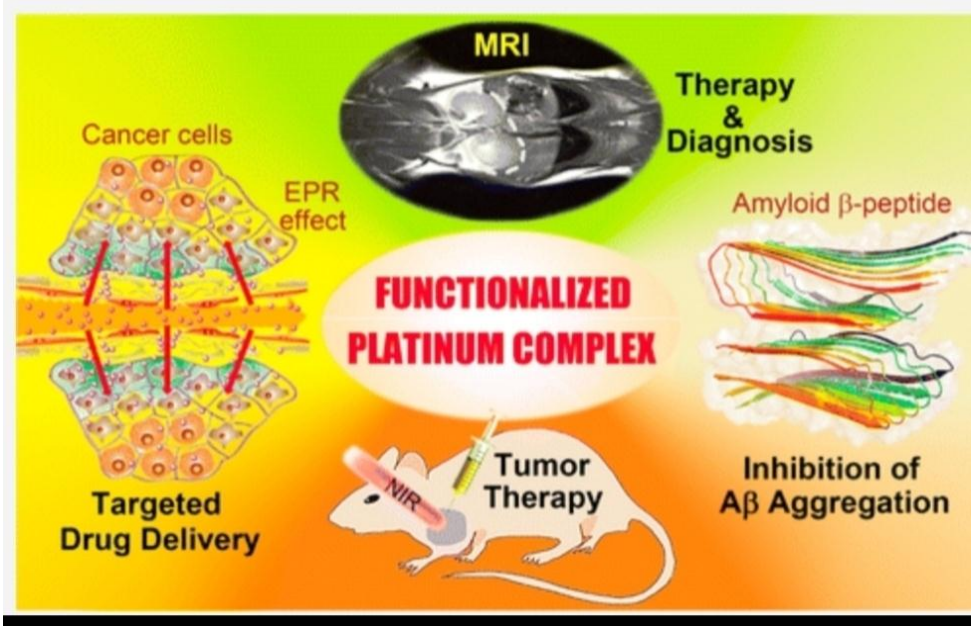


Figure 3 A general scheme for cellular response to platinum-induced DNA damage.



PROPERTIES OF METAL COMPLEXES AND METAL-BASED COMPOUNDS

Transition metals are member elements of the "d" block and are included in groups III-XII of the periodic table.1-structural and bonding; relative to organic molecules, metal complexes can aggregate to a wide range of coordination geometries that give them unique shapes. The bond length, bond angle and coordination site very depending ion the metal and its oxidation state. Metal-based complexes can be structurally modified to a variety of distinct molecular species that confer a wide spectrum of coordination no. and geometries, as well as kinetic properties that cannot be realized by conventional carbon –based compounds

SCOPE OF METAL COMPLEXES IN THE TREATMENT OF CANCER

Therapeutic potential of metal complexes in cancer therapy has attracted a lot of interest mainly because metals exhibit unique characteristics,such as a redox activity, variable coordination modes and reactivity toward the organic substrate .These properties become an attractive probe in the design of metal complexes that selectively bind to the bio molecular target with a resultant alteration in the cellular mechanism of proliferation. several metal –based compounds have been synthesized recently are products of drug design targeted at achieving specific objectives that the original compounds could not achieve and such compounds exhibit a different spectrum of cytotoxicity.

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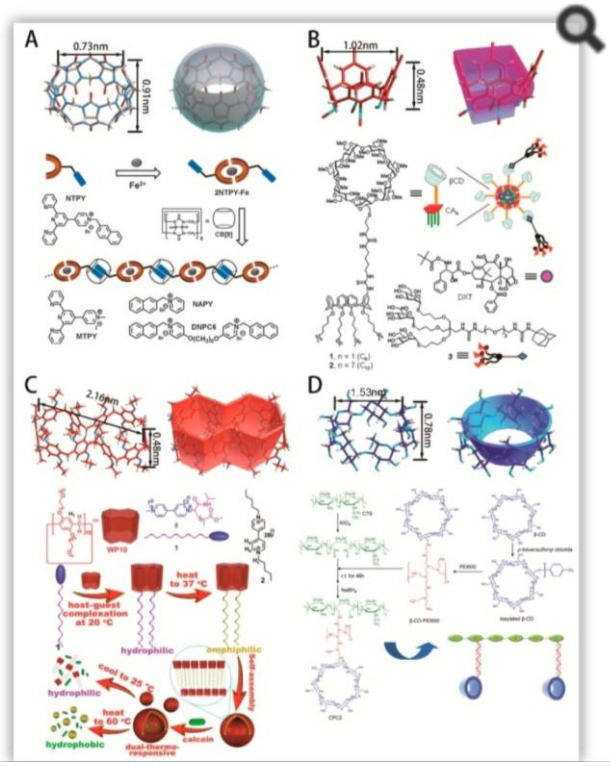
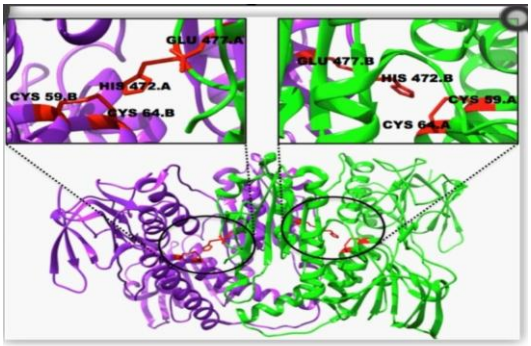
Figure 1





A 3D structure of the TrxR reductase homodimer (PDB entry 2J3N), with two chains in green and purple.

Note: The active site residues CYS 59.B, CYS 64.B, HIS 472.A and GLU 477.A represent the possible binding site for the gold(III) compounds.

Table 1 Medical and prospective medical uses of inorganic compounds.[a]

Element	*Compound*	*Uses*	*Trade names/comments*
Approved agents (mostly US or worldwide):			
Li	Li_2CO_3	Manic depression	Camcolit; Cibalith-S; Lithane (of many)
Fe	$[Fe(NO)(CN)_5]^{2-}$	Vasodilation	Nipride. For acute shock. NO release
Ga	$Ga(NO_3)_3$	Hypercalcemia of malignancy	Ganite. Possible anticancer agent. In clinical trials for use in lymphomas
As	As_2O_3	Anticancer agent	Trisenox. Use in acute promyelocytic leukemia
Ag	$AgNO_3$	Disinfectant	Neonatal conjunctivitis
	Ag(sulfadiazene)	Antibacterial	Flamazine; Silvadene; treatment of burns. 1% cream
Sb	Sb^{III}(tartarate)	Antiparasitic, leishmaniasis	Tartar Emetic Stibophen; Astiban
Pt	*cis*-$[Pt(amine)_2X_2]$	Anticancer agents	Platinol; Paraplatin; Eloxatine Testicular, ovarian, colon cancers
Au	$Au(PEt_3)$(acetyl-thioglucose)	Rheumatoid arthritis	Ridaura. Orally active
Bi	Bi(sugar) polymers	Antiulcer; antacid	Pepto-Bismol; Ranitidine Bismutrex; De-Nol
Hg	Hg-organic compounds	Antibacterial	Thiomersal; mercurochrome (amongst many)
		Antifungal	Slow release of Hg^{2+}
Agents in clinical trials:			
Pt	Polynuclear Pt^{IV} species	Anticancer agents	BBR3464, Satraplatin, AMD-473
			Expands spectrum of activity of cisplatin; overcomes resistance; oral activity?
Mn	Mn chelates	Anticancer agents	SOD mimics
Ru	*trans*-$[RuCl_4(Me_2SO)(Im)]^-$	Anticancer agent	NAMI-A; antiangiogenic?
V	$VO(maltate)_2$	Type II diabetes	BMOV; insulin mimetic
Ln	$Ln(CO_3)_3$	Hyperphosphatemia	Fosrenol; phosphate binder

IMMUNOTHERAPY TO TREAT CANCER

Immunotherapy is type of cancer treatment that helps your immune system fight cancer. The immune system helps your body fight infections and other diseases.

It is made up of white blood cells and organs and tissues of the lymph system. Immunotherapy is type of biological therapy treatment that uses substances made from living organisms to treat cancer.

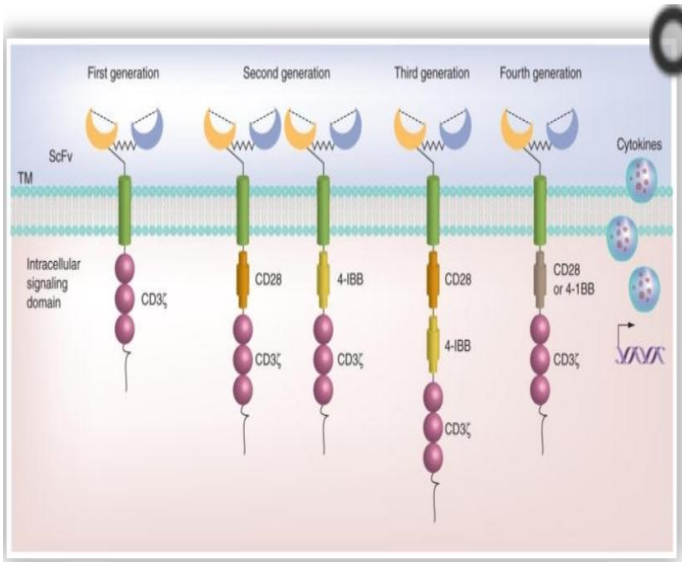
CHEMOTHERAPY TO TREAT CANCER

The FDP has approved a form of gene therapy called CAR T-cell therapy. It uses some of your own immune cells, called T cells, to treat your cancer. Doctors take the cells out of your blood change them by adding new genes so they can better find and kill cancer cells.

IMMUNOTHERAPY WITH CHEMOTHERAPY

Different types of chemo can be used alone or with one another, some studied have shown using a mix of chemotherapy and immunotherapy as a first strike against NSCLC to be a good approach .It helps your immune system find and destroy cancer cells.

Figure 2



Four Generations Of Chimeric Antigen Receptor Structure

Figure 4

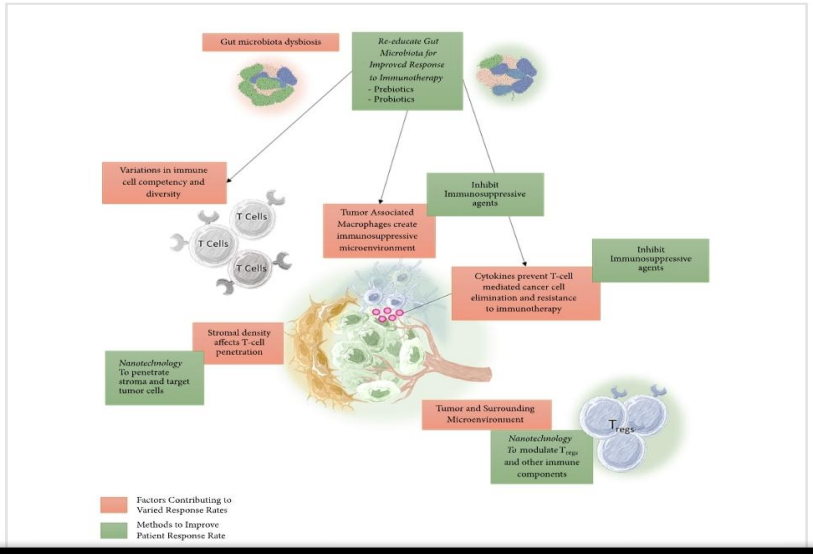
Overview of the factors contributing to varying response rates to immunotherapy and methods to overcome these barriers. Variations in immunotherapy response rates range from specific individual immune system diversity to the broad influence of the composition of the gut microbiota and are shown in red boxes. The proposed methods to overcome these barriers are indicated in green boxes. The gut microbiota can have overarching effects on patient response to immunotherapy due to the influence of the gut microbiota on the composition and function of the immune system.

7. Conclusions

Cancer immunotherapy represents a new frontier in cancer therapies that have begun to show promise since their initial conceptualization. However, patient response rates continue to fluctuate for reasons that are not well understood but have been considered from multiple standpoints, including immune competency and diversity, differing antigen specificity and expression levels, and more recently the role played by the gut microbiota. An improvement in the efficacy of immunotherapies will likely involve a more personalized and multimodal approach that cannot only target specific antigens that are present on a patient's tumor but is supplemented with agents such as epigenetic inhibitors and microbiota enhancers to elicit a more robust response. Thus, the complexity of the immune system and factors contributing to its activity are not well characterized, and additional research will require transdisciplinary approaches.

6. Future Directions in Improving Immunotherapies

Immunotherapy is now at the forefront of cancer treatment, but questions and challenges still remain around its efficacy, targeting, and toxicity. We have briefly detailed the latest developments in immunotherapy, including established and emerging targets and modalities, novel engineering strategies, combinations modalities, biomarkers, preclinical model approaches, strategies to mitigate toxicity, and clinical developments. Here, Figure 4 describes the overview of the factors contributing to varying response rates to immunotherapy and methods to overcome these barriers.



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