widespread use of penicillin will equally not result in an increasing incidence of infections resistant to penicillin.

CURRENT STATUS OF ANTIBIOTICS

The current state in the field of antimicrobials, resistance, and chemotherapy is certainly not limited to clinical microbiology as it was in the early years of the antibiotic era. Thus, it is not a single grand challenge; it is rather a complex problem requiring concerted efforts of microbiologists, ecologists, health care specialists, educationalists, policy makers, legislative bodies, agricultural and pharmaceutical industry workers, and the public to deal with. In fact, this should be of everyone's concern, because, in the end, there is always a probability for any of us at some stage to get infected with a pathogen that is resistant to antibiotic treatment. Moreover, even the behavioral patterns, such as hygienic habits or compliance with antibiotic treatment regimens, may have consequences that are not limited only to individual health issues but, on a larger scale, contribute to the interaction with the resistomes around us. In the following sections I will briefly touch upon some of the areas ranging from research to regulations to the cultural patterns that are important in dealing with the challenges of the antimicrobials, resistance, and therapy fields.

REFERENCES

1. L. Katz, R.H. Baltz, Natural product discovery: past, present, and future J Ind Microbiol Biotechnol, 43 (2016), pp. 155-176
2. J.O. Neil, Report on Antimicrobial Resistance (2016), https://amr-review.org

Chapter 2

METAL COMPLEX INTERACTIONS WITH DNA

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INTRODUCTION

Small organic molecules have been employed as therapeutic agents since the early twentieth century. Since that time, developments have progressed towards metal complexes as an additional area, providing most effective class of biological agents. For example, cis-diamminedichloridoplatinum(II) (cisplatin) was the first clinically proven platinum anticancer drug. Cisplatin itself and various analogues were found to be able to bind to cellular DNA, halting replication and inducing apoptosis.[1]. These compounds have several disadvantages, such as limited solubility, severely dose-limiting side effects such as nausea, neurotoxicity and nephrotoxicity and acquired resistance in some cancer types. The inherent problems accompanying chemotherapy necessitate the development of novel anticancer approaches. An example of such an approach is the development of compounds that can disrupt cancerous cellular machinery by non-classical interactions with nucleic acids and has been the focus of many medicinal chemists. The functions of DNA such as replication, transcription and regulation by specific protein interactions were intensely investigated. Small molecules that can induce or suppress cellular interactions related to DNA are of important as they manipulate the function of cells to produce a desired result, thereby allowing the diagnosis or treatment of disease.[2]. Transition metals are ideal for these purposes, as their unique properties can allow for specific interactions between DNA and other biomolecules and their spectroscopic characteristics facilitate their use as probes for biophysical studies. There is extraordinary interest in the development of transition metal complexes given the extensive array of readily available ligands for coordination and the different geometries, coordination numbers, redox potentials, kinetic and thermodynamic characteristics of the metals [3]. A large number of transition metal complexes has been widely used as cleavage agents for DNA and also for novel potential DNA-targeted antitumor drugs. This is very essential for further expected applications in many areas like biological and medicinal significance as potential artificial gene regulators cancer chemotherapeutic agents. Transition metals that have been extensively utilized in medicinal chemistry are platinum, ruthenium, titanium, rhodium, copper, palladium, gold and iron.

DNA is a critical therapeutic target that is responsible for, and the focus of, a variety of intracellular interactions [4]. Each of the complementary strands of DNA are stabilised by hydrogen bonding exist between adenine and thymine (A–T) and guanine and cytosine (G–C) nucleic acids. In most common DNA form, B-DNA, the strands are held in the anti-parallel double helix by stacking interactions between parallel oriented base.

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METAL COMPLEX DNA INTERACTIONS

The varied structural complexity and polymorphic nature of DNA presents a number of potential intermolecular interactions, like irreversible covalent binding, reversible groove association or intercalation. Transition Metal complexes can interact with DNA through covalent modes and three non-covalent modes viz. intercalation, groove binding and external static electronic effects [5].

The degree of variability. of transition metal complexes imparted by the metal, oxidation state, coordinated ligands, overall size and shape of the complex allows for a high degree of selectivity towards various biological targets. The size, charge distribution, stereochemistry, redox potential and other physical properties of the metal chelates can be varied readily during chemical synthesis and these substances would seem to be ideal pharmacological tools with which to investigate many functional systems in the living cell. Metal complex-DNA interactions shows the influence that the coordination geometry of the metal and the disposition of the ligands have on the binding activity. For example, square planar complexes permit deeper insertion of an intercalator when compared to octahedral or tetrahedral geometries [6]. Different transition metal complexes can undergo vastly different binding interactions with DNA. Different binding interactions of metal complexes with DNA were discussed in detail.

COVALENT BINDING

Covalent binding is a common method of DNA interaction for anticancer drugs. Cisplatin is the most clinically most successful DNA covalent binder, although it reacts with a diverse range of other biomolecules This binding will result in the unwinding of the double helix and subsequent inhibition of transcription this results in recognition by DNA damage-response proteins and following failed repair attempts, cell-induced apoptosis occurs [7].

INTERCALATION.

The process of insertion of a positively charged planar polycyclic aromatic molecule between two adjacent base pairs of DNA is known as intercalation. This insertion is stabilised by π–π stacking interaction between the base pairs and aromatic ring system which results in the lengthening, stiffening and unwinding of the DNA helix [8]. This effect dependent upon the “depth of insertion”. Intercalation is reversible, and is stabilised by a combination of electrostatic, hydrogen bonding, entropic, van der Waals and hydrophobic interactions. The positive charge of metal complexes allows improved solubility, selective cellular uptake via active transport and high DNA affinity. Many metal complexes

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of this type have been synthesised and some have exhibited higher cytotoxicity than carboplatin in human ovarian cancer cell lines.

GROOVE BINDING

Among the different modes of interactions of DNA with metal complexes, the groove binding plays an important role in the efforts of the drugs targeted to DNA. The formation of helix in DNA results in the presence of a major and minor groove which will provide sites for the binding of small molecules. The major and minor groove differ significantly in size, shape, hydration, electrostatic potential, and position of hydrogen bonding sites DNA has a distinct feature - two hydrophobic grooves that run along the surface of the molecule. The major groove is wider so the edges of the bases are more accessible. The width of the grooves varies but it was found to be sequence dependent. The Groove binding is based upon intermolecular interactions such as electrostatic and van der Waals attractions; however, it does not involve explicit stacking between base pairs, and relatively minor changes to the structure of the double helix occur because of this binding [9].

CONCLUSION

Metal complexes have proven themselves to be powerful tools when it comes to the diagnosis and treatment of disease. Metal complex-DNA interactions have been extensively researched. Combinations of these modes of interaction can be utilized to improve the binding affinity and selectivity of metal complexes. The design flexibility afforded by transition metals due to their inherent physiochemical variety and almost limitless range of ligands for coordination, makes metal complexes potent therapeutic and diagnostic agents that can be used to explore the structural diversity of DNA.

REFERENCES

1. Rosenberg, B., Vancamp, I., Trosko, J. e., & Mansour, V. H. Platinum Compounds: a New Class of Potent Antitumour Agents. *Nature*, (**1969)** 385–386.

2. Mjos, K. D., & Orvig, C. Metallodrugs in Medicinal Inorganic Chemistry. *Chemical Reviews* (2014) 114(8), 4540–4563.

3. Krause-Heuer, A.M., Price, W.S. & Aldrich-Wright, J.R. Spectroscopic investigations on the interactions of potent platinum(II) anticancer agents with bovine serum albumin. *Journal of Chemical Biology* (2012) **5**, 105–113.

ISBN: 978-93-5737-783-6

4. Quin, J. E., Devlin, J. R., Cameron, D., Hannan, K. M., Pearson, R. B., & Hannan, R. D. Targeting the nucleolus for cancer intervention. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease,* (2014) 1842(6), 802–816.
5. Arnott S. Major groove or minor groove?. *Nature* (1986) 320, 313.
6. Cusumano, M., Di Pietro, M. L., Giannetto, A., & Romano, F. Influence of DNA on the Rate of Ligand Substitution in Platinum(II) Terpyridine Complexes. *Inorganic Chemistry*, (2000). 39(1), 50–55.
7. Cepeda, V., Fuertes, M., Castilla, J., Alonso, C., Quevedo, C., & Perez, Biochemical Mechanisms of Cisplatin Cytotoxicity. *Anti-Cancer Agents in Medicinal Chemistry* (2007), 7(1), 3–1.
8. Arena, G., Scolaro, L. M., Pasternack, R. F., & Romeo, R. Synthesis, Characterization, and Interaction with DNA of the Novel Metallointercalator Cationic Complex (2,2':6',2''-terpyridine)methylplatinum(II). *Inorganic Chemistry*, (1995) 34(11), 2994–3002.
9. Oguey, C., Foloppe, N., & Hartmann, B. Understanding the Sequence-Dependence of DNA Groove Dimensions: Implications for DNA Interactions. *PLoS ONE*, (2010) 5(12), e15931.

Chapter 3

BIOSORPTION OF ARSENIC OVER PEELS OF VARIOUS FRUITS. A MINI-REVIEW

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Arsenic (As) contamination of water bodies is a significant global issue and its removal is a great worldwide concern owing to its toxic and carcinogenic nature. This metalloid can mainly exist in various forms such as As (0), As (III), As(V), and arsenide and among these, As (III) and As(V) are most prevailing in the aqueous environment. Both As (III) and As (V) are very toxic and As (III) is very much danger and versatile than As (V), and these can cause cancer of the skin, lungs, urinary bladder, liver, and kidney as well as pigmentation changes, hyperkeratosis, neurological disorders, muscular weakness, loss of appetite, and nausea. Around 300 million people all over the world became the victims of arsenic poisoning [1-3]. US Environmental Protection Agency (US EPA 1997) and the International Association for Research on Cancer (IARC 2004) classified arsenic as a group A and

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