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Review

Exploration of glycosylated-organotin(IV) complexes as anticancer drug candidates

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ABSTRACT

The design of metal-based chemotherapeutic drugs depends on choice of ligand framework, therefore, metals incorporated in a bioactive ligand scaffold hold promise for the improved pharmacokinetic profile and better efficacy of drugs. In this context, glycosylated-organotin(IV) antitumor agents are attractive and prove the state-of-the-art design for chemotherapy due to organotin-induced cytotoxicity. In recent years, many organotin(IV) complexes with glycosylated appendage have been developed and screened *in vivo* and *in vitro* for cytotoxic properties; the results exhibited high anticancer activity which could be attributed to the fact that glucoconjugation (anticancer therapeutic entity is linked to glucosamine, glucose or other sugars) improves cancer targeting and selectivity. However, there is a scarcity of data validating the mechanism of cell uptake and *in vivo* pharmacokinetic response of organotin(IV) glycoconjugates. Herein, we describe new leads in the synthetic design and validation of mechanistic pathway of tumor-targeting biologically active glycosylated-organotins, with a focus on the chemical and biological developments.

Sartaj Tabassum is working as Professor in the Department of Chemistry, Aligarh Muslim University, Aligarh. He was awarded Senor Research Fellowship (1988) and Research Associateship (1991) by CSIR New Delhi and in 1994 he was appointed as lecturer in the department of chemistry, Aligarh Muslim University. He has published 96 papers in the journals of international repute. He has presented his research work and delivered invited lectures in conferences/symposia. He is a life member of ICC, CRSI, ISCB, DNA Society of India and American Nano Society. He has successfully guided 15 Ph.D and 4 M.Phil students. He has successfully completed many research projects granted by TWAS, Italy, CSIR, UGC, New Delhi, DBT, Govt. of India. As a distinguished Scientist, Prof. Tabassum was awarded Overseas Associateship award in 2005 by DBT, Govt of India. He has signed several MoU and joint research collaboration with University of Camerino UNICAM, Italy, USM Malaysia and USTC Hefei, China. He has visited many countries for academic pursuit particularly, China, USA, Italy as fellow, visiting Professor and for the international conferences. Prof. Tabassum is working in the area of medicinal inorganic chemistry and his main focus is the design and synthesis of heterobimetallic complexes which have potential to act as cancer chemotherapeutics.

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Farukh Arjmand, born in November, 1964, currently working as Professor of Chemistry, Aligarh Muslim University, Aligarh,India since 2009. She has completed her masters and Ph.D in chemistry from Aligarh Muslim University, Aligarh and has vast research experience of 24 years in the specialization area of bioinorganic chemistry. Her research focus is on medicinal inorganic chemistry. She works on "Design and Synthesis of chiral metal-based antitumor chemotherapeutic drug entities" and in vitro interaction studies of metal-based compounds with biomolecules *viz.*, DNA, RNA and nucleotides. She has published more than 102 research articles pertinent to her specialization area in the peer reviewed journals of international repute, has contributed 42 articles to conferences/symposium and has two patents. She has contributed a chapter "Antitumor activity of tin complexes" to Encyclopedia of Metalloproteins (Springer, 2012). Dr. Arjmand has successfully guided 9 Ph.D and 2 M. Phil students and has run five major research projects as PI on the design of metal-based drug candidates awarded by UGC, CSIR and DBT, Govt of India (2001-09) and has visited many countries(China, USA, Eygpt) for academic pursuits. She has joint research collaborations with national and international research institutes, IIT Kharagpur, IICT, Hyderabad and ACTREC, Mumbai (India) USTC, China, USM, Malaysia and Materials Chemistry Laboratory Oujda, Morocco and Institut de Physique de Rennes – UMR 6251,université de Rennes 1, France.

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1. Introduction

World Health Organization (WHO) defines cancer as a leading cause of death worldwide, accounting for 7.6 million deaths in 2008 and anticipated to claim the lives of approximately 13 million people by 2030 [1]. Changes, or mutations, in the genetic material of normal cells can disrupt the balance of factors governing cell survival and division, causing the uncontrolled and pathological proliferation of abnormal cells which lead to cancer- a life-threatening disease. Chemotherapy is the primary mainstay treatment modality against cancer, which was initially fueled by the early discovery of bacteriostatic and anticancer properties of ruthenium polypyridyl complexes by Francis Dwyer in the 1950s (Fig. 1) [2] and later strengthened by the serendipitous discovery of the antiproliferative activity of a platinum complex- *cis*-diamminedichloroplatinum (II) (cisplatin [CPT]) by Barnet Rosenberg in 1969 (Fig. 2) [3]. Since the approval of cisplatin, in 1979 [4] as a chemotherapeutic drug for treating solid malignancies, several second generation platinum analogues have been screened as potential antitumor agents, but of these, only two (carboplatin and oxaliplatin) have entered worldwide in chemotherapeutic regimens (Fig. 2). Potentially, these complexes exhibit a broad antineoplastic spectrum and, in combination with other chemotherapeutic agents, could be highly effective in testicular, ovarian, colorectal, cervix, and lung cancers [4,5]. Regardless, the clinical and commercial success of current platinum drugs, downsides associated with them, especially the systemic toxicity and drug resistance have stimulated an extensive search for unconventional chemotherapeutic strategies [6–10].

In this context, organometallic compounds provide versatile platforms for anticancer drug design. Since organometallic

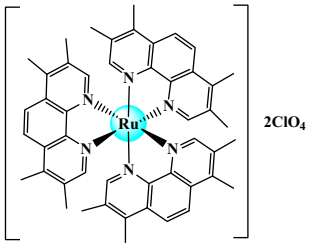
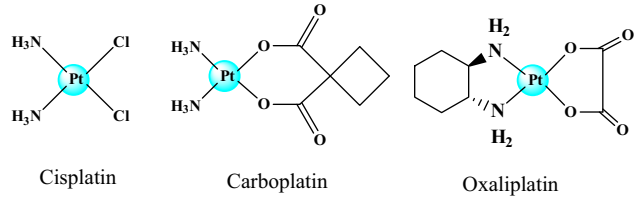


Fig. 1. Dwyer Ru(II) compound.



Cisplatin Carboplatin Oxaliplatin

Fig. 2. Pt-based anticancer complexes cisplatin, carboplatin and oxaliplatin (approved for worldwide clinical use).