Potentiating Chemotherapy using 'SS' Strategy of '*Sweetness*' and '*Synergy*'

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Cancer is the second leading cause of fatalities worldwide. The serendipitous discovery of anticancer activity of Cisplatin in 1965 by Prof. Rosenberg ushered in a new era of cancer chemotherapy. It is the preferred choice of treatment against a large variety of cancers. Despite its clinical success, cisplatin treatment has some drawbacks. Adverse side effects like nephrotoxicity, ototoxicity, anaemia are commonly observed in patients undergoing chemotherapy.

In this context, the selective accumulation of the cytotoxic drug at the tumor site is highly desirable to achieve improved efficacy and minimal side-effects. Glucose metabolism is typically upregulated in cancer cells as compared to the normal cells (Warburg Effect). An overexpression of Glucose Transporter (GLUT) family of proteins is observed in the cancer cells. GLUTs have emerged as an attractive target for a large number of targeted anticancer strategies. Recently, the disaccharide moiety of anticancer drug Bleomycin A_5 has been reported to exhibit preferential uptake in cancer cells [1,2]. However, there is contradiction in the chemical literature about the minimal epitope of this disaccharide which is necessary and sufficient for imparting the observed selectivity [3]. We have therefore decided to investigate this problem by carrying out a structure-activity relationship study on the bleomycin disaccharide. We have planned to exploit the glycan core of this natural product as a cancer targeting vector for fluorophores and cytotoxic payloads. In the first part of the talk, I will discuss about the synthetic efforts towards these target molecules.

Resistance to chemotherapy is a serious issue with the current treatment modalities. The synthetic chemist, therefore, must constantly update his/her arsenal and design molecules with novel mechanisms of action. In the second part of the talk, I will switch over to Inorganic Chemistry and discuss about the development and preliminary *in vitro* studies done on a class of high-valent Re(V) oxo compounds. The lead compound shows promising synergistic activity with the clinically approved drug cisplatin.

References:

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