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Review

Recent advances in the metallo-glycodendrimers and its potential applications

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A B S T R A C T

Ever since the discovery of the phenomenon of multivalent representation of sugar to enhance the binding affinity of specific carbohydrate-protein interactions, the quest for the construction of carbohydrate clusters, with precise geometries that are highly specific to lectin, has been the goal of synthetic chemists. In addition to multivalency, the presence of redox, fluorescence, radioactive nature of glyco-cluster will improve the prospect of direct readout of specific carbohydrate-protein interactions. To address this question, the design of metallo-glycodendrimers with precise sugar topology is critically important. In this review, we provides an overview of the important roles that metallo-glycodendrimers can play as lectin binding molecules, highlighting the unique properties metals can confer to these studies.

Shadab Ali Khan received his M.Sc. degree in Biochemistry from Amravati University (M.S.), India in 2003. He obtained his Ph.D. degree from National Chemical Laboratory, Pune, India in 2012 in Biotechnology. After Ph.D. he joined the group of Dr. Raghavendra Kikkeri as a Post Doctoral Research Associate at Department of Chemistry, Indian Institute of Science Education & Research (IISER), Pune, India. His research interests include Nanobiotechnology, biomedical applications of nanomaterials and glyconanotechnology.

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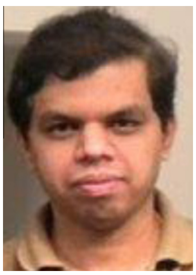

Raghavendra Kikkeri received his master degree from university of Mysore, where he studied organic chemistry as major, In 2001 he moved to Weizmann Institute of science, Israel, where he earned his Ph.D in organic chemistry under the guidance of Prof. Abraham Shanzer. After postdoctoral fellowship with Prof. Peter Seeberger and Prof. Ajit Varki at ETH Zurich, MPI Berlin and UCSD San Diego. He became Assistant professor at the Indian Institute of Science Education and Research (IISER) in Dec 2010. Recently, he started Max- Planck partner group in IISER, Pune.

Contents

1. Introduction

Lectins are specific carbohydrate-binding or carbohydrate cross-linking proteins. The interactions between lectins and sugars are involved in a large number of biological processes, such as cell adhesion and migration, phagocytosis, cell differentiation and apoptosis [1–4]. Over the past 120 years, numerous lectins have been isolated from plants, microorganisms, fungi, animals and viruses [5–7]. Lectins have been used as tools for the detection, isolation and characterization of various glycoproteins and for the clinical diagnosis of carcinoma and leukemia [8,9]. Despite the prevalence of lectin in biological systems, the binding between an individual lectin and monovalent carbohydrate are quite weak and not particularly specific [10,11]. Nature provides strong and specific responses by carbohydrate multivalency. In multivalent interactions, multiple copies of the ligand and receptors sequentially or simultaneously bind and significantly increase binding affinity for a meaningful and biologically relevant recognition processes [12,13]. A host of glycoclusters have been prepared and explored in different applications. It has been shown that multivalent mannose glycoclusters inhibited HIV infection [14,15]. Multivalent glycoclusters have also been shown to function against bacterial toxins [16,17] and against bacterial adhesion to human cells [18–20]. Multivalent glycoconjugates are also being used for stimulation of immune system [21–23]. Similarly, several glycoclusters have been used as a potential target for drug development, gene delivery and diagnostic tools [24–27]. Hence there is a need for new multivalent probe to study carbohydrate-protein interactions in order to unravel the finer details of these interactions. Research groups of Seeberger, Roy, Penadés and Marra have reported carbohydrate clusters on dendrimers, polymers, liposomes, micelles as well as cyclodextrin and calixarenes templates [28–36].

Interactions between carbohydrates and proteins can be studied by using a range of biophysical techniques. The strength of interactions between a given glycoclusters and the lectins have been calculated by Isothermal Titration Calorimetry (ITC), Surface Plasmon Resonance (SPR), Fluorescence Resonance Energy Transfer (FRET) and dialysis. Most glycoclusters reported to date are able to display inherent optical, electrochemical or gravimetric properties for bioimaging or biosensing processes [37–42]. Apart from the purely organic or nanoparticles based glycoclusters reported as lectin binders [43,44], it has recently been shown that metallo-glycodendrimers can also be a potential glycoclusters for lectins [45–47], with the number of reported example increasing rapidly over the past couple of years. In this review we aim to provide an overview of the important roles of the metallo-glycodendrimers. The