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Opinion

Recent Advances in the Development of Carbohydrate Derivatives as Anti-Infective Agents

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Received: January 29, 2019; **Published:** March 26, 2019

Carbohydrates are integral component of all cells and are involved in intercellular and intracellular events in living organisms. They not only act as cell surface receptors and also as signaling molecules. Carbohydrates are involved in molecular recognition and many other cellular processes. Several carbohydrate derived moieties have good range of pharmacological activities. This is an overview on the advance developments in carbohydrate-based molecules having promising anti-infective activities. Carbohydrate-based anti-infective agents can disrupt complex carbohydrate recognition events vital to the infective mechanisms of pathogens, representing an untapped wealth of therapeutics. The promise of carbohydrate-based anti-infective is that they are less prone to the evolution of microbial resistance, because, carbohydrate legends themselves are invariant, and carbohydrate recognition is essential to pathogenic function. As such, carbohydrate-based anti-infective can better thwart the looming public health threats posed by the evolution of resistant microbial strains targeting bacterial transglycosylase, the influenza coat proteins hemagglutinin and neuraminidase. Transglycosylase (TGase) is the enzyme responsible for assembling the carbohydrate backbone of the bacterial cell wall: it is essential, accessible, and less prone to evolving antibiotic resistance due to its recognition of the invariant oligosaccharide backbone of the peptidoglycan.

Routes for the specialized synthesis of carbohydrate-based substrate analogs, transition state inhibitors, and novel drug- like motifs are proposed for targeting gram-positive and Mycobacterial TGases. Hemagglutinin (HA) and neuraminidase (NA) are influenza coat glycoproteins that are susceptible to inhibition by sialic acid derivatives, which interfere with necessary recognition of sialosides (i.e. complex carbohydrates that end with a sialic acid). They are also targets of the adaptive immune response, which can generate neutralizing antibodies to antigenic protein epitopes, particularly with HA. Strategies for inhibition and immunization need to be improved, as high rates of viral mutation lead to resistance against anti-influenza agents e.g., the rapid emergence of Tamiflu resistant swine flu during the 2009 level-6 pandemic outbreak and antigenic drift (i.e., escape from protective immunity). Looming pandemic threats further hasten this need. Anti influenza agents are designed herein with focus on establishing a higher barrier to resistance and understanding how resistant mutations affect NA-sialoside interactions. Anti-infective agents are essential to preserving public health, but are increasingly compromised by the evolution of microbial resistance.

Developing carbohydrate-based anti-infective agents can disrupt or exploit invariant carbohydrate recognition processes critical to pathogen survival and infectivity, leading to important new therapeutics for effectively managing infectious disease, while minimizing problems associated with microbial resistance. Modifications of proteins and lipids by carbohydrates are very important processes which can regulate the structures and functions of these biomolecules. The goals of the research must be specifically develop new carbohydrate-based anti-infective agents that address the recent rise of resistant strains of pathogenic bacteria and influenza. Future studies and research focus must be in development of new tools that will help to understand carbohydrate recognition at molecular level, which in future can help in the carbohydrate-based drug discovery process.

Volume 14 Issue 4 April 2019