Sarkar, B.; Mahapa, A.; Chatterji, D.; Jayaraman, N., 2019, "Sugar vinyl sulfoxide glycoconjugation of peptides and lysozyme: Abrogation of proteolysis at the lysine sites", *Biochemistry*, *58*, 3561 – 3565.

The emergence of bioconjugation methodologies has given a new paradigm shift in the studies of biomolecules, their structures and functions. Bioconjugation methodologies permit covalent linkage of a chosen moiety onto the biomolecule in a benign manner, so as to engineer the biomolecular functional and structural properties. A number of chemical methods have been developed, particularly, in the bioconjugation of chemical moieties on to proteins, illustrating beneficial effects arising from such modified proteins. An intense area of development is the glycoconjugation methodologies, wherein carbohydrate moieties are covalently linked to proteins, thereby enabling de novo synthesis of glycan conjugated proteins. In many such methods, it is pertinent to modify the side chain functionalities of the proteins, amenable for subsequent covalent linkage with the carbohydrate moieties. In the present manuscript, we describe the development of a new method of the glycoconjugation of proteins, with the aid of a conjugate addition reaction of a vinyl sulfoxide with the amine functionality present at the side chain of lysine residue. The vinyl sulfoxide functionality is in-built within the sugar scaffold by judicious implementation of chemical conversions on a pyrano-sugar. The resulting sugar vinyl sulfoxide is developed as an excellent synthon for Michael addition reaction with amine functionalities present in peptides and proteins. In this manuscript, we demonstrate that side chain functionality of lysine in proteins can be covalently linked with a sugar moiety, with the aid of the sugar vinyl sulfoxide reactive moiety. This new method of bioconjugation is verified first with amino acids and peptides. Following these conjugations, occurring at physiological pH and temperature and without the necessity of a reagent to mediate the conjugate addition, a systematic study of bioconjugation of lysozyme with sugar vinyl sulfoxide is conducted. Bioconjugation occurs at all the lysine sites of the protein, under benign reaction conditions. The consequence of the glycoconjugation is evaluated further in the proteolysis with trypsin, which cleaves peptide bonds at the arginine and lysine residues of lysozyme. The proteolysis assays shows that the susceptible lysine sites of the protein do not undergo proteolysis, even when peptide bonds at the arginine sites are cleaved in the modified lysozyme. Further, the antimicrobial property of lysozyme on Gram-negative E. coli bacterial cells is assessed. The antimicrobial property of the modified lysozyme is retained as that of the native lysozyme.