Application of Organic Synthesis for Construction of complex bioactive compounds and biomolecules.

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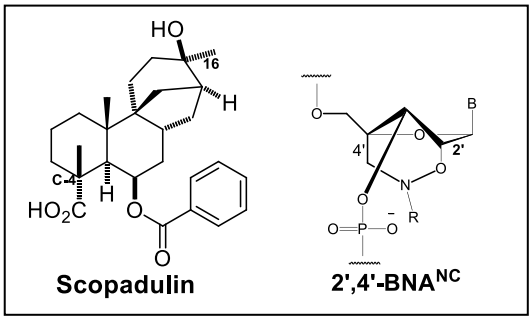
Abstract: Organic synthesis can be used for the construction of complex molecules having important biological activities. In this presentation, I will discuss about the synthesis of complex and synthetically challenging tetracyclic diterpene Scopaduin, an antiviral principle. This presentation also includes the synthesis of some artificial nucleosides, nucleotides and nucleic acids having superior biophysical properties. In addition to these some recent results in our laboratory will be disclosed.

The first total synthesis of (±)-scopadulin was accomplished by a stereoselective construction of a quaternary carbon at C-4, conversion of the hindered cyano group to a methyl group via the novel reaction for conversion of primary aliphatic amines into alcohols developed by us, and a highly chemo- and stereoselective methylation at C-16.

The novel bridged nucleic-acid analogue 2′,4′-BNANC (2′O ,4′C -aminomethylene bridged nucleic acid), containing a six-membered bridged structure with an N-O linkage, was designed and synthesized efficiently, demonstrating a one-pot intramolecular NC bond-forming key reaction to construct a perhydro1,2-oxazine ring. Three monomers of 2′,4′-BNANC (2′,4′-BNANC[NH], [NMe], and [NBn]) were synthesized and incorporated into oligonucleotides, and their properties were investigated and compared with those of 2′,4′-BNA (LNA)-modified oligonucleotides. Compared to 2′,4′-BNA (LNA)-modified oligonucleotides, 2′,4′-BNANC congeners were found to possess: (i) equal or higher binding affinity against an RNA complement with excellent single-mismatch discriminating power, (ii) much better RNA selective binding, (iii) stronger and more sequence selective triplex-forming characters, and (iv) immensely higher nuclease resistance, even higher than the Sp -phosphorthioate analogue. 2′,4′-BNANC-modified oligonucleotides with these excellent profiles show great promise for applications in antisense and antigene technologies.

2’,4’-BNANC modified siRNA (Short interfering RNA) was also designed, synthesized and evaluated for their gene-silencing properties. Positional effect of 2’,4’-BNA residues in siRNA was examined and some very interesting results were obtained. Caatioic phosphorthiate oligonucleotides were also synthesized and their biophysical properties investigated. The derivatives showed improved property.

As a whole, the construction of these important biomolecules will be discussed in this presentation.



Biography*:* **S. M. Abdur RAhman**, is a *Professor* of Clinical Pharmacy and Pharmacology, University of Dhaka (DU). He is the Dean, Faculty of Pharmacy, University of Dhaka. He did B.Sc.(honors) [1st class 1st position] & Masters [1st class 1nd position] from the Dept. of Pharmacy, University of Dhaka and PhD from Osaka University, Japan. He was awarded prestigious JSPS Postdoctoral Fellowship. He has published 65+ journals and conference papers. He has received 9 national and international awards. He has one PATENT. He is currently President, Dhaka University Pharmacy Alumni Association (DUPAA) (January 2017 to Date).

He is currently doing research in the areas of Bioactivity Directed Phytochemical Investigations of Indigenous Plants, Synthesis of Biological Investigations of Benzimidazole derivatives and Development of Novel Bridged Nucleic Acids for Gene Therapy and Diagnosis.

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