

## NMR and molecular dynamics approach for therapeutic use of a model heptapeptide: towards template design of peptide antagonists of glycoprotein IIbIIIa-fibrinogen binding

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The short peptides have been implicated to be of immense therapeutic use in lieu of their role as peptide hormones, growth factors and neuropeptides. However, their development as clinically useful drugs is limited by their poor metabolic stability and low bioavailability due to their inability to cross membrane barriers such as intestinal and blood brain barrier. To overcome these problems various strategies are being developed towards producing modified peptides and mimetics, which in turn have increased the chances of obtaining useful drugs structurally related to parent peptides, and improve the stability and bioavailability. Among such strategies are de novo designing (emphasizing the structural characterizations of peptides), and theoretical approach based on molecular simulation (for constructing useful model to reduce time and cost). The resulting models will help to isolate the factors behind folded structure formation, and contribute useful information about de novo peptide design. The NMR and molecular dynamics methods have been used to study the conformations of Arg-Gly-Asp (RGD)-containing model heptapeptide, GRGDSPC, which has been shown to be accessible to Glycoprotein IIbIIIa-fibrinogen binding mediated cellular behaviours such as thrombosis and metastasis. The formation of two fused weak  $\beta$ -turns of type-II (HB, 4 $\rightarrow$ 1), and type-II' (HB, 7 $\rightarrow$ 4) from simulation studies has been consistent with NMR data. The conformational transitions into additional multiple turns have been discussed. The existence of sustainable 'S' shaped molecular structure due to interconversions between multiple turns initiated at Asp<sup>4</sup>, Ser<sup>5</sup> and Cys<sup>7</sup> has been considered to be the biologically active part in binding interactions. This molecular shape, thus, may prove to define the template for the design of peptide antagonists of Glycoprotein IIbIIIa-fibrinogen binding.

### Biography

Ashok Kumar Kulkarni has completed his Ph.D in Biophysics, specializing in Peptide Biophysics from University of Gorakhpur, India. He has been involved in teaching and research for about 11 years in different postgraduate institutions and medical Colleges. He has presented 26 papers in international and national conferences, and has published various papers in reputed journals and full length papers in conference proceedings. He has delivered several invited lectures at various conferences and postgraduate institutions, and also acted as Resource Person at Academic Staff Colleges' Refresher Courses in Life Sciences. He is now Assistant Professor in the Physiology Department of Mediciti Institute of Medical Sciences, Hyderabad, A.P., India

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