PEPTIDE-BASED DENDRIMERS AND SECONDARY STRUCTURE MIMETICS

by

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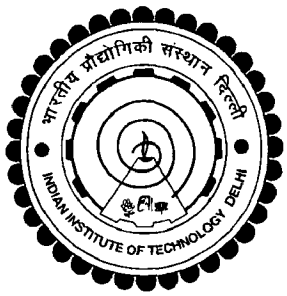
Submitted

In fulfillment of requirement of degree of

DOCTOR OF PHILOSOPHY

to the



Indian Institute of Technology Delhi

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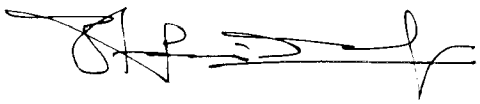
Dedicated to my dear parents

CERTIFICATE

This is to certify that the thesis entitled, **"Peptide-Based Dendrimers and Secondary Structure Mimetics",** being submitted by **Mr. Yogesh Kumar Sharma**, to the Indian Institute of Technology, Delhi, for the award of degree of '**Doctor of philosophy in Chemistry**', is a record of bonafide research work carried out by him. **Mr. Yogesh Kumar Sharma** has worked under my guidance and supervision and has fulfilled all the requirements for the submission of this thesis, which to my knowledge has reached the requisite standard. The results embodied in this thesis have not been submitted in part or in full, to any other University or Institute for award of any degree or diploma.



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ABSTRACT

This thesis, **"Peptide-Based Dendrimers and Secondary Structure Mimetics"** is concerned with dendrimers and peptidomimetics crafted from amino acids. Dendrimers are molecules that have attracted immense interest in chemistry, biology and material sciences, because of the challenges involved in their synthesis and their functional properties. Peptide dendrimers, with large size and surface area, are similar in many ways to globular proteins, except for the absence of secondary structural features, and can be considered as protein models. The *de novo* design of proteins is a challenge, and has achieved limited success because of the lack of predictability of 3D structure from primary structure. Dendritic architectures using peptide systems may provide an efficient strategy to circumvent protein folding problem, as dendritic peptides are topologically forced to adopt globular shapes, thus mimicking certain features of globular proteins.

Chapter 1 gives a detailed introduction to the history, dendrimer synthesis, recent developments and applications in the area of dendrimers.

Chapter 2 describes the design and synthesis of various peptide dendrimers with unusual architecture. A series of novel designer dendrimers was synthesized by employing a Huisgen 1,3-dipolar cycloaddition reaction, commonly called a click reaction. The dendritic structures reported here include symmetrical and unsymmetrical dendrimers, with a variety of cores such as triazole, cystine and Lys-Asp dipeptide.

Chapter 3 addresses the synthesis of multi-tier designer dendritic molecules incorporating an aromatic core and heterocyclic and peptide units. The versatility of the method is demonstrated by the synthesis of various multi-tier dendritic structures. 5-(azidomethyl)benzene-1,3-dicarbonyl was chosen as the scaffold, as this core unit allows the synthesis of various unsymmetrical dendrimers.

Chapter 4 reports the synthesis of various rigid core symmetric dendrimers using an oxidative coupling reaction using Cu catalyst. A Ni-catalyzed cross-coupling reaction was utilized for the synthesis of unsymmetrical dendrimers. The supramolecular gelation of these molecules was studied in a mixture of polar and non-polar solvents, and their self-assembling properties were demonstrated using state-of-the-art techniques like SEM, TEM and AFM. Photopolymerization of diacetylenic dendrimers in the gel state resulted in the formation of polydiacetylenes (PDA).

Chapter 5 deals with the design and synthesis of beta-turn secondary structure mimetics. This chapter describes 3,7-diazabicyclo[3.3.1]nonane (bispidine) as a scaffold for constructing open reverse turn structure in peptides. Various bispidine-peptide conjugates were designed and synthesized. Their conformations were studied by detailed NMR, CD and X-ray crystallographic methods.

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