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Role of Dendrimer Architecture in Host–Guest Interactions and Molecular Recognition

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Abstract: *Dendrimers are highly branched, monodisperse macromolecules with precisely controlled architectures that have emerged as versatile platforms for host–guest interactions and molecular recognition. Their unique structural characteristics, including a central core, repetitive branching units, multiple generations, and numerous terminal functional groups, enable selective encapsulation and binding of a wide range of guest molecules. These interactions are governed by electrostatic forces, hydrogen bonding, hydrophobic interactions, van der Waals forces, and π–π stacking. The architecture of dendrimers significantly influences their binding affinity, selectivity, loading capacity, and release behavior.*

Poly(amidoamine) (PAMAM), polypropylene mine (PPI), phosphorus, peptide, and carbosilane dendrimers have been extensively investigated for applications in drug delivery, biosensing, catalysis, molecular imaging, gene delivery, and environmental remediation. This review discusses how dendrimer architecture controls host–guest chemistry and molecular recognition mechanisms, summarizes recent advances, highlights current challenges, and presents future opportunities in biomedical and nanotechnological applications.

Keywords: Dendrimers, Host–Guest Chemistry, Molecular Recognition, PAMAM, PPI, Supramolecular Chemistry, Drug Delivery, Nanotechnology.

I. INTRODUCTION

Host–guest chemistry forms the foundation of supramolecular science, where non-covalent interactions govern selective molecular binding. Among various supramolecular hosts, dendrimers have attracted significant scientific attention because of their well-defined three-dimensional architecture, controlled molecular weight, high functionality, and tunable surface chemistry. Unlike conventional polymers, dendrimers possess monodispersity and predictable branching, enabling precise engineering of molecular recognition sites.

The architecture of dendrimers consists of three principal components: a central core, repetitive branching layers known as generations, and terminal functional groups. Each component contributes to the molecular recognition behavior. The internal cavities created during dendrimer growth can encapsulate hydrophobic molecules, while peripheral functional groups interact selectively with biomolecules, metal ions, drugs, proteins, nucleic acids, and small organic compounds.

The advancement of dendrimer chemistry has revolutionized targeted drug delivery, biosensing, catalysis, diagnostics, molecular imaging, and environmental applications by exploiting highly selective host–guest interactions.

II. STRUCTURAL COMPONENTS OF DENDRIMERS

The molecular architecture determines the recognition capability of dendrimers.

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Table 1. Structural Components Influencing Molecular Recognition

Structural Component	Function	Effect on Host–Guest Interaction
Core	Initiates dendrimer growth	Determines molecular geometry
Branching Units	Increase molecular size	Create internal cavities
Generations	Increase branching density	Improve encapsulation efficiency
Surface Groups	Functional recognition sites	Enhance selective binding
Internal Voids	Molecular storage	Host hydrophobic guest molecules
Flexible Linkers	Molecular adaptability	Improve guest accommodation

The progressive increase in generations produces larger cavities capable of accommodating diverse guest molecules while increasing the number of recognition sites.

III. TYPES OF DENDRIMER ARCHITECTURES

Several dendrimer families have been developed depending upon branching chemistry.

Table 2. Major Dendrimer Families

Dendrimer Type	Surface Functional Groups	Major Applications
PAMAM	Amine, Hydroxyl	Drug delivery, Gene delivery
PPI	Primary amines	DNA delivery
Phosphorus Dendrimers	Phosphonate	Catalysis
Carbosilane	Hydrophobic groups	Imaging
Peptide Dendrimers	Amino acids	Antimicrobial therapy
Polyester Dendrimers	Ester groups	Controlled drug release

PAMAM dendrimers remain the most widely studied because of their excellent biocompatibility and extensive functionalization possibilities.

IV. MECHANISMS OF HOST–GUEST INTERACTIONS

Host–guest interactions involve reversible, non-covalent molecular recognition.

Major interaction mechanisms include:

1. Hydrogen bonding
2. Electrostatic attraction
3. Hydrophobic interactions
4. Van der Waals forces
5. π–π interactions
6. Metal coordination

These interactions collectively determine binding affinity and specificity.

Table 3. Host–Guest Interaction Mechanisms

Interaction	Driving Force	Example Guest
Hydrogen bonding	Donor–acceptor interaction	Drugs
Electrostatic	Charge attraction	DNA
Hydrophobic	Nonpolar association	Paclitaxel
π–π Stacking	Aromatic interaction	Doxorubicin
Metal Coordination	Chelation	Cu^{2+}, Zn^{2+}
Van der Waals	Weak intermolecular force	Organic molecules

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V. INFLUENCE OF DENDRIMER GENERATION

Generation number strongly affects host–guest chemistry.

Lower-generation dendrimers possess fewer cavities and recognition sites, whereas higher generations exhibit enhanced encapsulation, increased molecular weight, and greater binding capacity.

Table 4. Effect of Generation on Molecular Recognition

Generation	Surface Groups	Recognition Efficiency
G0	Low	Low
G2	Moderate	Moderate
G4	High	High
G5	Very High	Excellent
G7	Extremely High	Superior

Higher generations improve drug loading but may increase steric hindrance and cytotoxicity.

VI. SURFACE FUNCTIONALIZATION AND RECOGNITION

Surface modification dramatically changes dendrimer behavior.

Common modifications include:

1. PEGylation
2. Acetylation
3. Carboxylation
4. Hydroxylation
5. Targeting ligands
6. Antibodies
7. Peptides
8. Folic acid

Table 5. Functionalization Strategies

Modification	Purpose	Application
PEG	Improve circulation	Drug delivery
Folic acid	Cancer targeting	Chemotherapy
Antibody	Cell-specific binding	Immunotherapy
Biotin	Biomolecular recognition	Biosensors
Carboxyl	Increase solubility	Drug carriers

VII. HOST–GUEST DRUG ENCAPSULATION

Dendrimers encapsulate therapeutic molecules through internal cavities while surface groups improve stability.

Examples include:

1. Doxorubicin
2. Methotrexate
3. Paclitaxel
4. Curcumin
5. Ibuprofen
6. Cisplatin

Table 6. Drug Encapsulation Using Dendrimers

Drug	Dendrimer	Interaction Type	Outcome
Doxorubicin	PAMAM G5	Electrostatic	Sustained release
Paclitaxel	PAMAM G4	Hydrophobic	Solubility enhancement

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Curcumin	PPI	Encapsulation	Increased bioavailability
Methotrexate	PAMAM	Ionic	Targeted delivery
Ibuprofen	PAMAM	Hydrogen bonding	Controlled release

VIII. MOLECULAR RECOGNITION IN BIOSENSING

Dendrimers improve biosensor sensitivity through multivalent interactions.

Applications include:

1. Glucose sensing
2. DNA detection
3. Protein recognition
4. Cancer biomarkers
5. Heavy metal sensing
6. Immunosensors

Table 7. Biosensing Applications

Target	Recognition Mechanism	Sensor
DNA	Electrostatic	Electrochemical
Glucose	Enzyme immobilization	Biosensor
Protein	Antibody binding	Immunosensor
Hg^{2+}	Chelation	Fluorescent sensor
Cancer marker	Aptamer recognition	Optical sensor

IX. FACTORS AFFECTING MOLECULAR RECOGNITION

Recognition efficiency depends upon several structural parameters.

Table 8. Factors Affecting Recognition

Parameter	Influence
Generation	Surface density
Surface charge	Electrostatic binding
Branch flexibility	Guest accommodation
Solvent polarity	Binding stability
pH	Protonation state
Temperature	Interaction strength

X. BIOMEDICAL APPLICATIONS

Host–guest interactions enable multiple biomedical uses.

Table 9. Biomedical Applications

Application	Role of Molecular Recognition
Drug delivery	Selective targeting
Gene therapy	DNA condensation
Cancer therapy	Ligand-mediated targeting
MRI imaging	Contrast enhancement
Vaccine delivery	Antigen presentation
Antimicrobial therapy	Membrane interaction

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XI. ADVANTAGES AND LIMITATIONS

Table 10. Advantages and Challenges

Advantages	Limitations
Precise architecture	Complex synthesis
High loading capacity	Costly production
Multiple binding sites	Cytotoxicity at high generations
Controlled release	Steric hindrance
Surface modification	Scale-up challenges
Excellent biocompatibility (modified forms)	Regulatory hurdles

XII. CONCLUSION

Dendrimer architecture plays a central role in determining host–guest interactions and molecular recognition through its highly organized, branched, and multifunctional structure. The number of generations, branching density, internal cavities, and surface functional groups collectively influence the affinity, selectivity, and capacity for binding guest molecules. These properties have established dendrimers as powerful supramolecular hosts for applications in targeted drug delivery, gene therapy, biosensing, catalysis, imaging, and environmental remediation.

Although challenges such as synthesis complexity, cytotoxicity of highly cationic dendrimers, and large-scale manufacturing remain, advances in surface engineering, biocompatible modifications, and stimuli-responsive designs continue to improve their performance. Future developments integrating dendrimer chemistry with nanotechnology, artificial intelligence, and precision medicine are expected to expand their role in next-generation molecular recognition systems and biomedical applications.

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