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Original Article

Nanosponges In Drug Delivery: Recent Advances, Applications, Challenges, And Future Perspectives

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ABSTRACT

Nanosponges are emerging as a novel class of nanostructured carriers that offer significant advantages in modern drug delivery systems. These three-dimensional porous networks, commonly prepared using cyclodextrins and suitable cross-linking agents, possess the ability to encapsulate a wide range of therapeutic molecules, including hydrophilic, hydrophobic, and biomacromolecular drugs. The unique architecture of nanosponges provides enhanced drug solubility, improved stability, controlled release, and targeted delivery, thereby overcoming many limitations associated with conventional dosage forms. Recent advancements in nanosponge technology have led to the development of stimuli-responsive, biodegradable, targeted, and multifunctional nanosponge systems with improved therapeutic performance. Various preparation methods such as solvent method, ultrasound-assisted synthesis, emulsion solvent diffusion, melt method, and microwave-assisted techniques have been successfully employed for nanosponge fabrication. Comprehensive characterization using particle size analysis, zeta potential measurement, SEM, TEM, FTIR, DSC, and XRD ensures the quality and efficacy of nanosponge formulations. Nanosponges have demonstrated promising applications in oral, topical, ocular, pulmonary, and parenteral drug delivery. Furthermore, their therapeutic potential has been extensively explored in cancer therapy, antimicrobial treatment, anti-inflammatory drug delivery, and neurological disorders. Despite numerous advantages, challenges such as large-scale production, regulatory approval, long-term safety evaluation, and formulation stability continue to hinder their widespread commercialization. Future research is focused on integrating nanosponges with personalized medicine, gene delivery, theranostics, artificial intelligence-driven formulation design, and green synthesis approaches. Overall, nanosponge technology represents a versatile and innovative platform with immense potential to revolutionize pharmaceutical drug delivery and improve therapeutic outcomes across a broad spectrum of diseases.

Keywords: Nanosponges, Drug Delivery Systems, Cyclodextrin Nanosponges, Controlled Drug Release, Targeted Drug Delivery, Pharmaceutical Nanotechnology.

INTRODUCTION

The advancement of nanotechnology has revolutionized pharmaceutical sciences by enabling the development of novel drug delivery systems that improve therapeutic efficacy and patient compliance. Conventional drug delivery systems often suffer from limitations such as poor aqueous solubility, low bioavailability, rapid degradation, frequent dosing, and non-specific distribution of drugs. To overcome these challenges, nanocarrier-based drug delivery systems such as liposomes, nanoparticles, dendrimers, micelles, and nanosponges have been extensively investigated (1,2).

Nanosponges are three-dimensional porous nanostructures capable of encapsulating a wide variety of therapeutic agents, including hydrophilic and hydrophobic drugs. Their unique architecture provides high surface area, tunable pore size, enhanced stability, and controlled drug release properties. These features make nanosponges promising carriers for targeted and sustained drug delivery applications (3).

Initially developed using cyclodextrin polymers, nanosponge technology has evolved significantly, leading to the development of polymeric, biodegradable, and stimuli-responsive nanosponges. Recent studies have demonstrated their potential in

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oral, topical, ocular, pulmonary, and parenteral drug delivery systems. Furthermore, nanosponges have shown remarkable utility in improving the solubility of poorly water-soluble drugs and enhancing therapeutic outcomes in cancer, infectious diseases, and neurological disorders (4,5).

Due to their versatility, safety, and cost-effectiveness, nanosponges have emerged as an attractive platform in modern pharmaceutical research. This review focuses on the structure, properties, advantages, recent developments, and pharmaceutical applications of nanosponges in drug delivery.

2. OVERVIEW OF NANOSPONGES

Nanosponges are nanosized, highly cross-linked polymeric structures containing interconnected cavities and pores capable of entrapping active pharmaceutical ingredients. They act as molecular sponges that absorb, encapsulate, and release drug molecules in a controlled manner (6).The porous architecture of nanosponges allows accommodation of molecules of different sizes and physicochemical characteristics. Depending on the polymer and cross-linking agent used, nanosponges can be engineered to provide desired release profiles and targeting capabilities (7).Nanosponges can exist as solid particles or colloidal dispersions with particle sizes generally ranging from 50 to 500 nm. They exhibit excellent thermal stability, biocompatibility, and loading efficiency, making them suitable for diverse therapeutic applications (8).

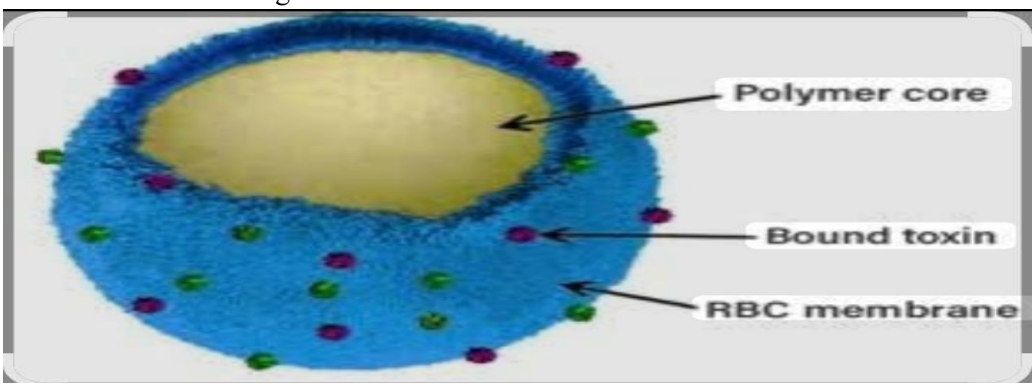

Figure 1. General Representation of Nanosponge Structure

2.1 Definition and Structure

Nanosponges are hyper-crosslinked polymeric nanoparticles composed of a three-dimensional network of polymers interconnected through cross-linking agents. The resulting structure forms nanoscale cavities capable of encapsulating drug molecules and protecting them from environmental degradation (9).

Cyclodextrin-based nanosponges are the most extensively studied systems. In these systems, cyclodextrin molecules are cross-linked using agents such as diphenyl carbonate, carbonyldiimidazole, or pyromellitic dianhydride to form a porous network (10).

The structure consists of:

• Polymer backbone

• Cross-linking bridges

• Nanocavities for drug entrapment

• Surface functional groups

The drug may be physically trapped inside pores or chemically associated with the polymer matrix depending on its physicochemical properties.

Component	Function
Polymer Matrix	Provides structural framework
Cross-linker	Forms porous network
Nanocavities	Drug encapsulation
Surface Groups	Enhance targeting and stability
Pores/Channels	Facilitate drug diffusion

Table 1. Structural Components of Nanosponges

2.2 Properties and Advantages

Nanosponges possess several unique physicochemical and biological properties that distinguish them from conventional drug delivery systems.

Property	Description
Nanoscale Size	Typically 50–500 nm
Porous Structure	High surface area for drug loading
Biocompatibility	Safe and non-toxic
Thermal Stability	Resistant to temperature variations
Chemical Stability	Protects drugs from degradation
Controlled Release	Sustained therapeutic action
High Entrapment Efficiency	Accommodates diverse drugs
Versatility	Suitable for multiple routes of administration

Table 2. Important Properties of Nanosponges

Parameter	Conventional Delivery	Nanosponges
Drug Solubility	Limited	Enhanced
Drug Stability	Moderate	High
Targeting Ability	Poor	Excellent
Drug Release	Immediate	Controlled
Toxicity	Higher	Reduced
Bioavailability	Lower	Improved
Patient Compliance	Moderate	Better

Table 3. Advantages of Nanosponges Compared with Conventional Systems

3. Materials Used in Nanosponge Preparation

The selection of suitable polymers and cross-linking agents is crucial in the fabrication of nanosponges, as these materials determine the structural integrity, drug-loading capacity, release characteristics, and biocompatibility of the final formulation. Various natural and synthetic polymers have been utilized to develop nanosponges with tailored properties for specific pharmaceutical applications (15).

3.1 Polymers Used in Nanosponge Preparation

Polymers form the backbone of the nanosponge structure and provide the porous network required for drug encapsulation. Cyclodextrins are the most widely used polymers because of their ability to form inclusion complexes with drug molecules. Other polymers such as ethyl cellulose, polymethyl methacrylate, polycaprolactone, and biodegradable copolymers have also been investigated for nanosponge synthesis (16,17).

Polymer	Characteristics	Applications
β-Cyclodextrin	High inclusion capacity, biocompatible	Oral and topical delivery
Hydroxypropyl-β-cyclodextrin	Improved aqueous solubility	Solubility enhancement
Ethyl Cellulose	Biodegradable, sustained release	Oral delivery
Polycaprolactone	Biocompatible and biodegradable	Controlled drug release
PMMA	Mechanical stability	Targeted delivery
Chitosan	Mucoadhesive and biodegradable	Nasal and ocular delivery

Table 4. Common Polymers Used in Nanosponge Preparation

3.2 Cross-Linking Agents

Cross-linking agents connect polymer chains and generate the porous three-dimensional architecture of nanosponges. The degree of cross-linking significantly influences pore size, drug loading, and release kinetics (18).

Cross-Linking Agent	Function
Diphenyl Carbonate (DPC)	Produces highly porous nanosponges
Carbonyldiimidazole (CDI)	Forms stable cross-linked networks
Pyromellitic Dianhydride (PMDA)	Enhances structural rigidity
Citric Acid	Biocompatible cross-linker
Epichlorohydrin	Produces stable polymeric matrices

Table 5. Common Cross-Linking Agents

3.3 Solvents Used During Preparation

Various solvents are employed during nanosponge synthesis depending on the polymer and cross-linker selected. Solvents facilitate polymer dissolution and improve reaction efficiency (19).

Solvent	Purpose
Dimethylformamide (DMF)	Polymer dissolution
Dimethyl Sulfoxide (DMSO)	Reaction medium
Ethanol	Purification and washing
Acetone	Solvent evaporation techniques
Water	Green synthesis approaches

Table 6. Solvents Used in Nanosponge Synthesis

3.4 Factors Affecting Material Selection

The choice of materials depends on:

- Drug physicochemical properties
- Desired release profile
- Route of administration
- Biocompatibility requirements
- Stability considerations
- Regulatory acceptance

Proper selection of polymers and cross-linkers enables the development of nanosponges with high entrapment efficiency, improved stability, and controlled drug release characteristics (20).

4. METHODS OF PREPARATION

Several techniques have been developed for nanosponge synthesis. The preparation method significantly affects particle size, morphology, drug loading capacity, and release behavior. Selection of a suitable method depends on the nature of the polymer, cross-linking agent, and intended application (21).

4.1 Solvent Method

The solvent method is one of the most commonly employed techniques for preparing cyclodextrin-based nanosponges. In this method, the polymer is dissolved in a suitable solvent and reacted with a cross-linking agent under controlled temperature conditions. After completion of the reaction, the product is purified and dried to obtain nanosponges (22).

Advantages

- Simple process
- High product yield
- Suitable for large-scale production

Limitations

- Use of organic solvents
- Additional purification steps required

4.2 Ultrasound-Assisted Method

In this technique, polymer and cross-linking agent mixtures are subjected to ultrasonic energy without using solvents. Ultrasonic waves promote efficient cross-linking and formation of porous nanostructures (23).

Advantages

- Solvent-free process
- Environmentally friendly
- Uniform particle size distribution

Limitations

- Specialized equipment required

4.3 Emulsion Solvent Diffusion Method

This method is widely used for preparing polymeric nanosponges. The polymer and drug are dissolved in an organic phase and emulsified into an aqueous phase containing stabilizers. Solvent diffusion and evaporation lead to nanosponge formation (24).

Advantages

- Suitable for hydrophobic drugs
- High drug entrapment efficiency

Limitations

- Residual solvent concerns

4.4 Melt Method

In the melt method, polymers and cross-linkers are heated above their melting points without the use of solvents. Cross-linking occurs during heating, resulting in nanosponge formation (25).

Advantages

- Solvent-free
- Economical

Limitations

- Not suitable for thermolabile drugs

4.5 Microwave-Assisted Synthesis

Microwave irradiation accelerates the cross-linking reaction and significantly reduces preparation time. Uniform heating improves nanosponge formation and reproducibility (26).

Advantages

- Rapid synthesis
- Reduced reaction time
- Energy efficient

Limitations

- Requires microwave reactor

4.6 Green Synthesis Approaches

Recent studies focus on eco-friendly preparation methods utilizing biodegradable polymers, aqueous media, and natural cross-linkers. Green synthesis minimizes environmental impact while maintaining formulation performance (27).

Method	Advantages	Limitations
Solvent Method	High yield, simple	Organic solvent use
Ultrasound Method	Solvent-free, eco-friendly	Specialized equipment
Emulsion Solvent Diffusion	High entrapment efficiency	Residual solvents
Melt Method	Economical	Not suitable for heat-sensitive drugs
Microwave Method	Fast synthesis	Equipment cost
Green Synthesis	Environmentally friendly	Scale-up challenges

Table 7. Comparison of Nanosponge Preparation Methods

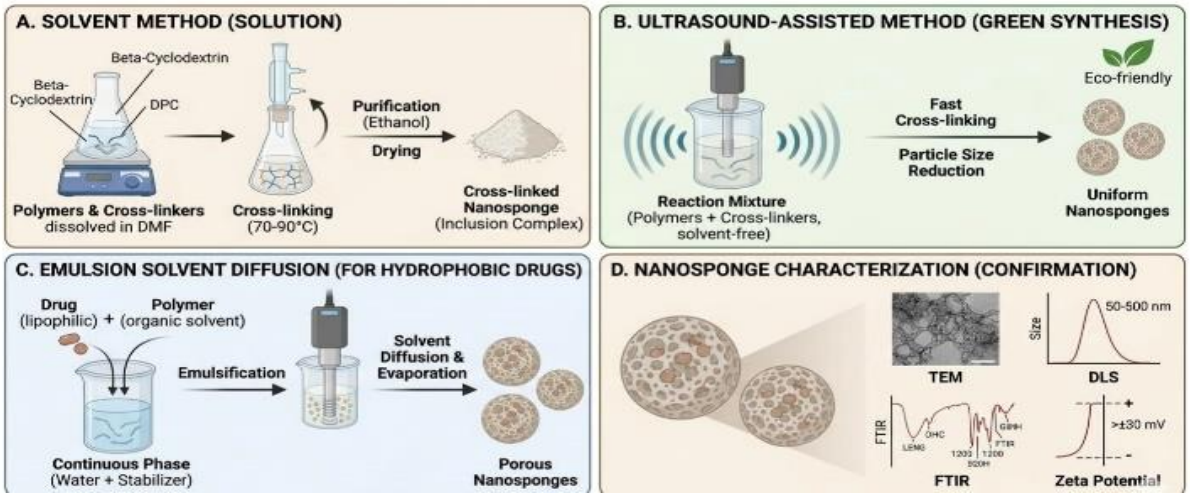

Figure 2: Preparation and Characterization of Nanosponges

5. CHARACTERIZATION OF NANOSPONGES

Characterization of nanosponges is essential to evaluate their physicochemical properties, drug-loading efficiency, stability, and drug-release behavior. Various analytical techniques are employed to ensure the quality and performance of nanosponge formulations. Proper characterization helps establish a correlation between structural properties and therapeutic efficacy (28).

5.1 Particle Size Analysis

Particle size is a critical parameter influencing drug loading, release kinetics, biodistribution, and cellular

uptake. Nanosponge particle size is commonly measured using Dynamic Light Scattering (DLS), laser diffraction, or nanoparticle tracking analysis (29).

Significance

- Influences drug release rate
- Affects stability and dispersibility
- Determines tissue penetration and bioavailability

Particle Size	Effect
<100 nm	Enhanced cellular uptake
100–300 nm	Optimal drug delivery
>500 nm	Reduced bioavailability

Table 8. Importance of Particle Size in Nanosponges

5.2 Zeta Potential

Zeta potential measures the surface charge of nanoparticles and predicts colloidal stability. Higher absolute zeta potential values indicate greater repulsive forces between particles, preventing aggregation (30).

Interpretation

Zeta Potential (mV)	Stability
±0–10	Highly unstable
±10–20	Relatively stable
±20–30	Moderately stable
> ±30	Highly stable

5.3 Surface Morphology

The morphology and surface characteristics of nanosponges are evaluated using:

- Scanning Electron Microscopy (SEM)
- Transmission Electron Microscopy (TEM)
- Atomic Force Microscopy (AFM)

These techniques provide information regarding particle shape, pore structure, and surface texture (31).

5.4 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectroscopy is used to identify functional groups and investigate drug-polymer interactions. Shifts in characteristic absorption peaks indicate successful encapsulation and compatibility between the drug and nanosponge matrix (32).

Applications

- Compatibility studies
- Confirmation of cross-linking
- Identification of chemical interactions

5.5 Differential Scanning Calorimetry (DSC)

DSC evaluates thermal behavior and physical state changes in nanosponge formulations. It is useful for determining melting points, crystallinity, and drug-polymer interactions (33).

Significance

- Detects encapsulation of drug
- Determines thermal stability
- Evaluates crystallinity changes

5.6 X-Ray Diffraction (XRD)

XRD analysis determines the crystalline or amorphous nature of the drug and nanosponge system. Drug encapsulation often results in reduced crystallinity, enhancing drug solubility and dissolution (34).

Technique	Purpose
DLS	Particle size measurement
Zeta Potential	Stability assessment
SEM	Surface morphology
TEM	Internal structure

FTIR	Drug-polymer interaction
DSC	Thermal behavior
XRD	Crystallinity analysis

Table 9. Characterization Techniques and Their Applications

5.7 Entrapment Efficiency

Entrapment efficiency represents the percentage of drug successfully incorporated into the nanosponge matrix relative to the total drug used during formulation (35).

Factors Affecting Entrapment Efficiency

- Polymer concentration
- Cross-linking density
- Drug solubility
- Preparation method

5.8 In Vitro Drug Release Studies

Drug release studies evaluate the release profile of encapsulated drugs under simulated physiological conditions. Commonly used dissolution media include phosphate buffer, simulated gastric fluid, and simulated intestinal fluid (36).

Objectives

- Determine release kinetics
- Predict in vivo behavior
- Optimize formulation performance

6. DRUG LOADING AND RELEASE MECHANISM

Drug loading and release are the fundamental functions of nanosponge-based drug delivery systems. The porous structure of nanosponges provides numerous cavities capable of entrapping active pharmaceutical ingredients and releasing them in a controlled manner (37).

6.1 Drug Loading Mechanism

Drug loading involves incorporation of drug molecules into nanosponge cavities through physical adsorption, inclusion complexation, diffusion, or molecular entrapment (38).

Steps in Drug Loading

Drug Solution

↓

Mixing with Nanosponges

↓

Drug Diffusion into Cavities

↓

Encapsulation

↓

Loaded Nanosponges

Factors Affecting Drug Loading

- Molecular size of drug
- Drug solubility
- Pore size of nanosponges
- Degree of cross-linking
- Drug-polymer affinity

6.2 Drug Release Mechanism

Drug release from nanosponges occurs through diffusion, desorption, erosion, swelling, or environmental stimuli. The release profile depends on the nature of the polymer, cross-linking density, and physicochemical properties of the drug (39).

Drug Release from Nanosponges

Drug Loaded

Nanosponges

↓

Penetration of Medium

↓

Drug Diffusion

↓

Controlled Release

↓

Therapeutic Action

6.3 Diffusion-Controlled Release

The majority of nanosponge systems release drugs by diffusion. After exposure to biological fluids, drug molecules gradually diffuse through nanosponge pores into the surrounding medium (40).

Advantages

- Sustained drug release
- Reduced dosing frequency
- Improved patient compliance

6.4 Stimuli-Responsive Release

Advanced nanosponges can release drugs in response to specific stimuli such as:

- pH changes
- Temperature
- Enzymes
- Redox conditions
- Light exposure

These systems provide site-specific and on-demand drug delivery (41,42)

7. Recent Advances in Nanosponge Technology

Nanosponges have emerged as one of the most promising nanocarrier systems due to their unique porous architecture, high drug-loading capacity, and ability to provide controlled and targeted drug delivery. Recent advances in nanosponge technology have focused on improving therapeutic efficacy, biocompatibility, targeting capability, and responsiveness to physiological stimuli. These developments have expanded the application of nanosponges beyond conventional drug delivery systems (43).

7.1 Stimuli-Responsive Nanosponges

Stimuli-responsive or "smart" nanosponges are designed to release drugs in response to specific environmental triggers such as pH, temperature, enzymes, redox potential, or light. These systems improve site-specific drug delivery and minimize adverse effects on healthy tissues (44).

Advantages

- Controlled drug release
- Improved therapeutic efficacy
- Reduced systemic toxicity
- Enhanced targeting efficiency

Stimulus	Mechanism of Drug Release	Therapeutic Application
pH	Release in acidic/basic environment	Cancer therapy
Temperature	Heat-triggered release	Hyperthermia treatment
Enzymes	Enzyme-mediated degradation	Infection targeting
Redox	Intracellular glutathione response	Tumor targeting

Light	Phototriggered release	Photodynamic therapy

Table 10:. Types of Stimuli-Responsive Nanosponges

7.2 Targeted Nanosponge Systems

Surface-functionalized nanosponges have been developed for active targeting of specific tissues and cells. Ligands such as antibodies, peptides, folic acid, and aptamers are attached to the nanosponge surface to enhance cellular uptake and target specificity (45).

Benefits

- Increased drug accumulation at target site
- Reduced off-target effects
- Improved therapeutic outcomes

7.3 Hybrid Nanosponges

Hybrid nanosponges combine nanosponges with other nanocarriers such as liposomes, metallic nanoparticles, hydrogels, and polymeric nanoparticles. These hybrid systems integrate the advantages of multiple delivery platforms (46).

Applications

- Combination drug therapy
- Controlled release formulations
- Theranostic systems

7.4 Biodegradable Nanosponges

Recent research emphasizes biodegradable nanosponges prepared from natural and synthetic biodegradable polymers. These systems undergo degradation after drug release, minimizing long-term toxicity and environmental concerns (47).

Common Biodegradable Polymers

- Chitosan
- Gelatin
- Polycaprolactone
- Polylactic acid (PLA)
- PLGA

7.5 Nanosponges for Biological Molecules

Modern nanosponge systems are capable of delivering proteins, peptides, nucleic acids, and vaccines. Their porous structure protects sensitive biomolecules from enzymatic degradation and enhances bioavailability (48).

Innovation	Key Benefit
Smart Nanosponges	Stimulus-triggered release
Targeted Nanosponges	Site-specific delivery
Hybrid Nanosponges	Multifunctional performance
Biodegradable Nanosponges	Improved safety
Gene Delivery Nanosponges	Nucleic acid protection
Vaccine Delivery Systems	Enhanced immune response

Table 11:. Recent Innovations in Nanosponge Technology

7.6 Nanosponges in Cancer Therapy

Advanced nanosponge formulations have demonstrated significant potential in cancer treatment through controlled release and targeted delivery of chemotherapeutic agents. These systems improve drug accumulation in tumor tissues while reducing systemic toxicity (49).

8. APPLICATIONS OF NANOSPONGES IN DRUG DELIVERY

Nanosponges have attracted considerable attention as versatile drug carriers due to their ability to encapsulate both hydrophilic and hydrophobic drugs. Their porous structure allows controlled release, improved stability, and enhanced bioavailability, making them suitable for various routes of administration (50).

8.1 Oral Drug Delivery

Oral administration is the most widely used route of drug delivery. Nanosponges improve the solubility and dissolution rate of poorly water-soluble drugs, thereby enhancing oral bioavailability (51).

Advantages

- Improved dissolution
- Enhanced gastrointestinal stability
- Sustained drug release
- Better patient compliance

Examples

- Itraconazole
- Curcumin
- Paclitaxel
- Resveratrol

8.2 Topical Drug Delivery

Nanosponges are extensively used in topical formulations such as creams, gels, lotions, and ointments. They provide sustained release of drugs at the skin surface and reduce local irritation (52).

Advantages

- Controlled drug release
- Improved skin retention
- Reduced irritation
- Enhanced patient compliance

Applications

- Acne treatment
- Antifungal therapy
- Anti-inflammatory therapy
- Wound healing

8.3 Ocular Drug Delivery

Ocular drug delivery remains challenging because of rapid tear turnover and limited corneal permeability. Nanosponge systems increase drug residence time on the ocular surface and improve drug penetration (53).

Advantages

- Prolonged precorneal retention
- Enhanced corneal permeation
- Reduced dosing frequency

Applications

- Glaucoma
- Conjunctivitis
- Dry eye syndrome
- Corneal infections

8.4 Pulmonary Drug Delivery

Nanosponges have demonstrated potential for pulmonary administration due to their small particle size and controlled-release characteristics. They enable direct delivery of drugs to the lungs, enhancing therapeutic effectiveness (54).

Advantages

- Rapid onset of action
- Reduced systemic exposure
- Improved lung targeting

Applications

- Asthma
- Chronic obstructive pulmonary disease (COPD)

- Pulmonary infections
- Lung cancer

8.5 Parenteral Drug Delivery

Parenteral administration allows direct delivery of nanosponge formulations into systemic circulation. Nanosponges improve the stability of injectable drugs and facilitate targeted delivery to diseased tissues (55).

Advantages

- Immediate therapeutic effect
- Controlled systemic release
- Enhanced targeting capability

Applications

- Cancer chemotherapy
- Antibiotic delivery
- Peptide delivery
- Protein therapeutics

8.6 Future Direction of Drug Delivery Applications

The integration of nanosponges with advanced targeting strategies, nanotechnology, and personalized medicine is expected to further improve drug delivery efficiency. Future research is focused on multifunctional nanosponges capable of simultaneous diagnosis and therapy, often referred to as theranostic nanosponges (56).

9. THERAPEUTIC APPLICATIONS OF NANOSPONGES

Nanosponges have gained considerable attention in pharmaceutical research due to their ability to enhance drug solubility, stability, bioavailability, and targeted delivery. Their unique porous structure enables encapsulation of a wide range of therapeutic agents, making them suitable for the treatment of various diseases. Recent studies have demonstrated significant applications of nanosponges in cancer therapy, antimicrobial treatment, inflammatory disorders, and neurological diseases (57).

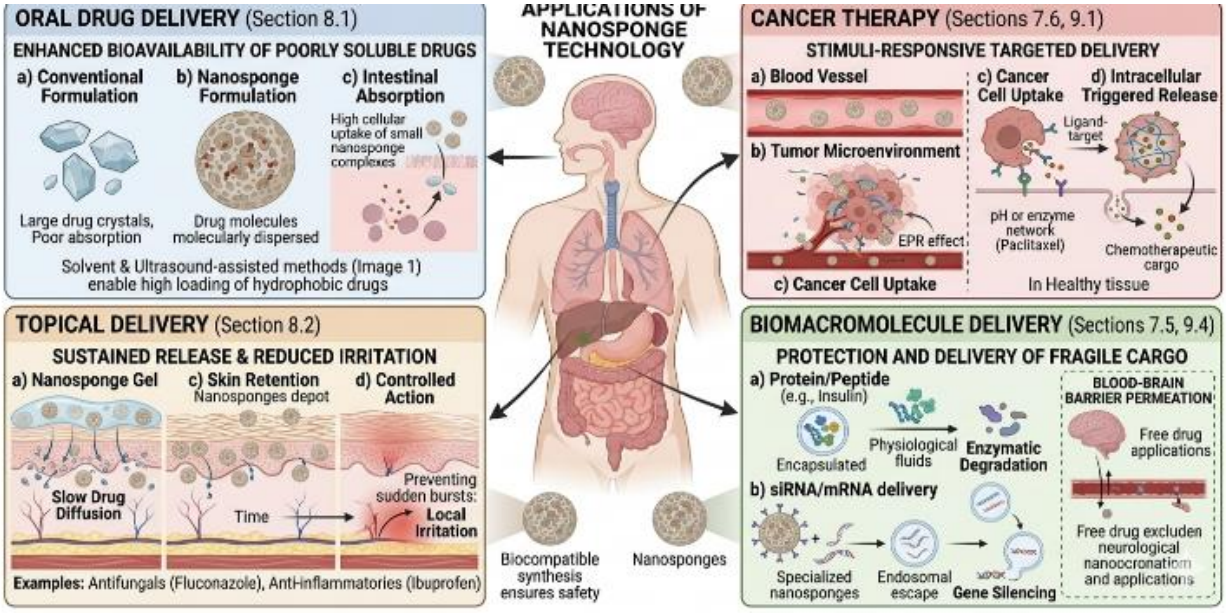

Figure 3: Application of Nanosponges

9.1 Cancer Therapy

Cancer remains one of the leading causes of mortality worldwide. Conventional chemotherapy often suffers from poor selectivity, systemic toxicity, and multidrug resistance. Nanosponge-based drug delivery systems have emerged as promising carriers for anticancer drugs due to their ability to provide controlled and targeted drug release (58).

Nanosponges can encapsulate chemotherapeutic agents such as paclitaxel, doxorubicin, camptothecin, and tamoxifen, improving their aqueous solubility and reducing adverse effects on healthy tissues. Surface-functionalized nanosponges further enhance tumor targeting through receptor-mediated uptake (59).

Benefits in Cancer Therapy

- Improved drug solubility
- Enhanced tumor targeting
- Sustained drug release
- Reduced systemic toxicity
- Improved therapeutic efficacy

Drug	Therapeutic Use	Benefit of Nanosponge Delivery
Paclitaxel	Breast and lung cancer	Improved solubility
Doxorubicin	Solid tumors	Reduced cardiotoxicity
Camptothecin	Colorectal cancer	Enhanced stability
Tamoxifen	Breast cancer	Controlled release

Table 11: Anticancer Drugs Delivered Using Nanosponges

9.2 Antimicrobial Drug Delivery

The emergence of antimicrobial resistance has created a need for more effective drug delivery systems. Nanosponges improve the delivery of antibiotics, antifungal agents, and antiviral drugs by enhancing their stability and maintaining therapeutic concentrations for prolonged periods (60).

Encapsulation within nanosponges protects antimicrobial agents from degradation and improves penetration into infected tissues. This approach may reduce dosing frequency and minimize resistance development.

Applications

- Bacterial infections
- Fungal infections
- Viral diseases
- Biofilm-associated infections

Advantages

- Improved antimicrobial activity
- Enhanced drug stability
- Sustained release
- Reduced frequency of administration

Drug	Infection Treated	Advantage
Fluconazole	Fungal infections	Enhanced penetration
Voriconazole	Ocular fungal infections	Sustained release
Ciprofloxacin	Bacterial infections	Improved stability
Acyclovir	Viral infections	Better bioavailability

Table 12:. Antimicrobial Applications of Nanosponges

9.3 Anti-inflammatory Drug Delivery

Inflammatory disorders require prolonged therapy, often associated with adverse effects due to repeated administration. Nanosponges offer controlled and localized drug delivery, reducing systemic exposure and improving therapeutic outcomes (61).

Anti-inflammatory drugs such as diclofenac, meloxicam, ibuprofen, and celecoxib have been successfully incorporated into nanosponge systems. Controlled drug release helps maintain therapeutic drug levels over extended periods.

Benefits

- Sustained anti-inflammatory action
- Reduced gastrointestinal side effects
- Improved patient compliance
- Enhanced local drug concentration

9.4 Neurological Disorders

Treatment of neurological diseases is often limited by the blood-brain barrier (BBB), which restricts drug penetration into the central nervous system. Nanosponges have shown potential in enhancing brain delivery of therapeutic agents through improved permeability and controlled release (62).

Nanosponge formulations have been investigated for the treatment of:

- Alzheimer's disease
- Parkinson's disease
- Epilepsy
- Brain tumors
- Neuroinflammatory disorders

Advantages in Neurological Therapy

- Improved BBB penetration
- Sustained drug release
- Enhanced bioavailability
- Reduced systemic toxicity

Disease	Drug Candidate	Expected Benefit
Alzheimer's Disease	Donepezil	Improved brain delivery
Parkinson's Disease	Levodopa	Sustained release
Epilepsy	Carbamazepine	Enhanced bioavailability
Brain Tumors	Temozolomide	Targeted delivery

Table 13: Neurological Applications of Nanosponges

10. ADVANTAGES OF NANOSPONGES

Nanosponges possess several advantages over conventional drug delivery systems due to their unique porous structure and versatile drug-loading capabilities (63).

1. Enhanced Drug Solubility:Nanosponges improve the aqueous solubility of poorly water-soluble drugs through inclusion complex formation and molecular encapsulation.

2. Controlled and Sustained Release:The porous matrix allows gradual drug release, maintaining therapeutic drug concentrations for extended periods.

3. Improved Stability:Encapsulation protects drugs from hydrolysis, oxidation, photodegradation, and enzymatic degradation.

4. Reduced Toxicity:Targeted and controlled drug delivery minimizes exposure of healthy tissues to drugs, reducing adverse effects.

5. High Drug Loading Capacity:Large internal cavities facilitate efficient incorporation of therapeutic molecules.

6. Versatility: Nanosponges are versatile nanostructured carriers capable of encapsulating hydrophobic and hydrophilic drugs, proteins, peptides, anticancer agents, and antimicrobial agents.

11. Challenges and Limitations

Despite their numerous advantages, nanosponge systems face several challenges that limit their widespread clinical and commercial application (64).

11.1 Manufacturing Challenges:Large-scale production of nanosponges remains difficult due to complex synthesis procedures, reproducibility issues, and process optimization requirements.

11.2 Drug Loading Limitations:Not all drugs are suitable for nanosponge encapsulation. Drug loading depends on molecular size, polarity, and affinity toward the polymer matrix.

11.3 Toxicity Concerns:Although generally considered biocompatible, long-term toxicity and biodistribution studies remain limited for several nanosponge formulations.

11.4 Regulatory Challenges:The absence of standardized regulatory guidelines for nanosponge-based formulations delays product approval and commercialization.

11.5 Stability Issues:Certain nanosponge formulations may experience aggregation, particle growth, or drug leakage during storage.

11.6 Cost of Production:Advanced preparation methods and specialized characterization techniques increase manufacturing costs.

12. Future Perspectives

Nanosponge technology has emerged as a versatile and promising platform in advanced drug delivery. Although significant progress has been made in recent years, continuous innovations in material science, nanotechnology, biotechnology, and pharmaceutical engineering are expected to further expand the scope of nanosponges in clinical medicine. Future research is directed toward developing safer, smarter, and more efficient nanosponge systems capable of overcoming current limitations and addressing unmet therapeutic needs (65)

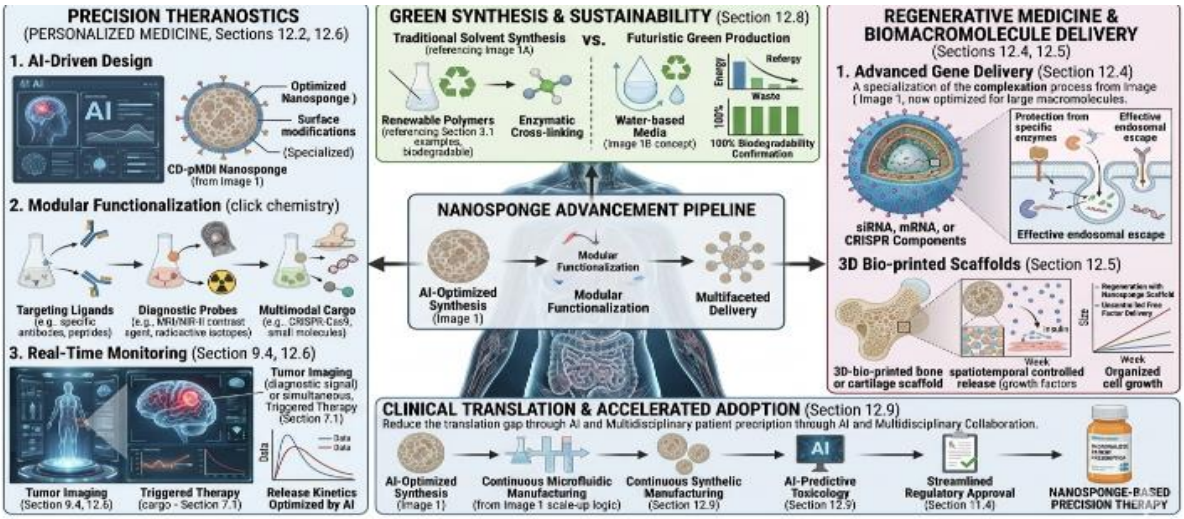

Figure 4 : Future presepective of Nanosponge

12.1 Development of Smart and Stimuli-Responsive Nanosponges

One of the most promising future directions involves the development of smart nanosponges capable of responding to specific physiological or external stimuli. These advanced systems can release drugs selectively in response to changes in pH, temperature, enzyme concentration, redox potential, magnetic fields, or light irradiation (66).

Such stimuli-responsive nanosponges may significantly improve therapeutic outcomes by ensuring that drugs are released only at the desired site of action. This approach minimizes systemic exposure, reduces adverse effects, and increases treatment efficacy, particularly in cancer and inflammatory diseases.

Potential Applications

- Tumor-specific drug delivery
- Infection-responsive antimicrobial therapy
- Site-specific anti-inflammatory treatment
- Precision medicine approaches

12.2 Personalized Medicine

The growing emphasis on personalized medicine presents a significant opportunity for nanosponge technology. Future nanosponge formulations may be customized according to individual patient characteristics, including genetic profile, disease state, metabolic status, and therapeutic requirements (67).

Personalized nanosponge systems could enable:

- Patient-specific dosing
- Reduced adverse effects
- Enhanced therapeutic efficacy
- Improved treatment adherence

Integration of pharmacogenomics and nanosponge-based drug delivery may play a critical role in tailoring treatments for chronic and complex diseases.

12.3 Targeted Drug Delivery Systems

Targeted drug delivery remains one of the most important goals of pharmaceutical research. Future nanosponges are expected to incorporate targeting ligands such as antibodies, peptides, aptamers, folic acid, and receptor-specific molecules to achieve highly selective delivery to diseased tissues (68).

Benefits of Targeted Nanosponges

- Increased drug concentration at target site
- Reduced toxicity to healthy tissues
- Lower therapeutic dose requirements
- Enhanced clinical effectiveness

Targeted nanosponge systems are particularly promising for cancer therapy, neurological disorders, autoimmune diseases, and infectious diseases.

12.4 Gene and Nucleic Acid Delivery

Recent advances in gene therapy have highlighted the need for safe and effective carriers capable of delivering nucleic acids. Nanosponges possess structural characteristics suitable for the delivery of:

- DNA
- siRNA
- mRNA
- microRNA
- CRISPR-associated gene-editing components

Future nanosponge-based gene delivery systems may provide improved protection against enzymatic degradation while enhancing intracellular uptake and transfection efficiency (69).

Potential Therapeutic Areas

- Genetic disorders
- Cancer gene therapy
- Rare diseases
- Regenerative medicine

12.5 Nanosponges for Protein and Peptide Delivery

Protein- and peptide-based therapeutics have gained considerable attention because of their high specificity and efficacy. However, their clinical application is often limited by instability and rapid degradation.

Future nanosponge systems may provide effective encapsulation and controlled release of biologics, improving stability and extending circulation time (70).

Potential Applications

- Insulin delivery
- Monoclonal antibodies
- Growth factors
- Therapeutic enzymes
- Vaccine antigens

12.6 Theranostic Nanosponges

Theranostics refers to the combination of diagnosis and therapy within a single platform. Emerging nanosponge systems are being engineered to simultaneously deliver therapeutic agents and diagnostic molecules such as fluorescent probes, contrast agents, and imaging markers (71).

Advantages

- Real-time monitoring of treatment
- Early disease detection
- Personalized treatment adjustment
- Improved therapeutic outcomes

Theranostic nanosponges are expected to become valuable tools in oncology, cardiovascular diseases, and precision medicine.

12.7 Artificial Intelligence and Machine Learning in Nanosponge Design

Artificial intelligence (AI) and machine learning (ML) are transforming pharmaceutical development. Future nanosponge research may increasingly utilize computational approaches to optimize formulation parameters, predict drug-loading efficiency, evaluate release kinetics, and identify suitable polymer-crosslinker combinations (72).

Applications of AI in Nanosponge Research

- Formulation optimization
- Prediction of physicochemical properties
- Drug-polymer compatibility assessment
- Scale-up process optimization

These technologies can significantly reduce development time and costs while improving formulation quality.

12.8 Green and Sustainable Nanosponge Technology

Environmental sustainability is becoming increasingly important in pharmaceutical manufacturing. Future research is expected to focus on green synthesis approaches utilizing:

- Renewable polymers
- Biodegradable materials
- Eco-friendly solvents
- Energy-efficient production methods

Green nanosponge technology may reduce environmental impact while maintaining formulation performance and safety (73).

Benefits

- Reduced environmental burden
- Improved biocompatibility
- Lower manufacturing hazards
- Enhanced regulatory acceptance

12.9 Clinical Translation and Commercialization

Despite encouraging laboratory results, only a limited number of nanosponge-based products have reached clinical development. Future efforts should focus on bridging the gap between research and commercialization through:

- Large-scale manufacturing processes
- Standardized characterization methods
- Comprehensive toxicological studies
- Regulatory framework development
- Cost-effective production technologies

Successful clinical translation will enable broader adoption of nanosponge technology in pharmaceutical products and healthcare systems (74).

CONCLUSION

Nanosponges are revolutionizing drug delivery by leveraging a unique, porous architecture that dramatically enhances drug solubility, loading capacity, and controlled release across various administration routes. By seamlessly integrating targeted, stimuli-responsive therapies with advanced diagnostics, these versatile nanocarriers are overcoming historical manufacturing and safety hurdles. Ultimately, driven by breakthroughs in AI and biotechnology, nanosponges are poised to become a cornerstone of next-generation personalized medicine, offering safer, more effective, and patient-centric treatments for complex diseases like cancer and neurological disorders.

REFERENCES

1. Allen TM, Cullis PR. Drug delivery systems: entering the mainstream. Science. 2004;303(5665):1818-1822.
2. Torchilin VP. Multifunctional nanocarriers. Nat Rev Drug Discov. 2014;13(11):813-827.
3. Trotta F, Cavalli R. Characterization and applications of nanosponges. J Incl Phenom Macrocycl Chem. 2009;65(1-2):209-213.
4. Swaminathan S, Cavalli R, Trotta F, Ferruti P, Ranucci E, Gerges I, et al. Cyclodextrin-based nanosponges for drug delivery. Int J Pharm. 2010;393(1-2):92-98.
5. Krabicová I, Appleton SL, Tannous M, Mahdi F, Singh N, Zhu H, et al. History of cyclodextrin nanosponges. Biomolecules. 2020;10(8):1125.
6. Trotta F, Dianzani C, Caldera F, Mognetti B. The application of nanosponges in drug delivery. Beilstein J Org Chem. 2014;10:2586-2599.
7. Selvamuthukumar S, Anandam S. Nanosponges: a novel class of drug delivery system. J Pharm Pharm Sci. 2016;19(2):235-248.
8. Khalid M, Ahmad M, Minhas MU. Nanosponges: a promising approach for drug delivery. Drug Dev Ind Pharm. 2021;47(4):535-547.
9. Ansari KA, Vavia PR. Trotta nanosponges for drug delivery. Drug Deliv. 2011;18(8):577-583.
10. Trotta F, Zanetti M, Cavalli R. Cyclodextrin-based nanosponges as drug carriers. Beilstein J Org Chem. 2012;8:2091-2099.
11. Shende P, Trotta F. Enhancement of drug solubility using nanosponges. J Pharm Sci. 2018;107(1):289-297.
12. Pawar AP, Shende PK. Controlled release properties of nanosponges. AAPS PharmSciTech. 2014;15(3):699-708.
13. Deshmukh K, Shaikh A. Stability enhancement using nanosponges. Drug Dev Res. 2017;78(8):429-437.
14. Caldera F, Tannous M, Cavalli R, Zanetti M, Trotta F. Evolution of cyclodextrin nanosponges. Nanomaterials. 2017;7(12):381.
15. Mohanraj V, Chen Y. Nanoparticles: a review. Trop J Pharm Res. 2006;5(1):561-573.
16. Swaminathan S, Pastero L, Serpe L, Trotta F, Vavia P, Aquilano D, et al. Cyclodextrin-based nanosponges encapsulating camptothecin. Int J Pharm. 2010;393(1-2):164-173.
17. Shringirishi M, Prajapati SK, Mahor A, Alok S, Yadav P, Verma A. Nanosponges: a potential nanocarrier for novel drug delivery. Int J Pharm Sci Res. 2014;5(5):1775-1784.
18. Trotta F, Caldera F, Tannous M, Cavalli R. Cyclodextrin-based nanosponges as versatile carriers. Curr Pharm Des. 2017;23(11):1688-1703.
19. Krabicová I, Appleton SL, Tannous M, Mahdi F, Singh N, Zhu H, et al. Cyclodextrin nanosponges and their applications. Biomolecules. 2020;10(8):1125.
20. Deshmukh K, Shaikh A, Jain A. Polymeric nanosponges for controlled drug delivery. Drug Dev Ind Pharm. 2019;45(4):555-568.
21. Selvamuthukumar S, Anandam S, Kannan K. Nanosponges: preparation and applications. Int J Pharm Pharm Sci. 2012;4(3):42-51.
22. Trotta F, Cavalli R. Synthesis and characterization of cyclodextrin nanosponges. J Incl Phenom Macrocycl Chem. 2009;65(1-2):209-213.
23. Caldera F, Trotta F, Cavalli R. Ultrasound-assisted preparation of nanosponges. Mater Sci Eng C. 2015;48:593-601.
24. Patel EK, Oswal RJ. Nanosponge preparation by emulsion solvent diffusion. J Drug Deliv Ther. 2012;2(4):134-140.
25. Shende P, Trotta F. Melt preparation technique for nanosponges. AAPS PharmSciTech. 2013;14(2):651-658.

26. Rao MRP, Bajaj AN. Microwave-assisted synthesis of polymeric nanosponges. Int J Pharm Investig. 2018;8(2):87-94.
27. Tannous M, Caldera F, Trotta F. Green synthesis approaches for cyclodextrin nanosponges. Molecules. 2021;26(4):1103.
28. Kaur G, Singh SK, Sharma V. Characterization techniques for nanosponge-based drug delivery systems. J Drug Deliv Sci Technol. 2020;57:101759.
29. Danaei M, Dehghankhold M, Ataei S, Hasanzadeh Davarani F, Javanmard R, Dokhani A, et al. Impact of particle size and polydispersity index on nanoparticle systems. Pharmaceutics. 2018;10(2):57.
30. Honary S, Zahir F. Effect of zeta potential on nanoparticle stability. Trop J Pharm Res. 2013;12(2):255-264.
31. Bhattacharjee S. DLS and zeta potential—what they are and what they are not? J Control Release. 2016;235:337-351.
32. Coates J. Interpretation of infrared spectra: a practical approach. In: Encyclopedia of Analytical Chemistry. Chichester: John Wiley & Sons; 2006. p. 10815-10837.
33. Giron D. Applications of thermal analysis and calorimetry in pharmaceutical development. Drug Dev Ind Pharm. 2002;28(3):315-331.
34. Byrn SR, Pfeiffer RR, Stowell JG. Solid-State Chemistry of Drugs. 2nd ed. West Lafayette: SSCI Inc.; 1999.
35. Bolmal UB, Manvi FV, Kothiyal P. Entrapment efficiency studies of nanosponge systems. Int J Pharm Sci Rev Res. 2013;20(1):90-94.
36. Costa P, Sousa Lobo JM. Modeling and comparison of dissolution profiles. Eur J Pharm Sci. 2001;13(2):123-133.
37. Mhlanga N, Ray SS. Nanosponge-based drug delivery systems: recent developments. Int J Biol Macromol. 2022;198:1-15.
38. Osman MA, Al-Harthi MA. Drug encapsulation mechanisms in nanoporous carriers. Drug Dev Ind Pharm. 2020;46(4):529-542.
39. Siepmann J, Peppas NA. Modeling of drug release from delivery systems. Adv Drug Deliv Rev. 2011;63(3):163-174.
40. Dash S, Murthy PN, Nath L, Chowdhury P. Kinetic modeling of drug release from controlled systems. Acta Pol Pharm. 2010;67(3):217-223.
41. Karimi M, Ghasemi A, Zangabad PS, Rahighi R, Basri SMM, Mirshekari H, et al. Smart micro/nanoparticles in stimulus-responsive drug delivery. Chem Soc Rev. 2016;45(5):1457-1501.
42. Langer R. Drug delivery and targeting. Nature. 1998;392(Suppl):5-10.
43. Kapoor B, Kaur R, Sharma N, Kaur G. Recent advances in nanosponge-based drug delivery systems. J Drug Deliv Sci Technol. 2022;69:103145.
44. Zhang Y, Chan HF, Leong KW. Advanced materials and stimuli-responsive drug delivery systems. Adv Drug Deliv Rev. 2013;65(1):104-120.
45. Bae YH, Park K. Targeted drug delivery to tumors: myths and reality. J Control Release. 2011;153(3):198-205.
46. Wang Y, Sun S, Zhang Z, Shi D. Nanomaterials for cancer precision medicine. Adv Mater. 2018;30(17):1705660.
47. Danhier F. To exploit the tumor microenvironment: biodegradable nanoparticles. J Control Release. 2016;244:108-121.
48. Riley RS, June CH, Langer R, Mitchell MJ. Delivery technologies for cancer immunotherapy. Nat Rev Drug Discov. 2019;18(3):175-196.
49. Wilhelm S, Tavares AJ, Dai Q, Ohta S, Audet J, Dvorak HF, et al. Analysis of nanoparticle delivery to tumors. Nat Rev Mater. 2016;1(5):16014.
50. Krishnamoorthy K, Rajappan M. Applications of nanosponges in pharmaceutical drug delivery. Asian J Pharm. 2021;15(2):135-146.
51. Loftsson T, Brewster ME. Pharmaceutical applications of cyclodextrins: improving drug solubility and bioavailability. J Pharm Sci. 2010;99(6):2373-2387.
52. Sharma R, Roderick B, Pathak K. Evaluation of nanosponge carriers for topical drug delivery. Drug Dev Ind Pharm. 2011;37(10):1237-1244.
53. Gaudana R, Ananthula HK, Parenky A, Mitra AK. Ocular drug delivery challenges and opportunities. AAPS J. 2010;12(3):348-360.
54. Patton JS, Byron PR. Inhaling medicines: delivering drugs to the body through the lungs. Nat Rev Drug Discov. 2007;6(1):67-74.
55. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as emerging

platforms for cancer therapy. Nat Nanotechnol. 2007;2(12):751-760.
56. Mura S, Couvreur P. Nanotheranostics for personalized medicine. Adv Drug Deliv Rev. 2012;64(13):1394-1416.
57. Singh R, Sharma P, Gupta A. Therapeutic applications of nanosponge-based drug delivery systems. Drug Dev Ind Pharm. 2022;48(8):1123-1136.
58. Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: progress, challenges and opportunities. Nat Rev Cancer. 2017;17(1):20-37.
59. Conde J, Oliva N, Artzi N. Implantable hydrogel embedded cancer nanosponges for therapy. Nat Mater. 2016;15(3):353-363.
60. Ventola CL. The antibiotic resistance crisis: causes and threats. P T. 2015;40(4):277-283.
61. Ricci EJ, Lunardi LO, Nanclares DMA, Marchetti JM. Sustained release systems for anti-inflammatory drugs. Drug Dev Ind Pharm. 2005;31(8):799-804.
62. Saraiva C, Praça C, Ferreira R, Santos T, Ferreira L, Bernardino L. Nanoparticle-mediated brain drug delivery. J Control Release. 2016;235:34-47.
63. Trotta F, Caldera F, Cavalli R. Cyclodextrin-based nanosponges: advantages and pharmaceutical applications. Curr Pharm Des. 2019;25(9):1021-1033.
64. Lammers T, Kiessling F, Hennink WE, Storm G. Drug targeting to tumors: principles, pitfalls and opportunities. J Control Release. 2012;161(2):175-187.
65. Caldera F, Trotta F, Cavalli R. Emerging trends in cyclodextrin-based nanosponge technology for pharmaceutical applications. Pharmaceutics. 2021;13(7):1012.
66. Qiu Y, Park K. Environment-sensitive hydrogels for drug delivery. Adv Drug Deliv Rev. 2012;64:49-60.
67. Ashley EA. Towards precision medicine. Nat Rev Genet. 2016;17(9):507-522.
68. Bertrand N, Wu J, Xu X, Kamaly N, Farokhzad OC. Cancer nanotechnology: the impact of passive and active targeting. Adv Drug Deliv Rev. 2014;66:2-25.
69. Wang H, Li J, Chen Y, Wei Y. Non-viral gene delivery systems for therapeutic applications. J Control Release. 2020;325:83-95.
70. Leader B, Baca QJ, Golan DE. Protein therapeutics: a summary and pharmacological classification. Nat Rev Drug Discov. 2008;7(1):21-39.
71. Kelkar SS, Reineke TM. Theranostics: combining imaging and therapy. Bioconjug Chem. 2011;22(10):1879-1903.
72. Paul D, Sanap G, Shenoy S, Kalyane D, Kalia K, Tekade RK. Artificial intelligence in drug discovery and development. Drug Discov Today. 2021;26(1):80-93.
73. Anastas PT, Eghbali N. Green chemistry principles and practice. Chem Soc Rev. 2010;39(1):301-312.
74. Ventola CL. The nanomedicine revolution: challenges and opportunities. P T. 2017;42(12):742-755.

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