Transforming therapeutics through biomaterials: A comprehensive insight into biomaterials' role in effective drug delivery and healthcare advancement

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ABSTRACT

Biomaterials are engineered substances designed to interact with biological systems for therapeutic or diagnostic purposes. Their inherent properties—including biocompatibility, biodegradability, and structural versatility—have driven major advancements in drug delivery technologies. The global biomaterials market size was estimated at USD 178.0 billion in 2023 and is projected to grow at a compound annual growth rate of 15.6% from 2024 to 2030. The growing incidence of musculoskeletal and chronic skeletal disorders is expected to drive demand for biomaterial-based implants, thereby contributing to market expansion. This review critically examines biomaterials, focusing on their classification into biobased, biodegradable, and biocompatible categories and analyzes their physicochemical properties and functional benefits. It highlights their applications in oncology, cardiovascular therapy, neurodegenerative diseases, and vaccination. Key challenges—including immunogenicity, cytotoxicity, and manufacturing complexities—are discussed, emphasizing the need for rigorous evaluation and adaptive regulatory frameworks. The review also explores recent advances in smart biomaterials for precision drug delivery, underscoring their potential to revolutionize personalized medicine through targeted, efficient, and patient-specific therapies.

Keywords:
Biomaterials; Drug delivery; Therapeutics; Healthcare; Applications; Artificial intelligence

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1. Introduction

Advancing efficient drug delivery systems (DDSs) is critical for improving patient outcomes across a wide range of medical conditions.[1,2] Patient recovery is influenced by the quality of healthcare, individual characteristics, and access to medical resources.[3,4] In developed regions, access to advanced medical care enhances outcomes, whereas patients in resource-limited settings often experience poorer prognoses due to infrastructural and therapeutic limitations. Preventive medicine—including screenings, vaccinations, and lifestyle interventions—plays a pivotal role in reducing disease burden and improving patient well-being.[5]

The evolution of medical technology is increasingly driven by innovative materials, alongside advances in electronics, software, and robotics.[6] These materials—engineered through interdisciplinary approaches involving materials science, nanotechnology, and biotechnology—have transformed diagnostics, implantable devices, regenerative medicine, and DDSs.[7,8] Polymers, in particular, have become indispensable, providing biocompatible and bioresorbable structures for medical devices, tissue engineering scaffolds, and controlled drug delivery platforms.[9-11]

Biobased and biodegradable polymers offer versatile engineering properties, enabling controlled degradation rates, tunable mechanical characteristics, and surface features compatible with biological tissues. Innovations in polymer science have contributed to the development of

bioresorbable stents, transforming cardiology by reducing long-term complications and eliminating the need for secondary interventions.[12] Controlled degradation is particularly crucial for temporary implants such as stents and scaffolds, aligning material breakdown with tissue healing and minimizing risks associated with permanent implants, including chronic inflammation and the need for surgical removal. Materials such as polylactic acid (PLA) and polyglycolic acid (PGA) degrade into non-toxic byproducts, in contrast to permanent metallic implants that can persist and cause complications.[13,14]

Nanomaterials—with unique properties at the nanoscale size—have further revolutionized medical technology. Their applications span targeted drug delivery, advanced imaging, and diagnostic platforms.[15,16] Quantum dots, with tunable fluorescence, enable precise imaging crucial for cancer diagnosis and monitoring, while carbon nanotubes and graphene-based materials offer lightweight, conductive solutions for neural interfaces and prosthetics.[17] Biological materials, including biomimetic polymers, enhance biocompatibility by mimicking natural tissue structures. Advances in tissue engineering and bioactive coatings on implants promote improved tissue integration and reduced rejection rates, supporting the broader goal of enhancing clinical outcomes.[18]

Metamaterial-based lenses and cloaking devices show promising potential to improve diagnostic imaging by providing superior resolution and sensitivity, thereby contributing significantly to early disease detection and personalized therapeutic planning.[19,20] Beyond imaging, innovative materials underpin the development of smart medical devices. Shape memory alloys facilitate the design of self-expanding stents capable of remote activation and controlled deployment, thereby reducing surgical invasiveness and improving patient outcomes.[19,21] Similarly, conductive polymers and flexible electronic substrates are critical for wearable biosensors and electronic skin technologies, facilitating continuous, real-time health monitoring and advancing the paradigm of proactive, personalized medicine. The development of bioactive glasses and glass-ceramics has expanded opportunities in drug delivery. These materials exhibit exceptional biocompatibility, bioactivity, and tunable degradation rates, allowing for the incorporation and controlled release of therapeutic agents. Their porous structures enhance drug-loading capacity and promote localized, sustained drug delivery, thereby improving therapeutic efficacy while simultaneously supporting tissue regeneration.[22-24]

This review highlights the pivotal role of biomaterials in advancing DDSs to optimize patient outcomes across diverse medical conditions. This study adopts a multidisciplinary perspective, integrating advances in materials science, nanotechnology, and biotechnology. Reference selection was guided by relevance and scientific credibility, covering biomaterials, polymers, nanomaterials, biomimetic polymers, metal–organic frameworks (MOFs), and the application of artificial intelligence (AI) and machine learning (ML) in drug delivery. Applications discussed include drug delivery, medical imaging, and regenerative medicine. Recent advances and landmark innovations are highlighted, ensuring a comprehensive and up-to-date analysis of the evolving landscape of medical technology driven by innovative materials.

2. Biomaterials in drug delivery and human applications

Biomaterials, engineered to interface with biological systems, have become essential components of DDSs and broader biomedical applications. Their ability to precisely control drug-release kinetics enhances bioavailability and enables targeted drug delivery to specific tissues or cells. By minimizing adverse effects and maximizing therapeutic efficacy, biomaterials have transformed healthcare practices and extended their influence across diverse scientific and technological fields.[4] The biomaterials market was valued at USD 123.8 billion in 2023 and is expected to grow at a compound annual growth rate of 12.6% from 2024 to 2032. Key drivers of this growth include rising demand for innovative biomaterials, an aging global population, increasing prevalence of chronic diseases such as cardiovascular and orthopedic conditions, and the expanding use of biomaterials in esthetic and cosmetic procedures.[25]

The biomaterials market has been experiencing rapid growth, driven by a growing range of applications across healthcare sectors, including orthopedics, cardiovascular care, dental treatments, and tissue engineering. Leading companies in the biomaterials industry include BASF SE, Covestro AG, Evonik Industries AG, Medtronic plc, Stryker Corporation, Corbion N.V., Zimmer Biomet Holdings, Inc., Royal DSM, Invibio Ltd., and Carpenter Technology Corporation.[25]

These companies are focusing on innovation, strategic partnerships, and global expansion to capture larger market shares. Furthermore, rising investments in regenerative medicine, along with ongoing technological advancements in biomaterial science, continue to fuel competitive activity and support the market's growth. The details on biomaterials types are presented in **Figure 1** and their applications are shown in **Figure 2**—organized by key regions and countries, including North America (United States and Canada), Europe (e.g., Germany, United Kingdom, France, Spain, and Italy), Asia Pacific (e.g., Japan, China, India, and Australia), Latin America (e.g., Brazil and Mexico), and the Middle East and Africa (e.g., South Africa and Saudi Arabia).[25]

In drug delivery, biomaterials enable the controlled, sustained release of therapeutic agents, thereby enhancing treatment effectiveness and improving patient compliance. Their specificity further supports targeted therapies, reducing systemic side effects.[26,27] Beyond drug delivery, biomaterials serve as key components in medical devices such as artificial

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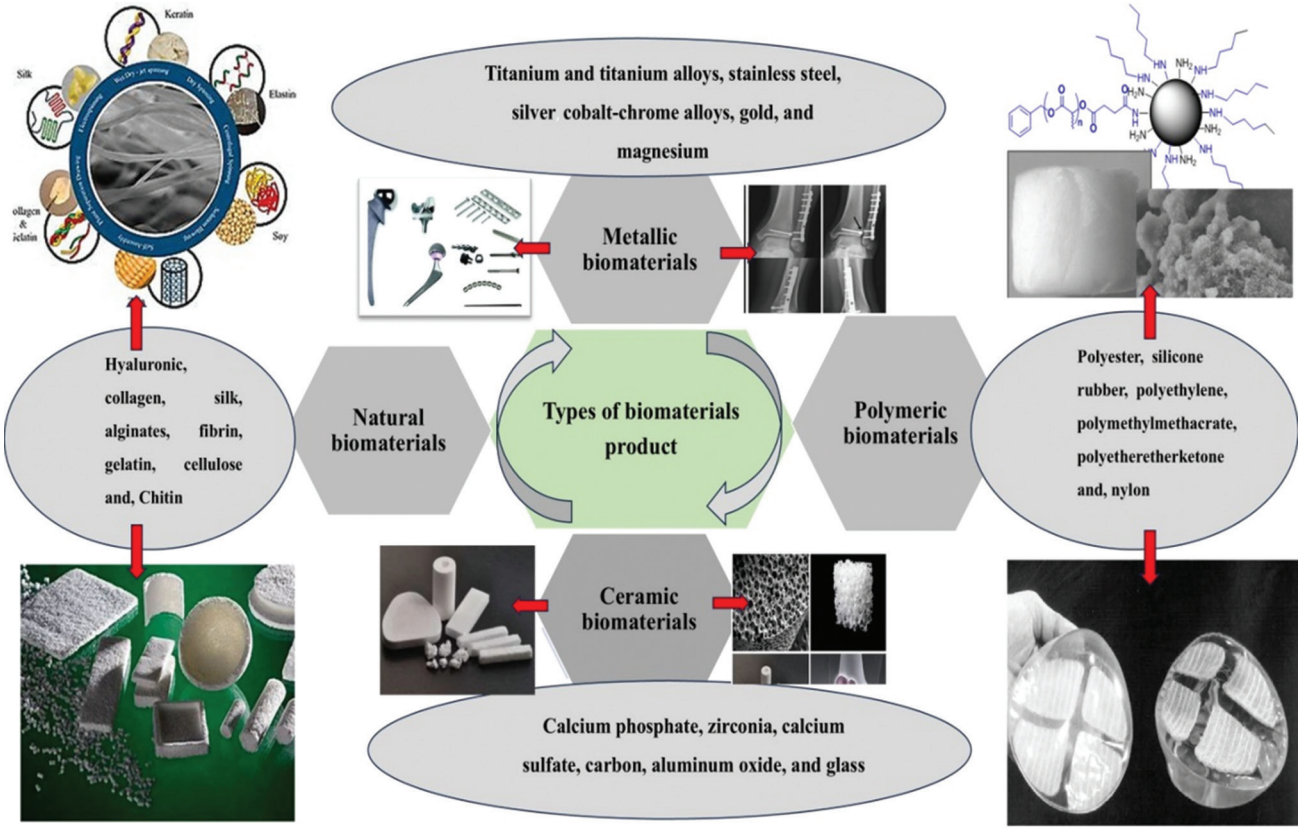

Figure 1. Types of biomaterial products. Figure created by the authors.

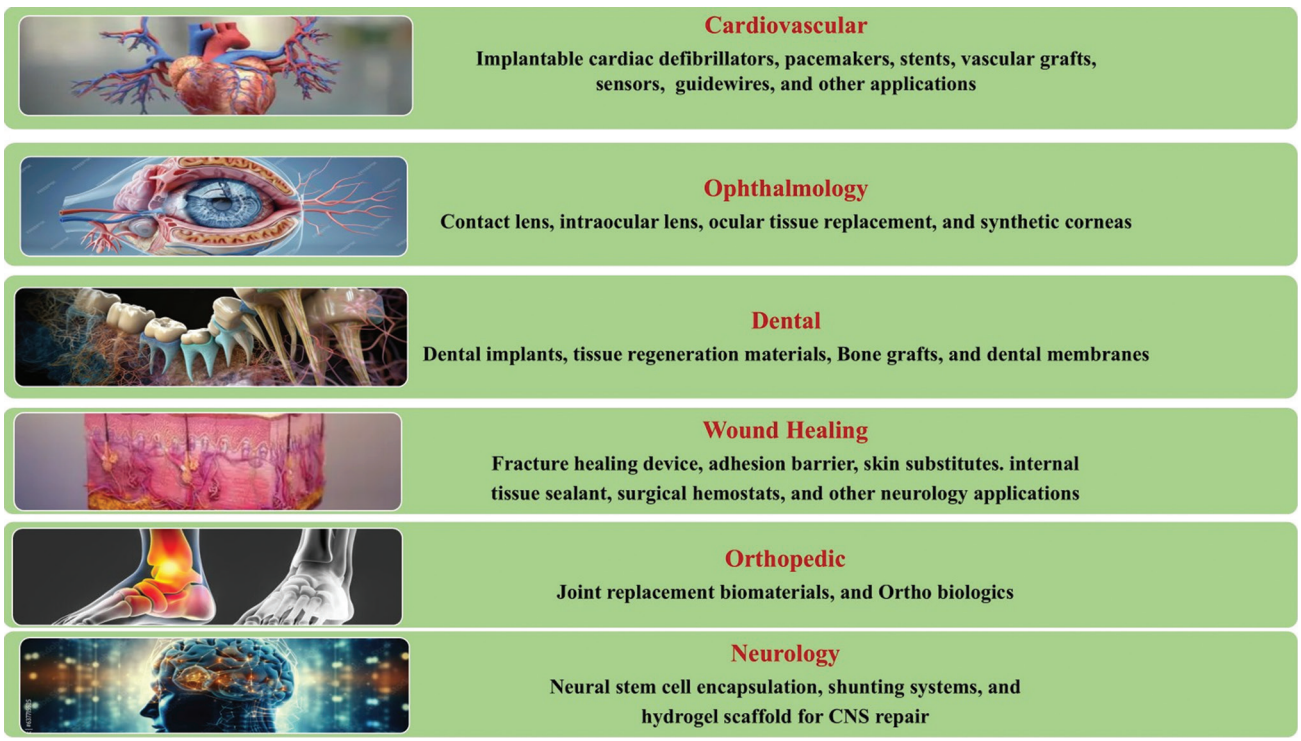

Figure 2. Applications of biomaterial products. Figure created by the authors.
Abbreviation: CNS: Central nervous system.

joints, dental implants, and tissue engineering scaffolds, promoting integration with host tissues and enhancing device longevity.[28]

The design of biomaterials for therapeutic use requires careful consideration of key parameters—including nanoparticle and microparticle size to optimize bioavailability and release profiles;

high surface area to enhance drug loading; biocompatibility and biodegradability to prevent immune responses and enable safe degradation; and mechanical, thermal, and sterilization properties appropriate for clinical application. Efficient drug loading, controlled release mechanisms, and compliance with regulatory standards are also critical to the success of biomaterials in advancing modern medicine.[26,28]

Beyond drug delivery, biomaterials have significantly advanced regenerative medicine. Scaffold materials with engineered microarchitectures guide tissue regeneration and offer promising avenues for developing functional tissues and organs. Hydrogels, in particular, support stem cell proliferation and differentiation, presenting new therapeutic opportunities for spinal cord injuries and degenerative diseases.[29] The versatility of biomaterials continues to drive innovation across healthcare, biotechnology, and nanotechnology.

A major application of biomaterials lies in the development of advanced DDSs. Engineered to encapsulate and release therapeutic agents in a controlled and targeted manner, these systems offer critical advantages, such as enhanced drug efficacy, reduced systemic toxicity, and prolonged therapeutic action—benefits that are particularly valuable for managing chronic conditions.[30] Biodegradable polymeric nanoparticles can be loaded with pharmaceutical compounds and administered to achieve sustained release at the site of action.[31] Commonly used biomaterials for drug delivery include polymers, lipids, and other biocompatible matrices designed to optimize drug loading, protect active agents, and regulate release kinetics.[32] A summary of widely used biomaterials in DDSs is provided in **Table 1**. A comparative table evaluating biocompatibility, drug-loading efficiency, targeting specificity, stability, and clinical development status across various DDSs would provide readers with deeper insights.

Tissue engineering utilizes biomaterials to develop functional tissues for regenerative medicine and transplantation. Researchers design scaffolds using biocompatible materials such as hydrogels, ceramics, and polymers to support cell attachment, proliferation, and differentiation. These scaffolds act as structural frameworks, ultimately facilitating the regeneration of functional tissues and organs, including bone, cartilage, and skin.[90] A list of commonly used biomaterials in tissue engineering and their applications is presented in **Table 1**. The choice of biomaterial depends on the specific tissue being engineered, the desired mechanical and biological properties, and the intended clinical application. Tissue engineering is a rapidly advancing field, with ongoing research focused on novel biomaterials and technologies aimed at enhancing tissue regeneration and transplantation outcomes.[91]

Biomaterials also play a pivotal role in the development of diagnostic tools, particularly by enhancing the sensitivity and specificity of detection methods. Nanoparticles, often coated with specific biomolecules, offer powerful capabilities for early disease detection. For instance, magnetic nanoparticles functionalized with antibodies can selectively bind to cancer cells, enabling magnetic separation and subsequent identification. This approach significantly improves diagnostic precision and enables early disease detection, which is crucial for effective treatment.[92-94] **Table 1** summarizes commonly used biomaterials in the fabrication of diagnostic tools, demonstrating their diverse applications in medical diagnostics.

In medical imaging, particularly in techniques such as magnetic resonance imaging (MRI), contrast agents are employed to enhance the visibility of specific tissues or structures. These agents possess magnetic properties and are introduced into the body to enhance tissue contrast, resulting in clearer and more accurate imaging outcomes.

In addition, biomaterials play a crucial role in regenerative medicine, particularly in stem cell therapy, where scaffolds and matrices guide stem cells to differentiate into specific cell types.[95,96] These strategies hold significant promise for treating conditions such as spinal cord injuries, neurodegenerative diseases, and cardiac damage. **Table 1** lists commonly used biomaterials in regenerative medicine, highlighting their applications, properties, and advantages.

Innovative biomaterials are increasingly used to develop three-dimensional (3D) cell cultures—known as organoids or spheroids—that more accurately replicate the *in vivo* environment than traditional two-dimensional (2D) cultures.[97] This advancement improves the reliability of drug screening and testing. **Table 1** lists biomaterials commonly utilized in drug screening and research, highlighting their applications and advantages. These biomaterials support more effective experimentation, facilitate drug development, and deepen understanding of disease mechanisms. In addition, biomaterials are used as contrast agents in imaging techniques such as MRI and ultrasound, enhancing tissue visibility for disease diagnosis and monitoring. **Table 1** lists common biomaterials used in bioimaging, along with their applications and advantages. These biomaterials contribute to improved bioimaging, enabling precise visualization and deeper insight into biological processes and pathological conditions.[98]

Biomaterials also play a vital role in vaccine development, particularly in messenger RNA (mRNA)-based vaccines such as those developed for COVID-19.[99] Lipid nanoparticles serve as key carriers for fragile mRNA molecules, protecting them and promoting efficient delivery into cells to trigger an immune response. **Table 1** lists biomaterials commonly used in vaccine development. These biomaterials significantly advance vaccine development, supporting the prevention of a wide range of infectious diseases.

3. Synthetic, biobased, and biodegradable biomaterials

Biodegradable polymers derived from renewable resources have gained prominence due to their environmental advantages. For example, polybutylene succinate (PBS) is a polymer synthesized from succinic acid and 1,4-butanediol, both of which can be sourced from crops such as corn. PBS is widely used in agricultural films and packaging due to its biodegradability.[101,102] PGA is another biodegradable, biobased polymer primarily used in the medical field for absorbable sutures and tissue scaffolds. Similarly, poly(3-hydroxybutyrate-co-3-hydroxyvalerate), a microbial copolymer that degrades

Table 1. Commonly used biomaterials in drug delivery systems

Biomaterial	Biocompatibility and drug-loading capacity	Targeting specificity and stability	Commercial status	Description	Applications	References
Liposomes	High biodegradability. Moderate to high drug-loading capacity.	Combines passive and active targeting specificity through ligand conjugation. Moderate intrinsic stability (enhanced through PEGylation).	Approximately 14 Śliposomal products (e.g., Doxil®, AmBisome®) are FDA- or EMA-approved.	Spherical lipid vesicles encapsulating hydrophobic or hydrophilic drugs.	Targeted drug delivery; gene therapy.	33
Chitosan	High biodegradability and low toxicity. Cationic mucoadhesive properties. High drug-loading capacity with the ability to encapsulate both hydrophilic and hydrophobic drugs.	Combines passive mucoadhesion with active targeting through ligands (e.g., folate-engineered NPs). Moderate, formulation-dependent stability.	Used in approved wound dressings and hemostatic agents; multiple chitosan-based NP systems in preclinical or early clinical trials (e.g., insulin, anticancer).	Biopolymer derived from chitin; forms hydrogels.	Oral drug delivery, wound dressings.	34
HA	Biodegradable and non-immunogenic. Highly biocompatible *in vivo* and suitable for ocular, dermal, and injectable applications. Supports versatile drug loading across hydrogels, nanogels, microspheres, nanoparticles, liposomes, and microneedles.	Binds CD44 and RHAMM receptors commonly overexpressed in tumors and inflamed tissues; enables receptor-mediated uptake and passive EPR/tissue accumulation; baseline HA degrades through hyaluronidase; stability improved through crosslinking (e.g., carbodiimides, BDDE).	Approved in dermal fillers (13+FDA products), viscosupplements, and ocular lubricants.	Natural ECM component.	Ophthalmology, joint injections, skin treatments.	35
PEG	Highly biocompatible, water-soluble, and chemically inert. Widely used in pharmaceutical formulations with minimal toxicity. PEGylation improves the solubility and stability of hydrophobic drugs and therapeutic proteins.	PEGylation prolongs circulation time through a "stealth" effect, enabling passive EPR/tissue accumulation; improves *in vivo* stability by shielding drugs from enzymatic degradation and clearance.	Numerous FDA-approved PEGylated drugs and proteins (e.g., pegfilgrastim, Adagen), as well as PEG-based hydrogels (e.g., OncoGel, Mebiol Gel), are in clinical trials.	Synthetic polymer enhancing drug solubility.	Used in NPs, drug conjugates.	36
Dendrimers	Generation- and surface-dependent; lower generation PAMAM (G5 and below) exhibit low toxicity, while cationic surfaces may induce hemolysis, which can be mitigated through PEGylation or acetylation. High drug-loading capacity through internal cavities and branching architecture.	Offers both passive targeting through size/EPR effect and active targeting through surface ligands (e.g., folate, HA, antibodies, PEG coatings); structurally stable with tunable cargo release through pH- or redox-sensitive linkers; surface modifications improve circulation and reduce leakage.	Mostly in preclinical studies; one dendrimer–docetaxel (DEP®) in Phase I trials; no approved dendrimer-based drug delivery systems yet.	Highly branched synthetic macromolecules	Targeted drug delivery, gene therapy	37
Polymeric micelles	Generally well-tolerated—PEG-based block copolymers (e.g., PEG-PLA, PEG-PCL) are	Passive targeting through the EPR effect; active targeting achievable with surface ligands or pH/redox-responsive	Several formulations are in clinical use or trials: Genexol-PM (approved in Asia);	Self-assembling nanostructures formed from amphiphilic block polymers.	Solubilization and delivery of hydrophobic drugs.	38

(Cont'd...)

Table 1. *(Continued)*

Biomaterial	Biocompatibility and drug-loading capacity	Targeting specificity and stability	Commercial status	Description	Applications	References
	commonly used, offering minimal toxicity and high drug-loading capacity for hydrophobic drugs. Loading efficiency is further enhanced through core modification.	triggers. Stability can be compromised upon dilution below the CMC; improved by core crosslinking or increased hydrophobicity.	NK-105, NC-6004, and NC-6300 are in Phase II–III clinical trials.			
Commonly used in tissue engineering						
Collagen	Highly biocompatible and biodegradable. A major ECM protein that supports cell adhesion, migration, and proliferation. Commonly used in the form of microspheres, nanoparticles, hydrogels, and scaffolds.	Passive targeting by mimicking tumor ECM; active targeting through collagen-binding ligands. Naturally degradable by collagenases; structural stability prolonged through crosslinking (e.g., EDC/NHS, AuNPs, aromatic agents), enabling sustained release.	Widely used in medical scaffolds and wound dressings; numerous preclinical drug-loaded systems developed (e.g., microspheres, hydrogels).	Major structural protein of the ECM.	Skin, bone, cartilage, nerve, and dental tissue engineering.	39
HA	Highly biocompatible and non-toxic. A natural component of the ECM. Non-immunogenic and FDA-approved for various biomedical applications.	High targeting specificity; forms hydrogels, micelles, nanogels, and conjugates. Strong active targeting through CD44, RHAMM, and LYVE-1 receptors, which are overexpressed in tumors, inflamed, and lymphatic tissues.	Approved in dermal fillers (e.g., Juvederm®, Restylane®), ocular drops, and joint lubricants; HA-based nanocarriers for cancer and arthritis are in clinical trials.	Natural connective tissue components.	Ophthalmology, osteoarthritis, and wound healing.	40
Decellularized ECM	Highly biocompatible. Facilitates removal of cellular components and minimizes immunogenicity while preserving native ECM proteins and GAGs. Supports host cell adhesion and regeneration. Highly versatile; can encapsulate bioactive molecules through hydrogels, absorption, or affinity binding.	Mimics native tissue to guide regeneration; 3D matrix provides localization cues and can be modified for active targeting. Mechanical properties are tissue-dependent and require crosslinking (e.g., UV, dehydrothermal) for improved durability.	Several products (e.g., AlloDerm®, Oasis®) are FDA-approved for regenerative use; drug-loaded dECM systems are preclinical with promising results in cartilage, trachea, and vascular tissues.	Acellular matrix retaining ECM structure.	Regeneration of heart, liver, kidney, and other tissues.	41
Silk	High biocompatibility. FDA-approved, non-toxic, and low immunogenicity after sericin removal. High drug-loading capacity. Encapsulates small molecules, proteins, and nucleic acids through adsorption, encapsulation, and conjugation.	Tunable surface for tissuespecific targeting; mild processing preserves bioactivity. βsheet structure enables controlled degradation; hydrogels and microspheres support sustained release (days to weeks).	NPs are in preclinical to early clinical stages. Widely used in sutures and scaffolds.	Natural fibrous protein.	Nerve regeneration, skin, and bone tissue engineering.	42

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Table 1. *(Continued)*

Biomaterial	Biocompatibility and drug-loading capacity	Targeting specificity and stability	Commercial status	Description	Applications	References
Alginate	Highly biocompatible and naturally derived; nontoxic and listed as FDA GRAS. Safely used in oral, ocular, topical, and wound applications. Offers good drug-loading capacity for both hydrophilic and hydrophobic drugs. Can form micro- or nanoparticles, hydrogels, capsules through ionic gelation, spray-drying, or emulsion techniques.	Passive mucoadhesion and EPR-based targeting effect; colon or tumor-specific delivery; ligand-conjugated composites (e.g., alginate–chitosan) enhance uptake. Gel stability tunable by Ca^{2+} crosslinking; degradable under physiological conditions; often combined with polymers or composites for enhanced mechanical strength.	Common in wound care (e.g., calcium alginate pads); drug-loaded alginate systems are in preclinical/early clinical stages.	Seaweed-derived hydrogel-forming polymers.	Drug encapsulation and 3D bioprinting.	43
PCL	Highly biocompatible, non-toxic, FDA-approved, and ISO-compliant. Demonstrated *in vivo* safety for long-term implants and drug delivery systems. Exhibits high drug-loading capacity and supports both hydrophilic and hydrophobic drugs.	Supports passive targeting through EPR; surface-modifiable. Semi-crystalline polymer with slow hydrolytic degradation (months to years).	FDA-approved in sutures (Monocryl™), contraceptive implants (Capronor™), and dermal fillers; drug-loaded PCL systems are in clinical/preclinical stages.	Biodegradable synthetic polymer.	Bone and cartilage tissue engineering.	44
Bioceramics (e.g., HAp, TCP)	Highly biocompatible and chemically similar to bone mineral. Osteoconductive, non-toxic, and bioresorbable, eliciting minimal immune response. Exhibits good to moderate versatility; HAp/TCP scaffolds, nanoparticles, and coatings can incorporate small-molecule drugs, antibiotics, proteins, and growth factors.	Local delivery through scaffold placement; surface tuning (e.g., carboxylic acids) enables controlled release. Offers high mechanical strength; degradation is tunable through porosity and composition.	Used in bone fillers, cements, and implants (e.g., porous TCP scaffolds); drug-loaded systems are mostly in the preclinical stage.	Ceramic materials are similar to bone mineral.	Bone and dental tissue engineering.	45
Commonly used in implantable devices						
Stainless steel	Good biocompatibility in bulk form; widely used in surgical implants. Surface modifications (e.g., passivation, coatings) enhance corrosion resistance and minimize cell irritation. High drug-loading capacity can be achieved through surface coatings	Primarily used for local delivery at implant sites (e.g., orthopedic, stents). Surface nanotexturing enhances cellular uptake and biomacromolecule delivery. Offers excellent mechanical strength; corrosion resistance is enhanced through chromium passivation, molybdenum addition, and surface treatments.	Widely used in orthopedic, dental, and cardiovascular implants. Drug-eluting stents using stainless steel combined with polymer are clinically approved.	Durable, corrosion-resistant steel alloy.	Stents, orthopedic implants.	46

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Table 1. *(Continued)*

Biomaterial	Biocompatibility and drug-loading capacity	Targeting specificity and stability	Commercial status	Description	Applications	References
	(e.g., dexamethasone CMC layers, chitosan–diclofenac multilayers, antibiotic-loaded bioactive glass/chitosan composites), enabling sustained local drug delivery.					
PMMA	High biocompatibility; widely used in bone cement, dental implants, and IOLs; non-toxic, non-immunogenic, yet non-biodegradable. Moderate drug-loading capacity; suitable for local delivery (e.g., antibiotics in bone cement).	Enables site-specific passive delivery (e.g., bone or joint infections). Mechanically strong and chemically stable, with a biphasic release profile (initial burst followed by sustained release).	Clinically used in orthopedic, dental, and ocular applications. Gentamicin-loaded PMMA bone cement is FDA-approved.	Biocompatible thermoplastic polymer.	Bone cement for joint replacements.	47
PEEK	Highly biocompatible and FDA-approved since the late 1990s. Chemically stable, wear-resistant, and possessing an elastic modulus similar to bone. Naturally bio-inert and typically requires surface modification. High drug-loading capacity can be achieved through surface coatings (e.g., porous PEEK with chitosan for pH-triggered doxorubicin release, gentamicin–chitosan systems, MOF–dexamethasone composites).	Used mainly for localized delivery at implant sites. Coatings and surface texturing support drug-loading, bone cell uptake, antibacterial activity, and angiogenesis. Extremely stable mechanically and chemically; highly resistant to wear and degradation.	FDA-cleared for spinal cages and dental or craniofacial implants. Drug-loaded or coated PEEK is in advanced preclinical and early clinical stages.	Biocompatible thermoplastic polymer.	Spinal implants, dental devices.	48
ZrO_2	Highly biocompatible, bioinert, and noncytotoxic to osteoblasts and fibroblasts. Forms a stable fibrous layer *in vivo*; yttriastabilized ZrO_2 is commonly used in dental and orthopedic implants. Exhibits high drug-loading capacity; mesoporous or hollow ZrO_2 nanostructures enable the incorporation of antibiotics, anticancer, antiinflammatory, and osteogenic agents.	Ideal for localized delivery. Surface nanotubes and coatings (e.g., PDA, RGD peptides) enhance drug release control and cell targeting. Offers excellent mechanical strength and corrosion resistance; performance is influenced by porosity and monoclinic/tetragonal phase ratio.	Widely used in dental and orthopedic implants. Drug-loaded ZrO_2 (e.g., $hmZrO_2$ nanocapsules) are in active preclinical development.	Bioceramic with excellent mechanical properties.	Dental implants, hip replacements.	49

(Cont'd...)

Table 1. *(Continued)*

Biomaterial	Biocompatibility and drug-loading capacity	Targeting specificity and stability	Commercial status	Description	Applications	References
Hydrogels	Highly biocompatible; soft, hydrated networks that mimic native tissues and induce minimal inflammation. Highly versatile; capable of encapsulating small molecules, proteins, genes, and cells.	Enable passive (depot-based) and active (stimuli-responsive) drug delivery triggered by pH, temperature, glucose, ultrasound, enzymes, or light. Stability is tunable through crosslink density and chemistry, affecting mechanical strength and degradation behavior.	Clinically used in contact lenses, wound dressings, and injectable depots; multiple smart hydrogel systems are in clinical trials and moving toward clinical translation.	Water-absorbent materials with tunable properties.	Drug delivery, tissue scaffolds.	50
Ta	Highly biocompatible, bioinert, noncytotoxic, and strongly osteoconductive. Exhibits high drug-loading capacity; porous 3D Ta scaffolds effectively deliver antibiotics (e.g., gentamicin) and anticancer drugs (e.g., doxorubicin, adriamycin).	Enables localized delivery at implant surfaces. Ta coatings on titanium nanotubes enable sustained antibiotic release. Exhibits excellent corrosion resistance and mechanical strength; performance is influenced by pore structure and phase composition (tetragonal/monoclinic).	Clinically used in orthopedic and dental implants (porous Ta scaffolds).	Biocompatible metal with high corrosion resistance.	Orthopedic implants, bone screws.	51
Used for diagnostic tools						
Polydimethylsiloxane	Highly biocompatible, bioinert, non-toxic; demonstrates excellent compatibility with tissues and blood. Resistant to biodegradation and oxidation. Offers high drug-loading capacity through surface coatings or integration into composite materials. Commonly used in controlled-release tablets (e.g., hydrochlorothiazide, acetaminophen).	Ideal for localized delivery through implant coatings. Adjustable porosity and channeling agents (e.g., PVP, PEG) enable controlled release. Stable elastomeric matrix offers excellent mechanical and chemical resilience, preserving release kinetics.	Proven in commercial implants (Norplant®, Compudose®) for sustained hormone delivery. Studied in thermogels (e.g., DOX) and antibiotic coatings in animal or *in vitro* models.	Microfluidic devices.	Transparency, flexibility, and ease of fabrication.	52
PE	Highly biocompatible; PE (including HDPE and UHMWPE) is chemically inert, non-toxic, and widely used in medical implants such as joint replacements, with minimal immune response. Due to its hydrophobic and non-porous nature, PE has limited drug-loading capacity; however, drug delivery is possible through surface coatings.	Primarily for site-specific delivery as a scaffold or coating on orthopedic implants. Mechanically robust, wear-and corrosion-resistant; excels in long-term load-bearing applications.	UHMWPE has been widely used in hip and knee implants since the 1960s; drug-loaded PE systems are mostly experimental/ preclinical.	Disposable pipettes and tubes.	Low cost, chemical resistance, and ease of molding.	53
PC	Biocompatible and widely used in FDA-cleared medical	Passive targeting through EPR; active targeting possible with	Preclinical stage—promising pharmacokinetics	Microplates and labware.	Clarity, durability, and heat resistance.	54

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Table 1. *(Continued)*

Biomaterial	Biocompatibility and drug-loading capacity	Targeting specificity and stability	Commercial status	Description	Applications	References
	devices; properties can be enhanced through PEGylation. Exhibits high drug-loading capacity; amphiphilic PEG–PC copolymer micelles effectively encapsulate hydrophobic drugs such as podophyllotoxin.	stimuli-responsive ligands. Crosslinked or core-stabilized micelles improved serum stability.	and tumor delivery shown *in vitro* and *in vivo*. No approved drug carriers to date.			
PU	Tunable chemistry allows the development of hemocompatible and biocompatible PUs for use in stents, catheters, foams, and coatings. Offers versatile drug-loading capacity; PU films, nanofibers, micelles, and coatings support the delivery of small-molecule drugs (e.g., gemcitabine, curcumin, doxorubicin, docetaxel).	Primarily localized delivery; pH/redox-responsive nanogels enable release in acidic/oxidative environments. Excellent mechanical strength and durability.	FDA-approved in biomedical devices (e.g., stents, catheters); drug-eluting PU coatings (e.g., DTX-stents) are in advanced preclinical or early clinical phases.	Catheters and tubing	Flexibility, durability, and biocompatibility.	55
AuNPs	Bioinert, non-cytotoxic, and tunable to minimize immune interactions. Toxicity depends on particle size, shape, and surface ligands. Exhibit highly versatile drug-loading capacity; can be functionalized with proteins (e.g., TNF), peptides, siRNA, small molecules, or surface coatings (PEG, zwitterionic ligands).	Passive (through EPR and active through ligands (e.g., antibodies, peptides); photothermal activation allows controlled release through NIR irradiation. Chemically and mechanically stable.	Multiple AuNP systems are in clinical trials.	Biosensors and NPs.	High surface area, conductive properties, and bioconjugation.	56
Hydrogels	Highly biocompatible, soft, and water-rich structures that mimic native tissues with low immunogenicity. Offers high drug-loading capacity; capable of encapsulating small molecules, proteins, DNA, and cells.	Passive (localized depot); tunable for pH, temperature, or enzyme-triggered controlled release. Crosslinking density and polymer type control swelling, degradation, and kinetics.	Approved for wound dressings, contact lenses, and dermal fillers. Smart hydrogels are in clinical trials.	Drug delivery and biosensors.	Water absorption, biocompatibility, and tunable properties.	57
Biodegradable polymers	Highly biocompatible and biodegradable, breaking down into non-toxic byproducts (e.g., lactic acid, glycolic acid). Offers good drug-loading capacity and is suitable for encapsulating both hydrophilic and hydrophobic drugs.	Tunable for local and systemic delivery, pH, temperature, or enzyme responsiveness. Degradation rate controlled through polymer type (e.g., PLGA, PCL, and PLA) and molecular weight.	FDA-approved in drug delivery systems (e.g., PLGA in Lupron Depot®, Gliadel® wafer). Widely used in implants and injectables.	Controlled drug release.	Biocompatibility and controlled degradation.	58

(Cont'd...)

Table 1. *(Continued)*

Biomaterial	Biocompatibility and drug-loading capacity	Targeting specificity and stability	Commercial status	Description	Applications	References
Used in regenerative medicine						
HA	Biocompatible, naturally occurring polysaccharide found in connective tissues; non-immunogenic. Can be chemically modified or formulated as NPs to carry both hydrophilic and hydrophobic drugs.	Targets CD44 receptors overexpressed in tumors and inflamed tissues; enzymatically degraded by hyaluronidase, with stability enhanced through crosslinking.	Approved in eye surgery, dermal fillers, osteoarthritis; drug delivery forms in clinical trials.	Dermal fillers, tissue scaffolds.	High water-binding capacity, lubricating ability, and biocompatibility.	59
Alginate	High biocompatibility. Naturally derived from brown algae; non-toxic and non-immunogenic. High drug-loading capacity; forms hydrogels and microspheres that efficiently encapsulate proteins, cells, and small molecules.	Primarily used for local delivery; can be modified for pH- or enzyme-triggered release. Stability depends on crosslinking type–chemical methods improve resistance in physiological conditions.	Used in wound dressings and cell encapsulation; drug-loaded systems are in preclinical/clinical phases.	Cell encapsulation, tissue engineering.	Gel-forming, biocompatible, and easy to shape.	60
PLGA	FDA- and EMA-approved; degrades into lactic and glycolic acids, metabolized through the Krebs cycle. Offers versatile drug-loading capacity. PLGA efficiently encapsulates small molecules, proteins, genes, and biologics through emulsification, spray-drying, electrospray, and microfluidics.	Surface-modified PLGA NPs (e.g., PEGylation, ligand conjugation), achieve prolonged circulation through EPR-mediated passive targeting and active targeting to specific tissues. Adjustable degradation (weeks to years) based on monomer ratio, molecular weight, and end-capping.	Established in products such as Lupron Depot® and Gliadel®, and in PLGA–PEG–PLGA thermosensitive hydrogels for local cancer treatment.	Drug delivery, scaffolds.	Biodegradable, tunable degradation rates, and biocompatible.	61
Decellularized tissues	High biocompatibility; decellularization significantly reduces immunogenicity while retaining essential ECM components (e.g., collagen, laminin, GAGs). Offers versatile drug-loading strategies; drugs, growth factors, and NPs can be incorporated through hydrogel formation, adsorption, affinity binding, coatings, or conjugation.	Enables localized delivery; tissue-specific microarchitecture enables site-specific release; dECM can be modified with NPs or ligands to enhance targeting. Structural and mechanical properties are tunable; optimized decellularization preserves integrity, while crosslinking enhances mechanical strength and modulates degradation kinetics.	Clinically used as scaffolds (e.g., heart valves, dermal matrices, vascular grafts).	Organ and tissue transplantation.	Retains natural ECM, minimizes immune response.	62
PCL	High biocompatibility; FDA-approved, non-toxic, chemically stable polyester; suitable for long-term implants and scaffolds. Highly versatile; used in NPs, microspheres,	Passive delivery through localized implants (e.g., bone, wound dressings); surface or compositional modifications (e.g., PCL–PEG conjugates, erythrocyte	FDA-approved for sutures, implants, and dermal fillers (e.g., Ellansé®); extensively used in clinical bone regeneration; drug-loaded	Scaffolds, tissue engineering.	Biodegradable, mechanical strength.	63

(Cont'd...)

Table 1. *(Continued)*

Biomaterial	Biocompatibility and drug-loading capacity	Targeting specificity and stability	Commercial status	Description	Applications	References
	electrospun fibers, films, and scaffolds for efficient loading of small molecules, peptides, and growth factors through emulsification, electrospinning, or microfluidics.	membrane coatings) enhance circulation time and targeting specificity. Semi-crystalline with a melting point of approximately 55°C and a glass transition temperature around –60°C.	PCL systems are in advanced preclinical development.			
Fibrin	Highly biocompatible; natural, biodegradable material that supports cell proliferation and promotes wound healing. High versatility; effectively encapsulates small molecules, proteins, and growth factors.	Facilitates localized delivery through direct application to the wound, bone, or injury site. Exhibits moderate stability; degrades over days to weeks, with degradation tunable through crosslinkers or inhibitors.	FDA-approved (e.g., Tisseel); used in hemostasis, tissue repair, and in clinical trials.	Wound healing, tissue engineering.	Natural clotting protein, supports cell migration.	64
Stem cells	Autologous or allogenic stem cells are generally well-tolerated immunologically. Moderate versatility; can be engineered to deliver drugs, genes, or NPs, and naturally secrete therapeutic factors.	High targeting specificity due to intrinsic homing capabilities toward injury, tumor, or inflamed tissues. Viability depends on the cell source, administration route, and host immune response; it requires optimized conditions for therapeutic efficacy.	Many stem cell therapies are in clinical trials and approved for some blood disorders and graft repair.	Regeneration of various tissues.	Pluripotent or multipotent cells for tissue repair.	65
MCF-7 cells	Used *in vitro* for cancer research and drug screening purposes—not as carriers but as target cells to evaluate drug efficacy and cytotoxicity.	Model for hormone-responsive breast cancer; used to assess targeting strategies.	Widely used preclinical model in laboratories, not for clinical use.	Breast cancer research, drug screening.	Representative for breast cancer.	66
A549 cells	A549 is a human lung adenocarcinoma epithelial cell line used in research as an *in vitro* model to assess NP uptake and drug cytotoxicity.	Applicable for passive and active targeting evaluations in lung cancer research (e.g., EGFR, folate targeting). High *in vitro* stability; easy to culture and highly reproducible across studies.	Preclinical use only; widely used for lung cancer drug screening and inhalation toxicity testing.	Lung cancer and respiratory disease studies.	Relevant for lung cancer.	67
Caco-2 cells	Caco-2 is a human colorectal adenocarcinoma cell line utilized *in vitro* studies—primarily to evaluate drug transport across intestinal barriers, rather than for drug delivery.	Model for passive diffusion and transporter-mediated uptake across the intestinal epithelium. High stability; differentiates into enterocyte-like monolayers, making it a robust model for permeability assays.	Preclinical use only; standard model for predicting oral drug absorption and permeability (e.g., BCS).	Drug transport and oral absorption studies.	Representative of the intestinal barrier.	68
Induced pluripotent stem cells	High biocompatibility; derived from a patient's own cells; immunologically compatible and ethically acceptable. Moderate versatility;	Allow site-specific targeting upon differentiation into desired cell types (e.g., neurons, cardiomyocytes). Requires careful control to avoid risks such as	In clinical trials for macular degeneration, Parkinson's, and spinal cord injury. No FDA-approved therapies yet.	Disease modeling and personalized medicine.	Derived from the patient's own cells.	69

(Cont'd...)

Table 1. *(Continued)*

Biomaterial	Biocompatibility and drug-loading capacity	Targeting specificity and stability	Commercial status	Description	Applications	References
	can be genetically engineered or differentiated to secrete therapeutic molecules.	teratoma formation if undifferentiated; stable once differentiated.				
3D cell models	High biocompatibility; mimics *in vivo* tissue architecture; supports natural cell–cell and cell–matrix interactions. Not used as carriers, but as target models to assess drug penetration, retention, and efficacy in 3D environments.	Simulates physiological tissue targeting; allows evaluation of therapeutic performance in complex microenvironments. More stable than 2D cultures; maintains phenotype and gene expression over time.	Preclinical tool; widely used in pharmaceutical research and development, but not for direct clinical use.	Physiologically relevant cell behavior studies.	Recapitulate tissue-like environments.	70
Hepatocytes	High biocompatibility; primary human hepatocytes are biologically relevant and accurately mimic liver function. Used to study drug metabolism, clearance, and hepatotoxicity.	Serve as target cells in liver-specific drug delivery studies (e.g., NP uptake through ASGPR receptors).	Primary human hepatocytes (considered the gold standard, but associated with high cost, limited supply, and restricted commercial availability), cell lines (e.g., HepG2, HepaRG; widely available and cost-effective for commercial use), and iPSC-derived hepatocytes (emerging models with growing commercial accessibility).	Liver metabolism and toxicity studies.	Essential for liver drug metabolism research.	71
THP-1 cells	THP-1 is a human monocytic leukemia cell line used *in vitro* to evaluate immune response, drug effects, and NP uptake by macrophages.	Serve as a target model for inflammation-related and immune-targeted drug delivery research.	Bioresearch suppliers like ATCC (American Type Culture Collection), Sigma-Aldrich, Thermo Fisher Scientific Inc., and ECACC (European Collection of Authenticated Cell Cultures)	Inflammation-related and immune response drug research.	Immunology and drug screening.	72
Zebrafish embryos	Zebrafish embryos are transparent and genetically similar to humans, enabling real-time *in vivo* studies. Used to evaluate drug toxicity, metabolism, biodistribution, and efficacy.	Facilitates visualization of drug targeting and organ-specific uptake (e.g., brain, liver, tumor). Genetically stable; embryos are robust and allow high-throughput screening.	Preclinical tool; extensively used in toxicity and pharmacology, but not used in humans.	High-throughput screening and developmental studies.	Transparent embryos for live imaging.	73

(Cont'd...)

Table 1. *(Continued)*

Biomaterial	Biocompatibility and drug-loading capacity	Targeting specificity and stability	Commercial status	Description	Applications	References
PLGA NPs	FDA-approved polymeric NPs degrade into lactic and glycolic acids, which are naturally metabolized. High versatility; suitable for delivering small molecules, proteins, peptides, and nucleic acids.	Enable passive targeting through the EPR effect; surface modification with ligands (e.g., antibodies, peptides) allows active targeting. High formulation-dependent stability; degradation tunable from days to months.	Used in approved drugs (e.g., Lupron Depot®); several formulations are in clinical trials.	Drug encapsulation and targeted drug delivery.	Controlled release.	74
Monoclonal antibodies	High biocompatibility; humanized or fully human monoclonal antibodies reduce immunogenicity and are well-tolerated clinically. High versatility; can be used directly as therapeutics or as drug conjugates.	Target antigens with high specificity (e.g., in cancer or autoimmune diseases). High *in vivo* stability; engineered for extended circulation and shelf life.	>100 FDA-approved monoclonal antibodies for cancer, autoimmune diseases, and infections.	Biologic drug development and immunotherapy.	High specificity and therapeutic potential.	75
Peptide nucleic acids	High biocompatibility; synthetic, non-charged backbone resists enzymatic degradation and minimizes toxicity *in vitro* and *in vivo*. Used therapeutically to bind complementary DNA or RNA with high sequence affinity and specificity.	Allows gene- or mRNA-specific targeting; often conjugated to targeting ligands. Exceptionally stable; resistant to nucleases and proteases, and stable in biological environments.	Used in gene editing, antisense therapy, and diagnostics in preclinical and early-phase clinical trials.	Genetic research, molecular biology, and gene therapy.	Sequence-specific hybridization.	76
Iron oxide NPs	Biocompatible when properly coated (e.g., dextran, PEG). High versatility; drugs, genes, or peptides can be conjugated to the surface or embedded in coatings.	Magnetically directed through external fields; surface ligands enable active targeting. Magnetically and chemically stable; prone to aggregation if uncoated.	Approved as MRI contrast agents (e.g., Resovist®, Ferumoxytol); in clinical trials for hyperthermia and drug delivery.	MRI contrast agents.	High relaxivity for sensitive MRI detection.	77
CNTs	Raw CNTs may elicit inflammation or cytotoxicity; functionalization improves compatibility. High versatility; capable of adsorbing or conjugating drugs, genes, and biomolecules onto/into their structure.	Surface can be modified with ligands (e.g., antibodies, peptides) for active targeting. Chemically stable but non-biodegradable without modification, raising long-term concerns.	Preclinical; extensively studied for cancer therapy, gene delivery, and biosensing; not yet FDA-approved.	Optical imaging, drug-delivery carriers.	Strong absorbance in the near-infrared region.	78
Fluorescent dyes	Generally biocompatible at low concentrations; certain dyes (e.g., cyanine dyes) exhibit better tolerability. Primarily used for labeling in tracking, imaging, or diagnostics.	High targeting specificity when conjugated to antibodies, peptides, or NPs for targeted imaging. Stability varies by type; organic dyes may photobleach.	Some dyes are FDA-approved (e.g., indocyanine green); others are widely used in preclinical imaging.	Various bioimaging techniques.	Bright fluorescence, broad color range.	79

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Table 1. *(Continued)*

Biomaterial	Biocompatibility and drug-loading capacity	Targeting specificity and stability	Commercial status	Description	Applications	References
Magnetic NPs	Magnetic NPs with coatings (e.g., dextran, PEG, silica) are biocompatible;uncoated cores may be toxic. Can be functionalized to carry drugs, genes, or proteins on or within the coating.	Directed using external magnetic fields; active targeting through surface ligands is possible. Magnetically and chemically stable, coatings prevent aggregation and oxidation.	FDA-approved for MRI contrast (e.g., Ferumoxytol); under investigation for magnetic hyperthermia and drug delivery.	MRI contrast agents.	Safe, non-toxic for *in vivo* imaging.	80
Silica NPs	High biocompatibility with surface modification; amorphous silica is less toxic than crystalline. Mesoporous silica provides a high surface area for loading drugs, genes, or imaging agents.	Surface easily functionalized with ligands (e.g., antibodies, peptides) for active targeting. Chemically stable; degradability tunable by particle size and porosity.	Preclinical and early-phase clinical trials for cancer therapy, imaging, and theranostics; not yet FDA-approved.	Labeling and tracking cellular events.	High stability, easy surface functionalization.	81
Biosensors	Biocompatibility depends on materials (e.g., enzymes, electrodes, polymers); generally, biocompatible when implanted. Used for detection, not drug delivery.	High specificity through biorecognition elements (e.g., antibodies, aptamers, enzymes). Stability enhanced with nanomaterials (e.g., graphene, gold); sensitive to pH, temperature, and biofouling.	Widely used in clinical trials; FDA-approved for glucose monitoring, pregnancy tests, and infectious disease diagnostics.	Detection of biomolecules in real-time.	High sensitivity and specificity.	82
Optical coherence tomography	Non-invasive, light-based imaging; typically does not require contrast agents. It is a diagnostic imaging tool, not a drug carrier.	High spatial resolution; enables localized tissue imaging (e.g., retina, coronary arteries, skin). Robust and reproducible; optical systems are durable and standardized.	Widely used; FDA-approved; standard imaging modality in ophthalmology, cardiology, and dermatology diagnostics.	Depth-resolved imaging in ophthalmology.	Real-time, non-invasive imaging.	83
Used in vaccine development						
Aluminum-based adjuvants	Widely used in licensed vaccines; may cause mild local inflammation. Moderate versatility; enhances immune recognition by adsorbing antigens (e.g., proteins, toxoids) onto their surface.	Non-specific targeting stimulates general immune activation without directing it to specific tissues or cells. Highly stable in vaccine formulations; preserves antigen integrity over time.	Used in many licensed vaccines (e.g., DTP, hepatitis B, HPV).	Enhance immune response and vaccine efficacy.	Proven safety and effectiveness in many vaccines.	84
mRNA vaccines	mRNA is non-infectious and non-integrating; LNPs may trigger mild immune responses. High versatility; encapsulate and protect mRNA for intracellular delivery.	Moderate targeting specificity; LNPs naturally accumulate in dendritic cells and muscle tissue at the injection site. Inherently unstable; requires –20–−80°C storage unless chemically optimized.	FDA-approved; used in COVID-19 vaccines (e.g., Pfizer-BioNTech, Moderna); clinical trials ongoing for cancer, flu, and RSV.	Deliver genetic material for immune response.	Rapid development, potential for personalized vaccines.	85
Viral vector vaccines	Uses non-replicating or attenuated viruses; may cause mild immune or	Moderate to high targeting specificity; natural viral tropism (e.g., adenovirus) enables	Used in vaccines like Oxford–AstraZeneca (COVID-19),	Modified viruses deliver antigens.	Strong and long-lasting immunity.	86

(Cont'd...)

Table 1. *(Continued)*

Biomaterial	Biocompatibility and drug-loading capacity	Targeting specificity and stability	Commercial status	Description	Applications	References
	inflammatory reactions. Deliver genetic material (e.g., DNA, RNA) encoding antigen directly into host cells.	targeted delivery to specific cell types. Stable at refrigerated temperatures; more stable than mRNA vaccines, but less stable than inactivated vaccines.	Ebola (Ervebo); many others in clinical trials.			
NPs (e.g., liposomes)	Highly biocompatible; especially when PEGylated; FDA-approved for clinical applications. High versatility; encapsulates hydrophilic (core) and hydrophobic (bilayer) agents.	Targeting through passive accumulation (EPR effect) or active ligand-conjugation for specific tissues or cells. Tunable stability based on lipid composition; PEGylation and pH-sensitive formulations improve durability.	Used in drugs like Doxil®, AmBisome®; multiple formulations in clinical use and trials.	Deliver antigens and adjuvants.	Improved stability and immune response.	87
Protein subunit vaccines	Generally safe and well-tolerated. Deliver antigenic proteins rather than therapeutic drugs.	Induce specific immune responses against the protein antigen; often enhanced with adjuvants. Stable at refrigerated temperatures; easier to store and transport than mRNA-based vaccines.	Used in vaccines like Hepatitis B, HPV (e.g., Gardasil), and COVID-19 (e.g., Novavax).	Use purified pieces of pathogens as antigens.	Safe, well-tolerated, no risk of causing disease.	88
LNPs	Composed of biodegradable lipids; generally well-tolerated, though mild inflammation may occur. Efficiently encapsulate nucleic acids (e.g., mRNA, siRNA) and small molecules.	Moderate to high targeting specificity; can be modified with ligands for targeted delivery; naturally accumulate in liver cells. Require cold storage (especially for mRNA delivery); PEGylation improves serum stability.	Used in mRNA COVID-19 vaccines (e.g., Pfizer-BioNTech, Moderna); in clinical trials for cancer and rare diseases.	Deliver mRNA and other vaccine components.	Facilitate cellular uptake, scalable, and adaptable for various pathogens.	90

Abbreviations: 3D: Three-dimensional; AuNPs: Gold nanoparticles; BCS: Biopharmaceutics Classification System; BDDE: 1,4-butanediol diglycidyl ether; CdSe: Cadmium selenide; CMC: Carboxymethyl cellulose; CNTs: Carbon nanotubes; dECM: Decellularized extracellular matrix; DOX: Doxorubicin; DTP: Diphtheria toxoid protein; ECM: Extracellular matrix; EDC: 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide; EPR: Enhanced permeability and retention; GRAS: Generally Recognized as Safe; FDA: Food and Drug Administration; GAG: Glycosaminoglycans; HA: Hyaluronic acid; HAp: Hydroxyapatite; HDPE: High-density polyethylene; HPV: Human papillomavirus; IOL: Intraocular lens; ISO: International Organization for Standardization; MOF: Metal–organic framework; MRI: Magnetic resonance imaging; NHS: N-hydroxysuccinimide; NIR: Near-infrared; NPs: Nanoparticles; PC: Polycarbonate; PCL: Polycaprolactone; PDA: Polydopamine; PE: Polyethylene; PEEK: Polyether ether ketone; PEG: Polyethylene glycol; PLA: Polylactic acid; PLGA: Poly(lactic-co-glycolic acid); PMMA: Polymethyl methacrylate; PU: Polyurethane; PVP: Polyvinylpyrrolidone; RGD: Arginine–glycine–aspartic acid (a cell adhesion motif); RSV: Respiratory syncytial virus; siRNA: Small interfering RNA; Ta: Tantalum; TCP: Tricalcium phosphate; TNF: Tumor necrosis factor; UHMWPE: Ultra-high-molecular-weight polyethylene; UV: Ultraviolet; ZrO_2: Zirconia; ASGPR: Asialoglycoprotein receptor; mRNA: Messenger RNA; EMA: European Medicines Agency; LNP: Lipid nanoparticle.

naturally, is commonly used in both packaging and biomedical applications.[103]

Blends of natural starch with other biodegradable polymers also offer sustainable alternatives for producing biodegradable bags and packaging films. Polyethylene (PE) glycol, depending on its molecular weight and formulation, can exhibit biodegradability and is often used in DDSs and pharmaceutical formulations.

However, not all biobased polymers are biodegradable. For example, PLA, derived from fermented plant starch (e.g., corn), is only biodegradable under industrial composting conditions, and its degradation in natural environments is limited. Biobased PE, manufactured using ethylene derived from sugarcane ethanol, shares the same molecular structure as conventional PE and is therefore non-biodegradable, despite offering a reduced carbon footprint. Similarly, biobased polyethylene terephthalate (PET), produced from renewable sources such as sugarcane-derived ethylene glycol, is chemically identical to petroleum-based PET and lacks biodegradability.[104] Biobased polyamides (e.g., nylon), which can be synthesized from castor oil, a renewable resource, also provide enhanced sustainability but do not undergo natural degradation in the environment.

Some synthetic polymers are biodegradable despite not being derived from renewable sources. For instance, polybutylene adipate terephthalate is commonly used in compostable products. Polycaprolactone is another non-renewable yet biodegradable polymer, utilized in biomedical devices, tissue engineering, and three-dimensional printing. Polyvinyl alcohol and polyethylene oxide, although synthetic, are biodegradable under specific environmental or processing conditions and are used in water-soluble packaging and DDSs.[105]

Many conventional polymers are neither biobased nor biodegradable. These include PE, polypropylene, polyvinyl

chloride, polystyrene, PET, polyurethane, acrylonitrile butadiene styrene, and polycarbonate.[106] Despite their widespread use in sectors such as packaging, construction, automotive, and consumer goods, these materials present long-term environmental concerns due to their resistance to degradation.

Nanotechnology-enabled biomaterials, including gold nanoparticles, carbon nanotubes, and electrospun nanofibers, have introduced new opportunities in precision medicine, facilitating highly targeted drug delivery, enhanced imaging techniques, and nanoscale tissue repair.[107] Biomaterials also include biologically derived constructs such as decellularized tissues, xenografts (e.g., porcine heart valves), and autografts (patient-derived tissues), all of which play a critical role in transplant and reconstructive surgery.[108]

4. Nanoparticles in drug delivery and diagnostics

Nanoparticles, particularly composed of biocompatible polymers and inorganic materials, have revolutionized modern medicine by enabling precise drug delivery and enhancing diagnostic imaging.

Polymeric nanoparticles are particularly versatile. Derived from biocompatible and biodegradable polymers, they can encapsulate a wide range of drugs—from hydrophobic molecules to water-soluble compounds—making them ideal for tailored drug delivery. Their structure and composition can be fine-tuned to regulate drug release, ensuring sustained therapeutic effects and minimizing side effects.[109,110] This capability supports personalized medicine, in which treatment is tailored to individual patient needs. Beyond drug delivery, polymeric nanoparticles also function as effective carriers for imaging agents. When loaded with fluorescent dyes or contrast materials, they enhance the accuracy of diagnostic techniques such as MRI and fluorescence imaging, allowing for early disease detection and high-sensitivity monitoring.[111]

Inorganic nanoparticles, such as gold and silver nanoparticles, offer distinct biomedical advantages. Gold nanoparticles are widely used in medical imaging due to their tunable optical properties (e.g., surface plasmon resonance), which improve the resolution of computed tomography scans. They also enable targeted drug delivery, as their surfaces can be functionalized with ligands or antibodies for selective interaction with disease-specific cells. This dual functionality in therapy and diagnostics has catalyzed their use in theranostics—an emerging field that integrates treatment and diagnosis.[112] Silver nanoparticles, known for their antimicrobial properties, are incorporated into wound dressings, topical creams, and surface coatings to control infections through the gradual release of silver ions. Their multifunctionality in both infection control and drug delivery highlights their versatility.

In tissue engineering, hydrogels serve as biocompatible scaffolds that support cell proliferation and tissue regeneration. They closely mimic the native extracellular matrix, creating a conducive environment for the formation of skin, cartilage, bone, and even complex organs such as the liver and heart.[113] This innovation has introduced new opportunities in regenerative medicine and personalized organ replacement, helping to address challenges such as organ donor shortages and immune rejection. Due to their adaptability, safety, and multifunctionality, hydrogels continue to advance healthcare by enabling novel therapeutic strategies and advancing the frontiers of regenerative medicine and precision drug delivery.[114]

5. Drug delivery vehicles: Structural diversity and functional capabilities

Several advantages of biomaterials include their biocompatibility and the ability to control drug loading and release kinetics. Biocompatibility ensures that materials interact safely with the body, avoiding immune reactions, inflammation, or toxicity—factors essential for clinical success. This is achieved through careful selection and modification of material properties, including chemical composition, surface characteristics, and mechanical strength—all of which are tailored to their intended medical use.[115] Equally critical is the precise control over drug loading and release rates, which determines how effectively a therapeutic agent is delivered. By engineering biomaterials to adjust factors such as porosity, degradation rate, and drug affinity, scientists can create systems that release drugs at optimal dosages over desired timescales. This personalization enhances treatment efficacy, reduces side effects, and enables long-term, patient-specific therapies, ultimately driving innovation in modern medicine.

Targeting and specificity are key advancements in biomaterial-based DDSs, enabling therapeutic agents to be targeted directly to diseased cells, tissues, or organs while minimizing their impacts on healthy tissues.[116,117] Unlike traditional systemic drug delivery, which often leads to broad exposure and side effects, engineered biomaterials—such as nanoparticles, liposomes, or drug-eluting implants—can be functionalized with ligands, antibodies, or peptides to selectively bind to target sites. This targeted approach is especially valuable in cancer therapy, gene therapy, and regenerative medicine, allowing for higher drug efficacy, lower toxicity, and improved patient outcomes. By delivering treatments directly to sites of pathology, biomaterials enhance precision medicine and open new possibilities for treating complex diseases with reduced systemic risks.

Stability and degradation are essential design considerations in biomaterial-based drug delivery, ensuring that therapeutic agents are released in a controlled manner while minimizing risks. A stable biomaterial must maintain its physical and chemical integrity during drug transport to prevent premature release and preserve drug efficacy. At the same time, many systems are engineered to degrade safely within the body, breaking down into non-toxic byproducts once their function is fulfilled.[117] This balance between sustained drug release and harmless degradation is critical for applications such as drug-eluting stents, tissue scaffolds, and biodegradable implants, ultimately enhancing treatment outcomes while reducing the need for surgical removal or long-term complications.

Immunogenicity refers to the potential of biomaterials to trigger immune responses, which can lead to inflammation,

rejection, or failure of medical interventions. To ensure safety and efficacy, it is crucial to design biomaterials that minimize immune recognition by selecting biocompatible materials and modifying surface properties to mitigate adverse reactions.[116,118] Reducing immunogenicity enhances the performance of DDSs, tissue engineering, and gene therapies, ultimately promoting safer and more effective treatments across diverse medical fields.

6. MOFs: Revolutionizing advanced drug delivery

MOFs are crystalline and highly porous materials constructed by coordinating metal ions or metal clusters with organic ligands to form 2D or 3D structures. Through careful selection of metal nodes and organic linkers, MOFs can be engineered with tailored physicochemical attributes—such as surface area, pore size, shape, morphology, and degree of hydrophilicity or hydrophobicity. This tunability makes MOFs highly adaptable for diverse applications, including gas storage, separation technologies, imaging, sensing, catalysis, energy storage and conversion, analytical chemistry, and biomedical uses.[119] In biomedicine, particularly, MOFs have emerged as promising candidates for DDSs due to their customizable porosity, structural flexibility, and amenability to functionalization.

One of the most significant advantages of MOFs is their high Brunauer–Emmett–Teller surface area, which allows for exceptional drug-loading capacities. They are capable of encapsulating a wide range of therapeutic agents—ranging from small drug molecules to peptides and even large biomacromolecules—often achieving encapsulation efficiencies approaching 100%. In addition, the physicochemical behavior of MOFs, such as biodegradability and release kinetics, can be finely tuned by modifying their metal nodes and linkers.[120] Notably, these modifications typically do not compromise the core structural or physicochemical integrity of the MOF. Surface coatings can be applied through simple aqueous adsorption, polymer grafting, or encapsulation with lipid or silica layers, thereby broadening the functional capabilities and enhancing the stability of MOF-based systems.[119]

In addition, due to the inherently weak coordinative bonds within MOF structures, these frameworks tend to degrade under physiological conditions, resulting in the gradual release of their constituent ligands. This feature imparts favorable biodegradability and biocompatibility, allowing MOFs to break down safely after fulfilling their therapeutic function. Moreover, several MOFs have demonstrated intrinsic bioactive properties that are beneficial in treating cancer and infections. For instance, certain iron-based nano-MOFs exhibit intrinsic antibacterial effects that work synergistically with encapsulated drugs to combat intracellular pathogens, as well as the ability to enhance radiotherapeutic efficacy in cancer treatments.[121] These findings provide new opportunities for the development of multifunctional nanoplatforms, where each component actively contributes to the therapeutic outcome, particularly in radiotherapy and antimicrobial therapies.

7. Classification of MOFs

Given the vast possibilities in choosing metal ions and organic linkers, thousands of MOFs have been synthesized with a wide range of structural and functional properties. For biomedical applications, particularly in DDSs, it is essential to consider both biocompatibility and toxicity during MOF design, as these characteristics are intrinsically linked to the nature of the metal centers and organic ligands used.[122] Therefore, only non-toxic and physiologically acceptable components should be selected.

The median lethal dose (LD_{50}) is commonly employed to estimate the toxicity of metal ions. Among the metals considered safe and widely used in DDS-related MOFs are potassium, zinc, zirconium, and iron, with reported oral LD_{50} values of 0.215 g/kg, 0.35 g/kg, 4.1 g/kg, and 0.45 g/kg, respectively. These metals form the backbone of the most commonly studied and applied MOFs for biomedical uses, particularly for drug delivery. Numerous studies have reported the use of iron-, zirconium-, potassium-, and zinc-based MOFs for encapsulating a wide range of therapeutic agents, including anticancer, antibacterial, and antiviral drugs.[119]

Notably, MOFs can also facilitate the co-delivery of multiple therapeutic agents, offering synergistic effects for complex disease treatments such as cancer and infectious diseases.[123] Due to their modularity, MOFs exhibit several desirable characteristics for pharmaceutical use, including high drug-loading capacities, enhanced drug solubility and stability, controlled release profiles, and the potential for targeted delivery—thereby improving overall drug bioavailability and therapeutic performance. MOFs designed for DDSs are classified primarily based on their metal ion composition, as outlined in **Table 2**.

8. AI and ML in drug delivery: Transforming precision and efficiency

AI and ML are rapidly transforming the pharmaceutical landscape, particularly in the field of drug development and delivery. The integration of AI and ML into the drug discovery streamlines early-phase processes by predicting molecular behavior, binding affinity, and toxicity with high accuracy (**Table 3**). This significantly reduces the reliance on traditional hit-and-trial methods, thereby accelerating the identification of viable drug candidates. AI also plays a pivotal role in the evolution of smart delivery systems, including nanoparticles and materials that respond to physiological cues such as pH, enzymes, and temperature.[124] These smart systems allow for targeted and controlled drug release, optimizing pharmacokinetics and improving patient compliance. In clinical trials, AI enhances patient recruitment and cohort design, supports predictive modeling, and enables virtual trials, thereby reducing costs, duration, and risk.

Beyond drug development, AI supports regulatory compliance and post-market surveillance by continuously analyzing real-world data to identify safety signals and optimize therapeutic protocols. Looking ahead, the convergence of AI with emerging technologies—such as clustered regularly interspaced short palindromic repeats (CRISPR), blockchain,

Table 2. Summary of various MOFs used for drulivery: Linkers, pore sizes, and loaded drugs

MOF type/name	Organic linker	Pore size (Å)	Loaded drugs
MIL-89 (Fe)	Muconic acid	11	Ibuprofen
MIL-88A (Fe)	Fumaric acid	6	Ibuprofen, Doxorubicin
MIL-100 (Fe)	1,3,5-Benzenetricarboxylic acid	25, 29	Gemcitabine monophosphate, Topotecan, Isoniazid, Doxycycline, Tetracycline, Docetaxel, Azidothymidine triphosphate
MIL-101 NH_2 (Fe)	Amino-1,4–benzenedicarboxylic acid	29, 34	Ibuprofen
MIL-53 (Fe)	1,4-Benzenedicarboxylic acid	8.6	Ibuprofen, Oridonin
MIL-101 (Fe)	2-Amino-1,4–benzenedicarboxylic acid	25–30	Ibuprofen, Azidothymidine triphosphate
ZIF-127	3,3',5,5'-Azobenzene	11.6	Caffeine
$Zn(TATAT)_3$/β DIF-H_2O	TATAT = 5,5'5"–(1,3,5-Triazine-2,4,6-triyl) tris(azanediyl)triso	17, 21	5-Fluorouracil
$ZnBDP_x$	1,4-Bis(1H-pyrazol-4-yl)-2-X-benzene (X=H, NO_2, NH_3, OH)	11	Mitoxantrone
Bio-MOFs/$ZnBDP_x$	–	11	Ketoprofen
ZIF-8	2-Methylimidazolate	11.6	Lansoprazole
Zr-MOFs/UiO-66	1,4-Benzenedicarboxylic acid	8/8	Azilsartan, Budesonide, Valsartan
UiO NMOFs	Amino-triphenyldicarboxylic acid	–	Ibuprofen, Doxorubicin

Abbreviations: BDP: 1,4-Bis(1H-pyrazol-4-yl)benzene; DIF: Diiron Framework; MOF:b Metal–Organic Framework; MIL: Matériaux de l'Institut Lavoisier; Nanoscale Metal–organic frameworks; NMOFs: NH_2: Amino Group; UiO: University of Oslo; TATAT: 5,5',5"-(1,3,5-Triazine-2,4,6-triyl)tris(azanediyl) trisbenzoic acid; ZIF: Zeolitic imidazolate framework.

Table 3. Overview of AI/ML-driven innovations in drug delivery highlighting collaborating organizations, applied methodologies, target applications, and observed impacts

Title/focus	Organization/ collaborator	Background/ context	AI/ML methodology	Application/case details	Outcome	Impact	References
AI-driven Personalized Drug Delivery	IBM Watson and Memorial Sloan Kettering Cancer Center.	IBM Watson used AI for personalized cancer therapy, especially for breast cancer.	AI processes vast literature, clinical trials, and patient records.	Analyzes genetic profiles, medical history, and treatment response to suggest optimal drug combinations and dosages.	Identified the best chemotherapy regimens for individual breast cancer patients.	Higher precision in treatment, minimized adverse effects, and improved patient-specific therapy.	125
ML in Nanomedicine Design	*In silico* medicine.	AI/ML for designing and optimizing nanoparticles in cancer drug delivery.	ML algorithms simulate drug interactions and predict nanoparticle structure and delivery.	Designed AI-powered nanoparticles to deliver drugs directly to tumor cells, avoiding healthy tissues.	Optimized size, shape, and material composition of nanoparticles.	Improved therapeutic index, reduced toxicity, and faster development of personalized nanomedicines	126
AI for Predicting Controlled Drug Release Profiles	Massachusetts Institute of Technology.	Critical to maintain drug levels in the body with fewer doses; tailored for chronic conditions.	AI trained on polymer properties, drug types, and environmental conditions.	Model predicts time-based drug release from polymer-based systems.	Successfully developed a steady release system for diabetes medication.	Reduced need for frequent dosing, better compliance, and improved long-term treatment outcomes.	127
AI for Optimizing mRNA Delivery through Lipid Nanoparticles	Moderna.	AI is used to handle the instability of mRNA in therapies like the COVID-19 vaccine.	ML models analyze formulation data for lipid nanoparticles.	Designed lipid nanoparticles to protect mRNA, ensure cell delivery, and enable protein expression	Used in the Moderna COVID-19 vaccine for an effective immune response.	Enabled rapid, scalable deployment of mRNA vaccines, vital during the pandemic	128
AI in Optimizing Drug Delivery Routes (Inhalation)	Bayer.	AI is used to improve respiratory drug formulations (e.g., asthma, COPD).	AI models simulate lung deposition, predict absorption, and analyze patient data.	Optimized particle size, formulation behavior during inhalation, and dose personalization.	Personalized dose and formulation based on disease severity and respiratory profile.	Faster development, better lung deposition, improved drug efficacy, and reduced physical trials.	124

Abbreviations: AI: Artificial intelligence; ML: Machine learning; COPD: Chronic obstructive pulmonary disease; mRNA: Messenger RNA.

nanorobotics, and the Internet of Things—promises to deliver ultra-precise, secure, and responsive DDSs. However, the field faces critical challenges, including issues of data quality and privacy, model interpretability (the black-box problem), and regulatory and ethical considerations. Ensuring transparency through explainable AI (XAI), safeguarding sensitive data, and building interdisciplinary governance frameworks will be essential to responsibly harness the full potential of AI and ML in drug delivery.[124,125]

9. Future prospects of AI and ML in drug delivery

The future of drug delivery is undergoing a significant transformation as AI and ML continue to advance, offering transformative solutions across therapeutic development and administration. Central to this evolution is the realization of fully personalized medicine, wherein AI enables dynamic, real-time adjustments in drug dosage and delivery based on continuous analysis of patient-specific data, such as genetic profiles, lifestyle factors, and physiological signals. Advanced predictive modeling will further allow anticipatory interventions in chronic diseases by forecasting disease progression and treatment requirements.

In addition, AI is expected to enhance integration with emerging technologies—such as CRISPR, nanorobotics, and smart implants—enabling precise, targeted delivery and autonomous therapeutic responses. The design of AI-optimized nanoparticles and controlled-release systems is anticipated to improve drug bioavailability, reduce side effects, and support time-dependent therapies. In addition, end-to-end AI-driven pipelines are likely to streamline drug discovery, formulation, clinical testing, and delivery, significantly shortening development timelines and reducing costs. Innovations such as virtual clinical trials and real-time safety monitoring will make development more agile and responsive. Importantly, AI also holds the potential to expand global healthcare access through affordable, scalable, and remotely managed delivery systems, particularly benefiting low-resource and underserved regions. As these technologies mature, emphasis on the development of ethical AI, XAI, and transparent regulatory frameworks will be essential to ensure trust, accountability, and equity in AI-driven healthcare.[124]

10. Limitations of the review

Despite offering a comprehensive overview, this review has certain limitations in its design. It follows a narrative approach without employing a systematic methodology, such as predefined inclusion and exclusion criteria, structured search strategies, or formal quality assessment of the included studies. As a result, there is a potential for selection bias and reduced reproducibility. The absence of quantitative synthesis, such as meta-analysis, further limits the ability to draw comparative conclusions across different biomaterials. In addition, some classes of biomaterials are discussed in greater depth than others, leading to an imbalanced content coverage. The review also does not sufficiently address regulatory challenges, clinical translation hurdles, or real-world applicability in low- and middle-income countries, which are critical for the successful integration of biomaterials into healthcare systems. Furthermore, there is limited discussion of potential biases within the cited studies and insufficient representation of the latest advancements published after the review's data cut-off. Lastly, while broad therapeutic applications are highlighted, some sections may overgeneralize findings without adequately considering context-specific factors, such as biocompatibility, degradation behavior, or economic feasibility.

11. Conclusions

Recent advancements in biomaterials have driven significant progress in drug delivery and precision medicine. The development of biomaterials that respond to physiological cues enables on-demand and site-specific drug release, significantly improving therapeutic outcomes. Coupled with innovations in nanotechnology and gene therapy, these materials are at the forefront of personalized medicine—allowing for the customization of treatment plans based on an individual's genetic makeup, disease profile, and physiological conditions. This tailored approach minimizes adverse effects and maximizes therapeutic efficacy, offering substantial benefits over conventional treatment strategies. Biomaterials have also enabled access to previously hard-to-reach areas of the body, such as the brain, thereby offering new opportunities for treating complex disorders like Alzheimer's disease and certain types of cancer. In regenerative medicine, scaffold-based biomaterials with intricate microarchitectures provide structural guidance for cell adhesion, proliferation, and differentiation, making them invaluable in tissue engineering applications. Likewise, hydrogels offer a supportive environment that promotes stem cell proliferation and tissue repair, further broadening their therapeutic potential. Moreover, the integration of real-time monitoring and feedback mechanisms into biomaterial-based DDSs allows for dynamic adjustment of drug release in response to the patient's needs. This level of control ensures optimal dosing and improves treatment adherence. As these technologies advance, there is a growing demand for updated and adaptive regulatory frameworks that can accommodate the complexity and precision of next-generation biomaterial applications, ensuring their safe and effective translation into clinical practice.

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