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REVIEW ARTICLE

Tailored Polymers in Therapeutics: Bridging Drug Delivery and Biomedical Engineering

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SUMMARY

Polymers have revolutionized the pharmaceutical and biomedical landscape by serving as adaptable and multifunctional materials in advanced drug delivery systems, tissue engineering, implants, and regenerative medicine. Their chemical versatility and tunable physicochemical properties enable precise control over drug release profiles, targeting, and biocompatibility, significantly enhancing therapeutic efficacy and patient compliance. Initially used as inert excipients, polymers have evolved into dynamic carriers that address formulation challenges such as poor solubility, instability, and non-specific biodistribution. Notably, polymer-based nanoparticles and hydrogels offer site-specific, controlled drug delivery with reduced systemic toxicity. Biodegradable polymers, particularly in injectable and implantable systems, eliminate the need for removal procedures, thereby improving patient safety. Innovations such as polymer-drug conjugates, programmable microdevices, and 3D-printed scaffolds are pushing the boundaries of precision therapeutics. Synthetic polymers offer consistency and thermal stability, while natural polymers provide superior biocompatibility and biodegradability, making their combined use highly effective. Despite the promising advancements, challenges remain in scalability, cost-efficiency, and long-term safety. Continued interdisciplinary research is crucial for addressing these hurdles. Looking forward, polymers are poised to play a pivotal role in the development of sustainable and smart drug delivery platforms, aligning with the goals of precision and personalized medicine. This review highlights the transformative role of polymers in current pharmaceutical innovations and future applications, underscoring their potential to reshape therapeutic strategies.

Keywords: *Smart polymers, hydrogels, tissue engineering, controlled release, 3d printed implants, regenerative medicine*

Terapötiklerde Özelleştirilmiş Polimerler: İlaç Taşıma ve Biyomedikal Mühendisliği Arasındaki Köprü

ÖZ

Polimerler, ilaç ve biyomedikal alanında ileri düzey ilaç taşıma sistemleri, doku mühendisliği, implantlar ve rejeneratif tıpta çok yönlü ve uyarlanabilir malzemeler olarak devrim yaratmıştır. Kimyasal çeşitlilikleri ve ayarlanabilir fizikokimyasal özellikleri sayesinde ilaç salım profilleri, hedefleme ve biyouyumluluk üzerinde hassas kontrol sağlanarak terapötik etkinlik ve hasta uyumu büyük ölçüde artırılmıştır. Başlangıçta inert yardımcı maddeler olarak kullanılan polimerler, kötü çözünürlük, kimyasal dengesizlik ve özgül olmayan biyodağılım gibi formülasyon zorluklarını aşabilen dinamik taşıyıcılara dönüşmüştür. Özellikle polimer bazlı nanoparçacıklar ve hidrojeller, sistemik toksisiteyi azaltırken hedefe yönelik ve kontrollü ilaç salımı sunar. Özellikle enjekte edilebilir ve implante edilebilir sistemlerde kullanılan biyobozunur polimerler, çıkarılma ihtiyacını ortadan kaldırarak hasta güvenliğini artırır. Polimer-ilaç konjugatları, programlanabilir mikrocihazlar ve 3B yazıcıyla üretilmiş iskeletler ve sürdürülebilir polimer yaklaşımları, hassas tedavi yaklaşımlarının sınırlarını zorlamaktadır. Sentetik polimerler tutarlılık ve ısıl stabilite sunarken, doğal polimerler üstün biyouyumluluk ve biyobozunurluk özellikleriyle dikkat çeker; bu nedenle birlikte kullanımları oldukça etkilidir. Tüm bu umut verici gelişmelere rağmen, üretim ölçeklenebilirliği, maliyet etkinliği ve uzun vadeli güvenlik konularında bazı zorluklar devam etmektedir. Bu engellerin aşılması için disiplinlerarası araştırmaların sürdürülmesi gereklidir. Geleceğe bakıldığında, polimerler sürdürülebilir ve akıllı ilaç taşıma platformlarının geliştirilmesinde kritik bir rol oynamaya adaydır ve bu durum hassas ve kişiselleştirilmiş tıbbın hedefleriyle örtüşmektedir. Bu derleme, polimerlerin güncel farmasötik yeniliklerdeki dönüştürücü rolünü ve gelecekteki uygulamalarını vurgulayarak, tedavi stratejilerini yeniden şekillendirme potansiyelini ortaya koymaktadır.

Anahtar Kelimeler: *Akıllı polimerler, hidrojeller, doku mühendisliği, kontrollü salım, 3B baskılı implantlar, rejeneratif tıp*

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INTRODUCTION

Polymers have emerged as cornerstone materials in biomedical and pharmaceutical advancements, underpinning innovations in drug delivery, tissue engineering, ophthalmic systems, implants, prosthetics, and regenerative medicine (El-Tanani et al., 2025; Lu, Cai, & Hu, 2024). Their remarkable chemical versatility and structural diversity enable the development of sophisticated delivery systems that prioritize therapeutic efficacy and patient well-being. The integration of polymer science with pharmaceutical research has reshaped formulation strategies, fostering precision in therapeutic interventions and elevating patient outcomes (Bharathy & Thanikachalam, 2024; Shergujri et al., 2025).

Despite the broad adoption of polymeric materials, a clear knowledge gap remains.While extensive reviews catalogue polymer platforms, fewer articulate how emerging polymeric systems are converging with digital design, smart implants, and next-generation manufacturing to address unmet therapeutic needs (Yue et al., 2025). In particular, the rapid advances in polymeric microneedles for transdermal and long-acting delivery (Chen et al., 2025; Mahajan et al., 2021; Meng et al., 2024), bioresorbable polymeric implants for tissue repair (Dobrzyńska-Mizera et al., 2024; Yu et al., 2023), and computer-assisted polymer design (Chou et al., 2025; Gao et al., 2024; Singh et al., 2020; Yue et al., 2025; Zhou et al., 2025) remain underreview in an integrated manner. Hence, this review aims to critically map and synthesize the state-of-the-art in advanced polymer platforms,focusing on how tailored polymeric materials, smart manufacturing, and multifunctional system design are enabling the next frontier of therapeutic delivery and regenerative medicine (Long et al., 2025; Nosrati & Nosrati, 2023; Son et al., 2024). By doing so, the review contributes to existing literature by delineating emerging trends, comparing traditional versus modern polymer approaches, and identifying future directions for translational research.

These macromolecules can be tailored to exhibit a spectrum of physicochemical properties by adjusting chain length, functional groups, and molecular interactions. Such adaptability allows precise control over surface and bulk characteristics to meet specific delivery goals (Chemban et al., 2022; Singh et al., 2022). Polymers serve diverse functions, including forming films, modulating rheology, enabling pH-dependent solubility, enhancing solubility, supporting sustained-release gelling, enhancing adhesion, and creating protective barriers—all of which optimize drug kinetics, stability, and safety (Alavi et al., 2024; Al-Sahlawi et al., 2024; Long et al., 2025; Nunziata et al., 2025).

Originally employed as inert excipients, polymers have evolved into dynamic carriers that address critical formulation challenges such as poor aqueous solubility, chemical instability, and non-specific biodistribution (Geszke-Moritz & Moritz, 2024; Singh et al., 2023). Their capacity to encapsulate fragile compounds and direct them to specific sites has transformed therapeutic approaches.

Notably, polymer-based nanoparticles and hydrogels have shown exceptional promise for targeted and controlled drug release, reducing systemic exposure while enhancing treatment accuracy. Bioresponsive polymers, which respond to physiological cues like pH, temperature, or enzymatic activity, mark a significant advance toward intelligent, patient-specific delivery systems (El-Tanani et al., 2025; Quader et al., 2022). Biodegradable polymers stand out for their ability to provide sustained release while being naturally metabolized or excreted, minimizing risks associated with long-term residue accumulation (Bachhav et al., 2025; Farjaminejad et al., 2024; Kurowiak et al., 2023; Ogay et al., 2020). These materials are particularly valuable in injectable and implantable systems, where durability and biocompatibility are paramount (Lu et al., 2025; Quader et al., 2022; Sharma et al., 2024).

Emerging developments now extend into polymeric microneedle systems for long-acting delivery and wearable diagnostics; recent reviews highlight the mechanisms, materials, and clinical applications of polymeric microneedles (Chen et al., 2025; Meng et al., 2024). Computer-assisted polymer design, leveraging artificial intelligence and machine learning, is accelerating the formulation of high-performance polymeric materials with tailored properties (Gao et al., 2024; Yue et al., 2025). In parallel, smart bioresorbable polymer implants enable structural repair combined with drug release and sensor integration, creating multifunctional therapeutic platforms (Dobrzyńska-Mizera et al., 2024; Heidari et al., 2024; Yu et al., 2023). These innovations reflect a paradigm shift—from traditional polymer use toward integrated, data-driven, and responsive polymer-therapeutic systems.

Synthetic and natural polymers each offer unique strengths. Synthetic variants are prized for their thermal stability, reproducibility, and processability, while natural polymers excel in biocompatibility and degradability (González et al., 2023; Meng et al., 2024). Together, they enable functions such as improving drug solubility and bioavailability through hydrogels and microparticles, refining drug distribution via nanoparticle carriers, delivering biomolecules to targeted sites, solubilizing hydrophobic drugs through micelle formation, enabling stimuli-responsive release, masking unpleasant tastes, and creating mechanically robust nanocomposites. Despite these advances, challenges persist, including scalability, production costs, regulatory hurdles, and potential long-term toxicity. Overcoming these hurdles will demand interdisciplinary collaboration, standardized data systems, and sustained innovation (Mukherjee et al., 2023; Nanda et al., 2022).

Looking ahead, polymers will remain pivotal in shaping the future of pharmaceuticals. Their evolving capabilities hold promise for advancing personalized therapeutics, sustainable drug delivery platforms, and integrated biotechnological systems, aligning with the growing needs of precision medicine (Dallaev, 2025; Huang et al., 2019; Rezaei et al., 2021).

HISTORICAL EVOLUTION OF POLYMERS IN BIOMEDICAL APPLICATIONS

The use of polymers in medicine dates back millennia, with natural polymers integral to traditional herbal remedies. Modern pharmacognosy has since advanced our understanding of these natural macromolecules, elucidating their mechanisms and therapeutic potential (Bhatia, 2016). This historical foundation has paved the way for the sophisticated integration of polymers into contemporary biomedical and pharmaceutical applications.

Emergence of synthetic polymers

The advent of synthetic polymers marked a transformative era in medical science, aligning with the birth of polymer science in the early 20th century. Hermann Staudinger's pioneering work in the 1920s established polymers as macromolecules, demonstrating their high molecular weight through physicochemical studies of rubber (Staudinger, 1920). His insights laid the intellectual groundwork for polymer science, earning him the Nobel Prize in 1953, a year that also saw the elucidation of DNA's structure, underscoring the broader significance of macromolecular science (Staudinger, 1953; Watson & Crick, 1953). Concurrently, Wallace Carothers' experiments in 1929 leveraged organic chemistry to synthesize polymers, further solidifying the field's foundations (Carothers, 1929). These milestones catalyzed the development of synthetic, water-soluble polymers as both therapeutic agents and components of drug delivery systems.

Polymer applications in wartime and beyond

The utility of synthetic polymers became particularly evident during World War II, with materials like polyvinylpyrrolidone finding widespread use in healthcare. This period also marked the introduction of polymer-drug conjugates, heralding the era of biologically active polymers. By the 1960s, efforts

to explore polymers as anticancer agents gained momentum, though early trials were hindered by toxicity concerns (Duncan et al., 2005). Despite these challenges, the groundwork laid during this time proved instrumental for subsequent innovations.

Foundations of modern polymer therapeutics

The 1970s ushered in a focused effort to design polymer-based therapeutics with tailored chemical and biological properties. This era saw the development of polymer-protein and polymer-drug conjugates, which have since become central to therapeutic strategies. A significant milestone came in 1994 with the introduction of the first synthetic polymer-drug conjugate for cancer therapy, combining hydroxypropyl methacrylate (HPMA) with doxorubicin (Duncan et al., 2005). The early 2000s marked further progress, with regulatory approvals for polymer-protein conjugates like PEG-interferon-α for chronic hepatitis and PEG-GCSF as a colony-stimulating agent. Additionally, polymer-based nanoparticles, such as paclitaxel-loaded systems, gained approval for treating metastatic breast cancer, highlighting the growing impact of polymers in precision therapeutics (Gandhi et al., 2012; Wang & Chang, 2023).

This historical progression—from ancient natural remedies to cutting-edge synthetic polymer conjugates—illustrates the dynamic evolution of polymers in medical science. This development embodies a synergy between scientific discovery and clinical innovation, laying a strong foundation for future advancements in polymer-based therapeutics.

RECENT ADVANCES IN BIOMEDICAL POLYMER APPLICATIONS

Polymers have become indispensable in modern biomedical applications, driving innovations in drug delivery, tissue engineering, and nanomedicine. Their chemical and structural versatility enables the design of tailored systems that improve therapeutic precision and patient outcomes across multiple delivery routes and clinical use cases. Recent work emphasizes not only novel materials but also manufacturing strategies such as 3D printing, electrospinning, and microfluidics, alongside design paradigms like stimuli-responsiveness, multi-functionality, and materials informatics, which together elevate polymer platforms from passive carriers to active, adaptive therapeutic systems (Clegg et al., 2024; Lu, Cai, & Hu, 2024).

Advanced polymeric drug delivery systems

Advanced polymeric drug delivery systems encompass far more than gastrointestinal targeting; they represent a platform technology for transporting therapeutic agents to a wide array of anatomical sites using tailored polymer architectures (Waqar et al., 2024; Zhang & Tian et al., 2024). Natural polymers like chitosan, alginate, pectin, xanthan, and guar gum have long been central to gastroretentive and mucoadhesive systems due to their inherent biocompatibility, ability to adhere to biological tissues, and safety profile (Harun-Or-Rashid et al., 2023; Turac et al., 2024). However, recent advances highlight the shift toward multifunctional systems, combining natural and synthetic polymers with nanomaterials, to address diverse therapeutic needs far beyond the gastric environment (Bachhav et al., 2025). Hybrid polymer matrices often integrating biodegradable synthetic elements like PLGA, polycaprolactone, and nanofibers are engineered for enhanced mechanical strength, controlled and responsive release, and compatibility with a variety of delivery routes, including transdermal, pulmonary, and ocular applications (Geszke-Moritz & Moritz, 2024; Shergujri et al., 2025). For example, polymeric microneedle arrays and patches, often made with smart blends of synthetic and natural polymers, now enable minimally invasive transdermal delivery of proteins, vaccines, and long-acting small molecules (Meng et al., 2024; Wang et al., 2022). In pulmonary delivery, polymeric nanoparticles and microparticles provide extended airway residence and targeted lung transport, with engineered release profiles and minimal toxicity (Mukherjee et al., 2023). In ocular and intranasal formulations, mucoadhesive

polymer-based hydrogels prolong drug retention time on mucosal surfaces and enhance therapeutic efficacy in eye and central nervous system diseases (Lu et al., 2024; Shergujri et al., 2025). For tumor and tissue targeting, polymers are tailored for stealth coating and ligand-mediated active targeting, exemplified by polymer-drug conjugates and nanocarriers loaded with chemotherapeutics or gene-editing agents (Geszke-Moritz & Moritz, 2024). Gene delivery is rapidly evolving through polymeric vectors, which protect nucleic acids from enzymatic degradation and facilitate cellular uptake, often utilizing biodegradable and stimuli-responsive carriers for enhanced safety and efficacy (Dallaev, 2025) (Figure 1.).

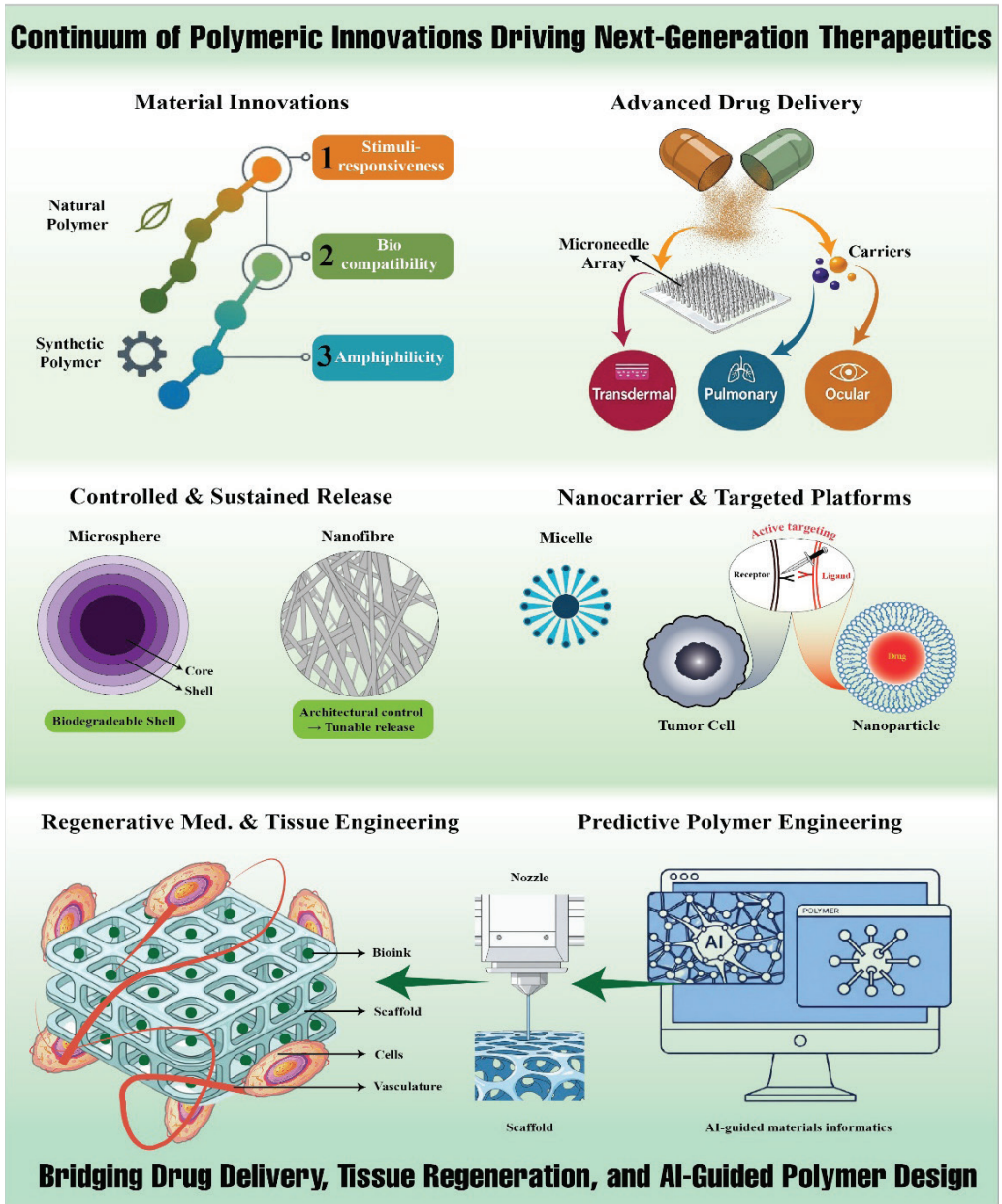

Figure 1. Advancements in polymeric drug delivery systems

Across all modalities, advances in computer-assisted design and machine learning have accelerated the development of intelligent polymer systems, enabling modular carriers that respond to physiological pH, temperature, or enzyme presence (Yue et al., 2025). These strategies are particularly prominent in the design of injectable hydrogels and nanocomposite scaffolds for localized, sustained delivery, regenerative medicine, and tissue engineering (Lu et al., 2024; Shergujri et al., 2025). The transition to composite and multifunctional polymer systems incorporating smart materials and bioresponsive mechanisms marks a major transformation in how drugs, biologics, and genetic therapies are transported within the body. Comparative studies now recommend hybrid designs that blend natural and synthetic polymers when both biofunctionality and structural robustness are critical, while also addressing manufacturing complexity and regulatory hurdles (Turac et al., 2024).

Innovations in controlled and sustained release

Modern controlled-release systems emphasize architectural design including core shell particles, layered films, and porous nano fibres and stimuli responsive chemistries that enable predictable long-term release and on-demand activation (Gaydhane et al., 2023). Electrospun nano fibres composed of PLGA, PCL, and PEG blends are especially valuable for local delivery in bone regeneration or wound healing, providing high surface area, tunable porosity, and controllable drug loading heterogeneity. These systems allow rapid adjustment of release kinetics via fiber diameter, porosity, and multilayer configurations (Fei et al., 2008; Wildy & Lu, 2023). However, scale-up and batch variability remain practical limitations compared with established microsphere technologies. PLGA hydrogels and depot systems have gained renewed attention for long-acting systemic delivery. Engineered PLGA based depots and hydrogel composites mitigate initial burst release and provide weeks tomonths release with predictable degradation, rivaling polymeric microspheres for sustained dosing (Cordovez et al., 2011; Marquina et al., 2023; Visan &Negut, 2024; Wan, Bao, & Burgess, 2022). Major limitations include burst control, polymer-acidification effects on labile drugs, and sterilization-related degradationissues that can be addressed through polymer blending, buffering excipients, or coreshell architectures (Gaydhane et al., 2023; Visan &Negut, 2024).

Nanocarriers, micelles, and targeted platforms

Polymeric nanoparticles, micelles, and polymer-lipid hybrids have matured significantly. Polymeric micelles enhance solubilization and tumor targeting via the enhanced permeability and retention (EPR) effect, and modern designs now incorporate ligands and stimuli cleavable linkers to achieve site-specific release (Beach et al., 2024; Harun-Or-Rashid et al., 2023). These platforms are promising for poorly water-soluble anticancer agents, though their clinical translation depends on circulatory stability and manufacturing reproducibility (Mahajan et al., 2023; Marquina et al., 2023). Recent reviews identify micelles demonstrating both *in vivo* stability and ligand integrity as the most promising for clinical success (Beach et al., 2024).

Comparative performance (nanocarriers vs microspheres). Nanocarriers excel at systemic targeting and intracellular delivery (for nucleic acids or small molecules), whereas microspheres and depots are preferred for localized, long-duration release (Marquina et al., 2023; Wan, Bao, & Burgess, 2022). The selection depends on therapeutic goals, drug stability, and regulatory considerations;nanoparticles demand extensive biodistribution studies, while depots follow clearer device-based regulatory pathways (Marquina et al., 2023).

Polymers in tissue engineering and regenerative medicine

Tissue engineering scaffolds now integrate multiple functionalities: mechanical support, cell instructive cues, controlled release of bioactive agents, and,

increasingly, biosensing. Natural polymers such as collagen, gelatin, and chitosan provide biocompatible cell matrices, whereas synthetic polymers like PCL, poly(lactic-co-glycolic acid) (PLGA), and PEG derivatives offer tunable mechanical properties and degradation rates. Current advances focus on functionally graded scaffolds, bioinks for 3D printing, and nanocomposite hydrogels, enhancing vascularization and tissue integration (Clegg et al., 2024; Lu, Cai, & Hu, 2024; Mahajan et al., 2023). Smart and stimuli-responsive scaffolds. Hydrogels responsive to pH, enzymes, temperature, or redox conditions enable on-demand drug release synchronized with the body's healing phases. Such responsiveness reduces dosing frequency and promotes localized therapeutic activity, though material design must prevent premature activation or degradation (Lu et al., 2024). Recent preclinical and early-clinical evidence supports several hydrogel classes for wound and tissue repair (Clegg et al., 2024).

Comparative assessment

To strengthen scientific rigor, the selection and optimization of polymeric systems should be guided by comparative performance metrics that ensure therapeutic reliability and clinical applicability. These include the reproducibility of the release profile (burst versus sustained), mechanical matching with the target tissue, stability of the incorporated drug during processing and *in vivo* conditions, nature of biodegradation byproducts, and the scalability and robustness of sterilization methods. For instance, PLGA microspheres provide predictable degradation kinetics but may create acidic microenvironments that compromise the stability of protein-based drugs, while electrospun fibers offer high drug loading efficiency yet encounter significant challenges during scale-up manufacturing (Gaydhane et al., 2023; Visan &Negut, 2024). Similarly, polymeric micelles are highly effective for delivering hydrophobic molecules; however, their stability and pharmacokinetic behavior often necessitate additional modifications such as PEGylation or crosslinking to ensure prolonged systemic circulation and controlled release (Beach et al., 2024; Harun-Or-Rashid et al., 2023). Therefore, system selection must balance pharmacokinetics, biocompatibility, degradation behavior, and manufacturability to achieve optimal clinical outcomes (Marquina et al., 2023).

Predictive polymer engineering

A defining trend in polymer research is the integration of AI-driven materials informatics and additive manufacturing to accelerate polymer discovery and predict *in vivo* behavior (Lu et al., 2024). This data-driven paradigm enables rational selection of polymer chemistries and scaffold architectures tailored for therapeutic use, minimizing trial-and-error and facilitating regulatory acceptance. Future progress will depend on interdisciplinary collaboration across materials science, biomedical engineering, and regulatory sciences to deliver clinically impactful polymer systems (Clegg, 2024; Lu et al., 2024).

POLYMERIC PLATFORMS IN DRUG DELIVERY

Overarching design principles and tailored therapeutic approaches

The diverse polymeric platforms in drug delivery, spanning film coatings, capsules, vesicles, micelles, microspheres, nanoparticles, hydrogels, and gene vectors, collectively embody a unified, tailored polymeric approach to therapeutics (Figure 2.) built upon several overarching design principles (Kurul et al., 2025; Zhang et al., 2025a). At their core, these systems harness structure-function relationships that govern their therapeutic performance: biocompatibility and biodegradability for safe *in vivo* application and predictable clearance (Bachhav et al., 2025), amphiphilicity and self-assembly for organizing both hydrophilic and hydrophobic agents (Krishnan et al., 2022), stimuli-responsiveness for spatiotemporal control in response to pH, temperature, enzymes, or redox gradients (Rosario & Ma, 2024), and surface functionalization for selective targeting via passive or ligand-mediated routes

(Shanahan et al., 2025). These shared design principles create a modular framework where polymer selection, architecture, and function are rationally engineered for specific therapies, transforming conventional delivery into precision nanomedicine (Rodriguez-Cruz et al., 2025; Zhang et al., 2022). This progression from basic coatings to multi-responsive nanocarriers reflects the field's conceptual maturation (Balcerak-Woźniak et al., 2024). Diverse polymeric systems represent context-specific applications of these strategies, enabling protection from the GI tract environment, in situ depot formation, or targeted cytosolic release. Such conceptual linkage, transcending single-platform descriptions, is now central to advanced polymer-based therapeutics (Kurul et al., 2025).

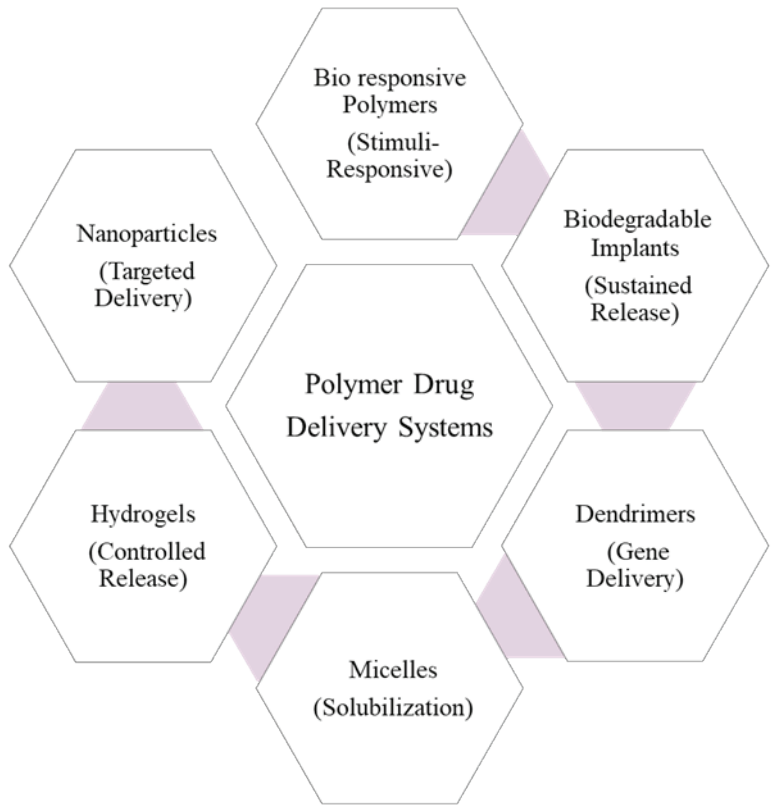

Figure 2. Polymeric platforms in drug delivery

Film coatings

Film coatings enhance both the mechanical integrity and release control of dosage forms (Rosario & Ma, 2024). Common polymer choices (shellac, zein, cellulose acetate phthalate, glyceryl stearate, Eudragit®) function as either rapid-release films or diffusion-controlling barriers (Rosario & Ma, 2024). More recent variants—such as pH-sensitive and nanocomposite coatings enable on-demand, location-specific drug release (Xu et al., 2025a). These innovations expand applications to transdermal, implantable, and ocular platforms, exemplifying how surface and stimuli-responsive engineering guide modern coating utility (Rosario & Ma, 2024; Xu et al., 2025b).

Capsules and encapsulation systems

Traditionally, both hard-shell and soft-shell capsules are made of gelatin and are used for various drugs requiring rapid release. Hydroxypropyl methylcellulose (HPMC) capsules, favored for plant-based and stability advantages, have gained wide acceptance (Al-Tabakha, 2010; Zhang et al., 2025a). Latest strategies feature ultra-thin polymer shells, hybrid encapsulation, and biodegradable nano-/micro-capsules for

targeted and delayed delivery (Zhang et al., 2025b). These advances in capsule materials and architectures illustrate modular polymer adaptation for modern pharmaceutical demands.

Polymer vesicles (polymersomes)

Polymersomes are self-assembled vesicles from amphiphilic block copolymers or graft copolymers, offering high stability and tunable permeability for targeted or triggered release. Smart vesicles offer co-delivery, imaging, and sequential release via multi-compartmental structures (Krishnan et al., 2022; Yetisgin et al., 2025), highlighting the design flexibility that distinguishes polymersomes from liposomes.

Polymeric micelles

Micelles self-assembled from amphiphilic copolymers enable solubilization and targeting of poorly water-soluble drugs in a stable core–shell structure (Kehrein et al., 2024; Krishnan et al., 2022). Recent variations include actively targeted micelles, enzyme or pH-responsive versions, and scalable microfluidic manufacturing aimed at translation to clinical use (Kehrein et al., 2024; Li et al., 2025a). The synergy of self-assembly, ligand targeting, and stimuli-responsiveness positions micelles as dynamic platforms for next-generation therapies.

Polymeric microspheres and microcapsules

Microspheres and microcapsules encapsulate both hydrophilic and hydrophobic agents, releasing drugs via engineered core–shell structures (Shendge et al., 2024; Sumathi, 2025). Modern approaches, such as multi-layering, in situ forming capsules, and ligand-functionalization, advance the targeting and dynamic release control (Shendge et al., 2024; Wan, Bao, & Burgess, 2022). Such developments demonstrate how design principles like biodegradability and functionalization extend microspheres to multifunctional therapeutic carriers.

Polymeric nanoparticles

Nanoparticles below 1 μm allow precise release kinetics, improved stability, and effective targeting when constructed from biodegradable polymers (e.g., PLGA) (Geszke-Moritz & Moritz, 2024; Islam et al., 2025). Newly engineered versions with ligand conjugation, hybrid systems, and multimodal properties have matured to preclinical and clinical application, uniting targeting, imaging, and on-demand release (Kaur et al., 2023; Kurul et al., 2025; Mahajan et al., 2022; Shanahan et al., 2025).

Polymeric hydrogels

Hydrogels of hydrophilic polymer networks excel for local/systemic delivery, wound healing, and tissue applications, thanks to tunable porosity and compatibility (Lohani et al., 2025; Shergujri et al., 2025). Stimuli-responsive, nanoparticle-loaded, and 3D-printed hydrogels now enable targeted, sustained, and tissue-integrated therapies (Delgado-Pujol et al., 2025; Karchoubi et al., 2024; Lohani et al., 2025).

Polymeric vectors for gene delivery

Polymeric vectors shield nucleic acids from degradation and facilitate cell uptake in RNA-based therapies. Recent breakthroughs include polymer-lipid hybrid nanoparticles and CRISPR delivery scaffolds, improving transfection and control (Gameiro et al., 2024; Hou et al., 2021; Maeki et al., 2024; Ullah et al., 2025). The design of these systems demonstrates functional integration across platforms from classic drug to advanced gene delivery.

Innovations in controlled and sustained release

Polymers form the foundation of controlled-release technology, leveraging biodegradable building blocks (PLGA, PCL, PEG) for tailored kinetics (Bachhav et al., 2025; Senthilkumar et al., 2025). Electrospun nanofibers, microneedles, and 3D-printed depots deliver localized, precise dosing (CeCe et al., 2024; Meng et al., 2024; Razzaghi, 2025). Integration of smart polymers, hybrid structures, and digital fabrication opens new frontiers for truly personalized, responsive therapy (Bernatoniene et al., 2025; Panchpuri et al., 2025).

SMART AND STIMULI-RESPONSIVE POLYMER GELS FOR PRECISION MEDICINE

Hydrogels have emerged as versatile platforms for advanced drug delivery, leveraging their water-absorbent, biocompatible nature to encapsulate diverse therapeutics. Their design, guided by polymer composition, crosslinking density, and responsiveness to environmental cues like pH or temperature, enables precise control over drug release, aligning with the demands of precision medicine (van der Meel et al., 2019).

Responsive hydrogel

pH-sensitive hydrogels, such as those based on poly(acrylic acid) (PAA) or chitosan, tailor drug release to specific physiological environments. For instance, PAA hydrogels achieved 80% methotrexate release within 48 hours at pH 5.5, mimicking tumor microenvironments, while limiting release at physiological pH (Jiang et al., 2019). Liu et al. (2017) developed an injectable thermoresponsive hydrogel based on alginate-graft-PNIPAM that effectively released ~70% of doxorubicin within 24 hours at 37 °C, demonstrating potential for localized, tumor-targeted chemotherapy.

Nanoparticle-infused gel matrices

Integrating nanoparticles into hydrogels improves drug stability and release kinetics. Alginate hydrogels embedded with PLGA nanoparticles sustained curcumin release over seven days, achieving 85% cumulative release and accelerating wound healing (Kass & Nguyen, 2022). Similarly, liposome-encapsulated gels protect drugs from degradation, while polymeric nanoparticles enhance tissue penetration and bioavailability (Abbas et al., 2022; Mou et al., 2022). Magnetic nanoparticles within gels enable site-specific delivery via external magnetic fields, offering promise for localized cancer therapies (Liu et al., 2020; Wang & Chang, 2023).

Biodegradable and dual-responsive gel platforms

Biodegradable hydrogels, crafted from natural polymers like chitosan, alginate, or hyaluronic acid, or synthetic polymers like PLGA and PEG, degrade into non-toxic byproducts, eliminating the need for surgical removal (Yuan et al., 2023). Dual-responsive hydrogels, sensitive to combined stimuli such as pH and temperature or electric fields, provide unparalleled precision. For example, pH- and temperature-sensitive gels target acidic tumor environments, while electro-responsive systems enable on-demand release (Naik et al., 2020; Yadav et al., 2021).

Targeted and nanocomposite gels

Functionalized hydrogels with ligands, such as antibodies or peptides, direct drugs to specific cells, enhancing therapeutic specificity for conditions like cancer (Deng et al., 2022; van der Meel et al., 2019; Wang & Chang, 2023). Nanocomposite gels incorporating carbon nanotubes, graphene, or silica nanoparticles bolster mechanical strength and drug-loading capacity, enabling sustained release and improved tissue penetration (Rao et al., 2022; Sun et al., 2021).

SMART POLYMERS FOR STIMULI-RESPONSIVE DRUG DELIVERY

Recent advances in polymer engineering have led to the development of smart polymers—materials capable of altering their physicochemical behavior in response to specific environmental stimuli. These stimuli can be physical (e.g., temperature, light, ultrasound, mechanical force), chemical (e.g., pH, ionic strength), or biological (e.g., enzymes, biomolecules), enabling highly controlled and site-specific drug release.Smart polymeric systems are designed to either passively target pathological tissues—leveraging the Enhanced Permeability and Retention (EPR) effect—or to actively engage in triggered delivery. Biochemical targeting, in contrast, involves conjugating specific ligands (e.g., antibodies, peptides) to polymer carriers for precise cellular interactions. In triggered systems,

drug release is activated by external or internal cues, aligning with the core principles of precision medicine, which further refines delivery specificity, ensuring drugs are released only under designated conditions (Kaur et al., 2014; van der Meel et al., 2019). Smart polymers thus offer innovative solutions for personalized, responsive therapeutics.

3D-PRINTED POLYMERIC SCAFFOLDS IN REGENERATIVE MEDICINE

Three-dimensional (3D) printing of polymeric scaffolds is revolutionizing the landscape of precision medicine and regenerative therapies by enabling the fabrication of patient-specific structures with complex anatomical geometries and tailored mechanical properties. This technology integrates biocompatible polymers with digital design, facilitating the creation of scaffolds that closely mimic native tissues, guide cellular behavior, and support controlled drug delivery (Anand et al., 2020a, 2020b; Qi et al., 2025). The following sections outline innovations across bone, nerve, and spinal tissue engineering, highlighting how materials, architecture, and multifunctionality converge to push the boundaries of polymer-based scaffold design.

Biomimetic bone scaffolds

Oladapo et al. (2023) developed 3D printed composite scaffolds designed to replicate the hierarchical structure and mechanical strength of natural bone. By combining polyetheretherketone (PEEK) with bioceramic fillers, they achieved implants that not only possess stiffness compatible with cancellous bone but also promote bone cell proliferation. The team demonstrated that tunable porosity and pore geometry, optimized through computational modeling and additive manufacturing, can strike a balance between mechanical integrity and nutrient diffusion. Surface modifications, including nano-roughening and tailored wettability, further enhanced osteointegration by creating favorable microenvironments for osteoblast adhesion (Oladapo et al., 2021). Recent advances in PEEK-based scaffolds highlight immunomodulation and angiogenesis as additional functional dimensions. Zhao et al. (2025) fabricated a multifunctional astragalus polysaccharide (APS)-coated, strontium-doped bioactive glass (SrBG)-reinforced PEEK scaffold (APS/PSBPK) that promotes M2 macrophage polarization, reduces inflammation, and enhances vascularization alongside osteogenic differentiation. This scaffold demonstrated superior in vivo bone regeneration through synergistic immune regulation and growth factor signaling (Zhao et al., 2025). Similarly, Mi et al. (2024) showed that nano-hydroxyapatite (nHA) and carbon fiber (CF)-reinforced PEEK scaffolds fabricated by fused deposition modeling (FDM) exhibit enhanced bioactivity and mechanical properties suitable for load-bearing bone defects, with significant improvements in osteoblast adhesion and proliferation (Mi et al., 2024). Furthermore, Qi et al. (2025) demonstrated that 3D-printed bioceramic scaffolds can modulate immune microenvironments and counteract bone aging by delivering anti-osteoporosis drugs, providing a therapeutic strategy for osteoporotic bone defects (Qi et al., 2025). These findings collectively underscore how biomimetic scaffold design integrates structural, immunomodulatory, and bioactive features to optimize bone regeneration.

Natural polymer-based hydrogels: Alginate and Carrageenan

Biopolymers such as alginate and κ-carrageenan have gained attention for their intrinsic biocompatibility and gel-forming ability, rendering them ideal for scaffold fabrication via extrusion-based 3D printing. Stavarache et al. (2024a) successfully printed hydrogel scaffolds composed of sodium alginate and κ-carrageenan, demonstrating their suitability for cell culture and tissue regeneration applications. These scaffolds exhibited rapid gelation upon crosslinking and maintained structural fidelity, with high porosity and interconnectivity—attributes essential for vascularization and cell migration (Stavarache et al., 2024a). In a subsequent study, Stavarache et al. (2024b) introduced carboxymethyl cellulose (CMC)

to the alginate/κ-carrageenan blend, improving printability, mechanical strength, and moisture retention. These composite scaffolds retained high cytocompatibility and mechanical resilience, exhibiting resistance to collapse during handling. Such enhancements underline the adaptability of natural polysaccharide blends for replicating soft tissue architectures with precise dimensional control (Stavarache et al., 2024b). Additional studies further validate the versatility of alginate-based systems. Jahani et al. (2024) demonstrated that alginate-chitosan composite hydrogels with controlled rheological properties and crosslinking behavior yield scaffolds with enhanced mechanical strength and cellular integration for cartilage tissue engineering (Jahani et al., 2024). Chowdhury et al. (2025) incorporated nano-hydroxyapatite (nHAP) into alginate-gelatin formulations, tuning mechanical, rheological, and osteogenic properties for bone regeneration applications (Chowdhury et al., 2025). These findings collectively emphasize how strategic polymer blending and nanocomposite integration advance natural hydrogel scaffolds from simple matrices to mechanically robust, bioactive platforms.

Self-sensing and smart nanocomposite scaffolds

Schneider et al. (2024) introduced an advanced scaffold platform using 3D-printed PEEK reinforced with conductive nanofillers to create self-sensing smart nanocomposites. Incorporating carbon nanotubes and graphene nanosheets endowed the scaffold with piezoresistive sensing capabilities, enabling detection of micro-deformations—mimicking the self-monitoring behavior of native bone. These scaffolds demonstrated high compressive strength (≥ 80 MPa) combined with strain-monitoring resolutions below 0.1%, proving suitable for load-bearing orthopedic applications. Cytocompatibility assays confirmed that their conductive properties can support osteogenic differentiation, indicating potential for "smart implants" capable of real-time monitoring of bone healing (Schneider et al., 2024).Building on this paradigm, Zaszczyńska et al. (2024) reviewed piezoelectric polymers and ceramics for bone tissue engineering, emphasizing how piezoelectric scaffolds—particularly those based on polyvinylidene fluoride (PVDF), poly-L-lactic acid (PLLA), and barium titanate (BTO)—generate electrical signals in response to mechanical stress, promoting osteoblast activity and mineralization (Zaszczyńska et al., 2024). Li et al. (2025b) recently fabricated BTO/β-tricalcium phosphate (β-TCP) piezoelectric composite scaffolds using digital light processing (DLP) 3D printing; under ultrasound stimulation, these scaffolds exhibited significantly enhanced alkaline phosphatase activity and osteogenic gene expression, validating the therapeutic potential of piezoelectric biomaterials (Li et al., 2025b). The integration of sensing, actuation, and bioelectric stimulation into 3D-printed scaffolds reflects a transformative shift toward intelligent, responsive regenerative platforms.

Scaffold design for spinal cord regeneration

Khaledian et al. (2024) reviewed the latest developments in 3D-printed scaffolds aimed at repairing spinal cord injuries. Polymers such as poly(lactic-co-glycolic acid) (PLGA), PEEK, and polycaprolactone (PCL) were designed into anisotropic structures that aligned neural growth and accommodated gradient release of growth factors and chemokines. The 3D architecture incorporated microchannels to guide axonal extension, while polymer blends enabled sequential degradation, optimizing the timing of therapeutic release. *In vivo* studies in animal models showed that neuro-conductive scaffolds with VEGF-loaded microspheres supported neovascularization and improved functional recovery (Khaledian et al., 2024). These findings underscore the crucial role of polymer engineering not only in structural healing but also in precision-controlled biochemical signaling—vital for functional tissue regeneration.Further supporting this direction, Zhu et al. (2025) highlighted integrated 3D-printed BDNF/collagen/chitosan scaffolds that accelerate neural regeneration following spinal cord injury by providing structural support, biochemical cues, and controlled neurotrophic factor release (Zhu et al., 2025). Chen et al. (2024) reviewed biomaterial-based strategies for spinal cord repair, emphasizing that conductive polymer hydrogels (e.g., polypyrrole)

combined with electrical stimulation enhance axonal guidance and remyelination (Chen et al., 2024). Ma and Li (2025) demonstrated that 3D-printed scaffolds incorporating neural progenitor cells and growth factors using microscale continuous projection printing can promote host axonal extension and exogenous cell integration at injury sites (Ma & Li, 2025). Harley-Troxell et al. (2025) developed PLGA/graphene oxide nerve guidance conduits via 3D printing, showing improved biocompatibility and enhanced neural differentiation (Harley-Troxell et al., 2025). Collectively, these studies demonstrate that advanced 3D printing strategies, when coupled with multifunctional polymer composites, provide spatiotemporal control over neural regeneration and functional recovery.

POLYMER SYSTEMS IN THERAPEUTICS

Polymer-based therapeutic platforms have evolved from laboratory innovations into clinically relevant systems (Bai & Tirella, 2022; Tewari et al., 2022; Wang et al., 2023; Yusuf et al., 2023). These systems, incorporating widely approved polymers such as PEG, PLGA, and PCL, offer significant improvements in drug solubility, stability, targeting, and release kinetics, representing a cornerstone of modern pharmaceutical science (Desai et al., 2025; Önel, 2022; Palma, 2025; Thapa & Kim, 2023).

Recent years have seen rapid progress, particularly in oncology and anti-infective applications, driven by regulatory approvals and robust late-stage clinical trials (Abdullah et al., 2025; Alam, 2023; Jia et al., 2023; Nirmala et al., 2023). With more than 50 FDA- and EMA-approved polymer therapeutics as of 2025, the translational landscape is robust, yet faces challenges around scalability, immunogenicity, and complex-generic regulatory pathways (Gultepe et al., 2026; Patil et al., 2024; Scott et al., 2023). Recent and ongoing clinical investigations (Table 1.) and recent FDA/EMA approvals are summarized (Table 2.), with outcomes and status validated.

Table 1. Recent and ongoing clinical investigations of polymeric therapeutics (Phases 1–3, 2023–2025)

Trial Name/ID	Polymer System	Therapeutic Agent/ Indication	Status/ Completion	Key Outcomes/ Notes	Sponsor	Reference
SHIELD II (NCT02468778)	PLEX hydrogel (PolyPid)	Doxycycline / SSI prevention (colorectal surgery)	Completed (June 2025), NDA in 2026	38% SSI/mortality reduction, positive topline results	PolyPid Ltd.	PolyPid, 2025; ClinicalTrials.gov, 2025
OTX-TKI (NCT05695417)	Elutyx hydrogel insert	TKI/ Diabetic retinopathy	Ongoing, completes Q2 2026	Sustained retinal delivery; Phase 2 showed good tolerability	Ocular Therapeutix	ClinicalTrials.gov, 2025
STELLAR-303 (NCT05613124)	Polymeric nanoparticle (albumin)	Zanzalintinib /Renal cell carcinoma	Ongoing, completes Q4 2025	Tumor microenvironment modulation, FDA app. 2025	Exelixis	Exelixis, 2025; ClinicalTrials.gov, 2025
Explore-CKD (NCT05182840)	PLGA microsphere	Lorundrostat /CKD with hypertension	Ongoing, interim Q4 2025	Long-acting release; ASN presentation 2025	Mineralys	MineralysTherapeutics, 2025; ClinicalTrials.gov, 2025
ORIGIN 3 (NCT04716231)	PEGylated conjugate	Investigational biologic/ Myasthenia gravis	Ongoing, update Nov 2025	Immunomodulation, all enrollment is complete	Vera Therapeutics	VeraTherapeutics, 2025; ClinicalTrials.gov, 2025
HRS9531 Obesity (NCT05991598)	Polymeric LAI depot	GLP-1 agonist/ Obesity	Ongoing, Phase 3 at ObesityWeek 2025	3-month sustained release; weight management	Hengrui/ Kailera	Hengrui Pharma, 2025; ClinicalTrials.gov

Table 2. Recent FDA/EMA polymer drug approvals

Product Name	Polymer System	Agent / Indication	Approval Date	Notes / Sponsor	Reference
Inlexzo	Intravesical polymeric system	Gemcitabine/ BCG-unresponsive bladder CA	Sep 2025	Bladder gel, 1st for instillation/ PolyPid	FDA, 2025; EMA, 2025; PolyPid, 2025
Bondlido	Polymeric patch hydrogel	Lidocaine/ Postherpetic neuralgia	Sep 2025	Transdermal hydrogel/ Medherant/BioPharma	FDA, 2025; EMA, 2025; MedherantLtd, 2025
Dextenza*	Elutyx hydrogel insert	Dexamethasone/ Ocular (conjunctivitis, expansion)	2021, 2025 (Pediatric)	>24 hydrogel approvals, 30-day release	FDA, 2025; Ocular Therapeutix, 2025
Neulasta Onpro	PEG conjugate, on-body	Pegfilgrastim/ Neutropenia (biosimilar wave)	2024	2002 original; biosimilars 2022-24	FDA, 2025; AmgenInc, 2024
Lupron Depot	PLGA microspheres	Leuprolide/ Prostate cancer, endometriosis	Expansions 2023–24	Biodegradable, pediatric/ oncology doses	FDA, 2024; AbbottLaboratories, 2024
Nubeqa (EU)	Polymeric nanoparticle (albumin)	Darolutamide/ Prostate cancer (HRR+)	Q2 2025 (EMA)	Dual US/EU; expanded indication	EMA, 2025; Bayer AG, 2025
Trodelvy	Hydrophilic polymer conjugate	Sacituzumab govitecan / TNBC	Q3 2023 (EMA)	First-in-class ADC	EMA, 2023; GileadSciences, 2023
Columvi	PEG-bispecific antibody	Glofitamab/ DLBCL	Q2 2023 (EMA)	T-cell engager, polymer stabilized	EMA, 2023; Roche, 2023
Inaqovi	Oral polymeric combo	Decitabine/ cedazuridine/ AML	EMA 2023	Polymer for oral bioavailability	EMA, 2023; TaihoOncology, 2023
Voranigo	Poly-enabled small molecule	Vorasidenib/ CNS glioma	Sep 2025 (EMA)	First approved CNS penetrant	EMA, 2025; Servier, 2025

*Expansion or additional indication approvals.

FUTURE PERSPECTIVES AND EMERGING TRENDS

The future of polymer-based biomedical applications lies in the convergence of material science, biotechnology, and data-driven design. As personalized medicine gains momentum, polymers will play a critical role in tailoring drug delivery systems to individual patient profiles. The integration of AI and machine learning in polymer engineering is expected to revolutionize formulation optimization, enabling predictive modeling of polymer-drug interactions, release kinetics, and therapeutic outcomes.

A significant trend involves the development of multi-functional, stimuli-responsive polymers capable of responding to multiple physiological cues—such as pH, temperature, redox potential, and enzymatic activity—allowing on-demand, site-specific drug release with minimal off-target effects. These smart systems are being increasingly adapted for cancer therapy, gene delivery, and implantable biosensors.

Biodegradable and bioresorbable polymers will continue to be at the forefront, especially in the design of implantable devices, 3D-printed scaffolds, and injectable hydrogels for tissue engineering and regenerative medicine. Innovations in natural-synthetic hybrid systems are expected to harness the biocompatibility of natural polymers and the tunable functionality of synthetics, creating next-generation platforms with enhanced mechanical strength and biological performance.

Additionally, green polymer chemistry is gaining importance, driven by sustainability concerns. The shift toward eco-conscious, renewable, and non-toxic polymeric systems will be vital for aligning pharmaceutical development with global environmental goals.

Finally, regulatory harmonization and translational scalability remain critical challenges. Bridging the gap between laboratory-scale innovation and clinical-grade production will require robust manufacturing practices, interdisciplinary partnerships, and advances in polymer characterization and standardization.

In conclusion, polymer science stands at a transformative juncture. By embracing cross-disciplinary innovation and sustainability, future polymeric systems are poised to drive next-generation therapeutics—precise, responsive, patient-friendly, and globally accessible.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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