

ADVANCES IN CONTROLLED DRUG DELIVERY SYSTEMS

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Abstract: Controlled drug delivery systems are designed to regulate the amount of drug reaching the body over time rather than releasing the entire dose immediately. Their main purpose is to maintain drug exposure within a useful therapeutic range, reduce unnecessary fluctuations, decrease dosing frequency, and improve treatment convenience. This review summarizes the development and current principles of controlled drug delivery, beginning with conventional modified-release systems and extending to osmotic, transdermal, implantable, gastroretentive, stimuli-responsive, and nanocarrier-based platforms. The role of pharmacokinetic properties such as half-life, absorption, distribution, and therapeutic index is considered because these factors determine whether a drug is a suitable candidate for controlled release. Major release models, including zero-order, first-order, Higuchi, Hixson-Crowell, and Korsmeyer-Peppas approaches, are discussed as practical tools for interpreting release behaviour. The review also considers polymeric biomaterials, hydrogels, biodegradable polymers, liposomes, lipid nanoparticles, and microfluidic manufacturing. Recent directions include microneedles, three-dimensional printing, programmable dosage forms, stimuli-responsive carriers, and artificial-intelligence-assisted formulation. Although these technologies offer improved temporal and spatial control, translation is still limited by reproducibility, stability, dose dumping, toxicity, scale-up, sterilization, regulatory requirements, and the gap between laboratory and clinical performance. Future progress will depend on combining sound pharmacokinetic design with robust materials, manufacturing control, and patient-specific approaches.

Keywords: controlled drug delivery; sustained release; modified release; pharmacokinetics; release kinetics; polymeric biomaterials; osmotic systems; nanocarriers; stimuli-responsive delivery; targeted delivery; personalized drug delivery.

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1. INTRODUCTION

For many medicines, therapeutic success depends not only on the pharmacological activity of the drug but also on how the drug is presented to the body. A potent compound may still perform poorly if it is eliminated too quickly, absorbed incompletely, distributed to unwanted tissues, or produces concentrations that move outside the therapeutic range [1,3,20]. This understanding helped transform the dosage form from a passive carrier into an important part of therapy [21,22]. The foundations of controlled delivery were established through several landmark developments. Higuchi described mathematical relationships for drug release from matrices, providing a basis for comparing formulations [18,19]. The elementary osmotic pump demonstrated that a dosage form could approach constant-rate delivery under gastrointestinal conditions

[14]. Langer and Folkman subsequently showed that macromolecules could be released from polymeric matrices, helping establish the feasibility of sustained delivery for proteins and peptides [2,6]. The central pharmacokinetic idea is simple. Immediate-release dosing often produces repeated peaks and troughs in plasma concentration. For drugs with short half-lives or narrow therapeutic windows, these fluctuations can result in concentrations above the toxic range or below the minimum effective concentration. Controlled delivery attempts to regulate drug input so that it better matches drug elimination, thereby extending the time during which exposure remains therapeutically useful [1,10,11]. Controlled systems may also reduce dosing frequency and improve adherence. They can be particularly useful when prolonged treatment is required or when local delivery can reduce systemic exposure. However,

controlled release is not appropriate for every drug. Very short or very long half-lives, very large doses, narrow absorption windows, and certain rapidly acting drugs can make the approach impractical. Dose dumping, difficulty with dose adjustment, higher manufacturing costs, and more demanding quality and regulatory requirements are additional concerns [5,33]. Modern controlled delivery is moving beyond simple time-based release. Targeted nanocarriers, responsive biomaterials, external triggers, and programmable devices aim to control delivery spatially or conditionally, releasing a therapeutic agent closer to the site or time at which it is needed [46,47,51-59]. The goal is therefore not simply longer release, but more predictable and clinically useful control of therapeutic exposure.

2. CLASSIFICATION OF DRUG DELIVERY SYSTEMS

Terminology in drug delivery is not always used consistently. Immediate release describes dosage forms that provide rapid availability without a deliberate release-controlling feature. Modified release is the broader category in which release differs from immediate release. Delayed release postpones the beginning of release, as with enteric or colon-targeted systems. Extended or sustained release prolongs drug availability and commonly reduces dosing frequency. Controlled release generally implies a more deliberately regulated release rate, while targeted, pulsatile, and stimuli-responsive systems add spatial or conditional control [1,7,13,17]. Controlled systems can be classified in several complementary ways. By release pattern, they may be extended, controlled, pulsatile, biphasic, targeted, or stimuli-responsive. By mechanism, the major groups include diffusion-controlled, dissolution-controlled, osmotic, swelling-controlled, erosion-controlled, chemically controlled, ion-exchange, and externally regulated systems [1,25,26]. A single formulation may belong to more than one category. For example, a pH-responsive colon-targeted formulation can be delayed-release by pattern and stimuli-controlled by mechanism.

The most useful classification is often the one that connects the release profile with the clinical purpose. A system may be selected to provide rapid initial exposure followed by maintenance, maintain a relatively constant rate, produce pulses at defined times, or concentrate delivery at a particular site. Understanding the intended clinical profile helps the formulator select an appropriate material and mechanism.

Table 01: Classification of drug delivery systems by release pattern, representative technology, kinetic behavior, and typical use.

Class	Representative technology	Kinetic signature	Typical use
Immediate	Conventional	Rapid,	Rapid

Immediate release	tablet, capsule, solution	uncontrolled	onset; acute or rescue therapy
Delayed release	Enteric coating; colon-targeted capsule	Lag phase followed by release	Protect acid-labile drugs or target distal gut
Sustained/extended release	HPMC matrix; wax matrix; coated pellets	First-order or Higuchi	Reduce dosing frequency and smooth peaks
Controlled release	Osmotic pump; reservoir; transdermal patch	Approximately constant rate	Stable exposure when a controlled input is needed
Pulsatile/programmed	Rupturable coat; time-controlled tablet; actuated implant	Defined lag followed by pulse	Chronotherapy and intermittent delivery
Biphasic	Loading-dose layer plus sustained core	Initial burst plus maintenance	Rapid onset with prolonged effect
Targeted/stimuli-responsive	Ligand-decorated carrier; responsive nanoparticle	Site- or trigger-dependent	Increase local exposure and reduce unwanted.

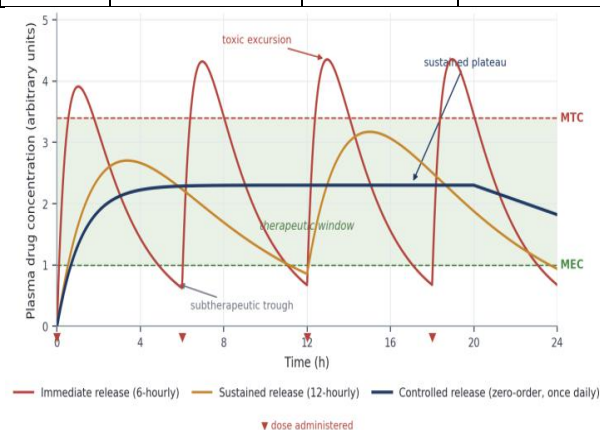


Figure 01: Schematic comparison of plasma drug concentration-time profiles for immediate-, sustained-, and controlled-release systems.

3. PHARMACOKINETICS OF DRUG DELIVERY SYSTEMS

Pharmacokinetics provides the quantitative basis for designing a controlled-release system. Before choosing

a formulation, the formulator should understand the drug's absorption characteristics, elimination half-life, volume of distribution, clearance, therapeutic window, and absorption site [1,10,11].

Absorption describes movement of the drug from the administration site into systemic circulation. For oral delivery, absorption is influenced by dissolution, lipophilicity, ionization, molecular size, transporters, and efflux mechanisms. Because controlled-release systems deliberately alter the rate at which drug becomes available for absorption, the relationship between dissolution and permeability is particularly important. The Noyes-Whitney relationship illustrates how diffusion, surface area, and solubility influence dissolution [11,24].

After absorption, distribution determines how much drug remains in plasma and how much reaches tissues. Volume of distribution is an apparent parameter linking the amount of drug in the body with its plasma concentration. Protein binding and tissue partitioning can change the relationship between total plasma concentration and pharmacological effect. Nanocarriers can alter distribution substantially because the carrier changes the biological behaviour of the associated drug [49,50].

The Biopharmaceutics Classification System (BCS) is also useful for oral controlled delivery [9]. Class I drugs have high solubility and permeability and are often suitable for conventional matrix or osmotic systems. Class II drugs have low solubility but high permeability, so release control may need to be combined with solubilisation. Class III drugs have high solubility but low permeability and may benefit from gastroretentive or permeation-enhancing strategies. Class IV drugs have both low solubility and low permeability and may require lipid systems, nanocarriers, prodrugs, or alternative routes [9].

Thus, controlled release should be designed around the biological behaviour of the drug rather than around the dosage form alone.

Table 02: Biopharmaceutics Classification System and implications for controlled delivery.

BCS class	Solubility / permeability	Main limitation	Typical strategy
I	High / High	Gastric emptying or formulation factors	Matrix or osmotic systems
II	Low / High	Dissolution	Combine solubilisation with rate control
III	High / Low	Permeation; narrow absorption window	Gastroretentive or mucoadhesive systems
IV	Low / Low	Both solubility	Nanocarriers, lipid systems,

		and permeability	prodrugs, or alternative routes
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4. DRUG RELEASE KINETICS

Release-kinetic models help describe how a drug leaves its dosage form and provide a framework for comparing formulations. They should be used as interpretive tools rather than as proof of a mechanism. Zero-order release describes a constant amount of drug released per unit time. It is desirable when maintaining a relatively stable input rate is important and can be approached with osmotic pumps, membrane-controlled reservoirs, transdermal systems, and some surface-eroding polymers [14,26,28]. First-order release describes a rate that depends on the amount of drug remaining in the dosage form. The release rate therefore decreases as the formulation becomes depleted. This behaviour can occur with water-soluble drugs in porous matrices and with simple dissolution-controlled systems [24,29]. The Higuchi model relates cumulative release to the square root of time and is widely used for diffusion-controlled matrices. Its assumptions include diffusion under sink conditions, a defined geometry, excess drug loading relative to solubility, and limited matrix swelling or dissolution [18,19,25]. The model is particularly useful for non-eroding or slowly eroding matrices, although its assumptions must be checked before interpretation. The Hixson-Crowell relationship accounts for changing surface area as particles dissolve and can be useful when dissolution changes the geometry of the dosage form [23,24]. The Korsmeyer-Peppas model is an empirical power-law approach that can help distinguish diffusion-dominated and anomalous release in suitable geometries [20,21,25]. Its exponent is geometry-dependent, so the value should not be interpreted without stating the dosage-form geometry and the assumptions used. The Peppas-Sahlin model separates contributions from diffusion and polymer relaxation and is useful for swellable hydrophilic matrices [22]. Baker-Lonsdale and Weibull models can also be used for spherical systems and flexible empirical fitting, respectively [27-30]. Model selection should not rely only on a high correlation coefficient. Adjusted statistical measures, information criteria, residual analysis, and mechanistic plausibility provide a more reliable basis for selecting a model [24,30]. Dissolution profiles are commonly compared using model-independent approaches such as difference and similarity factors, while in vitro-in vivo correlations can connect dissolution behaviour with pharmacokinetics. A Level A IVIVC provides the strongest point-to-point relationship and can be particularly valuable during formulation development and post-approval changes [11,31,32].

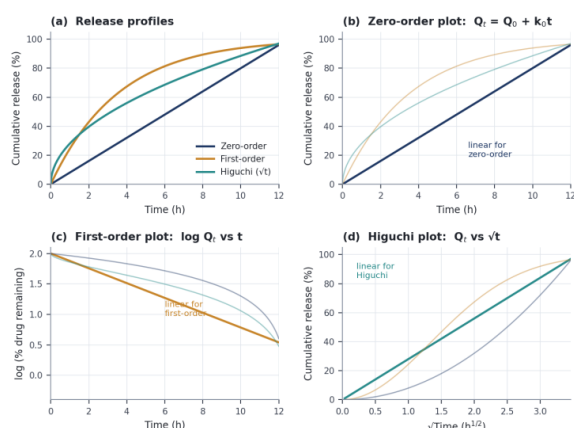


Figure 02: Characteristic zero-order, first-order, and Higuchi release profiles and their linearised representations.

5. CONVENTIONAL AND CONTROLLED DELIVERY SYSTEMS

Immediate-release dosage forms remain important because they are simple, inexpensive, robust, and well understood. They are particularly suitable when rapid onset is the main therapeutic requirement [1,7]. Their main limitation is that the formulation provides little control after administration. The full dose can become available rapidly, producing a high peak followed by decline governed largely by the drug's own elimination.

For drugs with narrow therapeutic windows, repeated immediate-release dosing may produce concentrations that move between ineffective and potentially toxic ranges. Frequent dosing can also make adherence more difficult in chronic therapy. Some drugs present additional challenges: acid-labile compounds may degrade in the stomach, drugs with extensive first-pass metabolism may lose much of their dose before reaching systemic circulation, and proteins and peptides are often unsuitable for conventional oral administration [1,5,7].

Controlled delivery places a rate-regulating mechanism between the drug and its absorption environment. The intended result is a smoother exposure profile, longer duration of action, fewer administrations, and, in some cases, lower peak-related toxicity. Local implants and targeted systems can further reduce systemic exposure by concentrating release near the site of action [4,39]. These benefits do not eliminate the need for careful formulation design. Controlled products may cost more to manufacture, can be difficult to adjust after administration, and may present serious risks if the rate-controlling structure fails. Crushing or splitting some products can also disrupt the intended release profile. Therefore, the decision to use controlled delivery should be based on the drug's pharmacokinetic needs, therapeutic objectives, and manufacturing feasibility rather than on the assumption that prolonged release is always preferable [5,33].

6. Controlled Drug Delivery: Mechanisms and Architectures

Controlled delivery systems use physical or chemical barriers to regulate drug transport. Each mechanism has characteristic materials, mathematical behaviour, and potential failure modes [1,12,25,26].

6.1 Diffusion-controlled systems

In reservoir systems, the drug is enclosed within a polymeric membrane and release is governed by membrane permeability. Fick's law relates release to membrane area, diffusion coefficient, partition coefficient, concentration gradient, and membrane thickness. When the core remains saturated, the concentration gradient can remain relatively constant and near-zero-order release may be achieved. Examples include ocular inserts, membrane-coated implants, transdermal patches, and coated multiparticulates [12,16]. Membrane failure is a critical concern because it can produce rapid release.

6.2 Dissolution-controlled systems

Dissolution control can be achieved by coating pellets with polymer layers of different thicknesses, embedding drug in slowly dissolving matrices, or altering the drug's own dissolution through salt formation, complexation, or polymorph selection. The approach is useful when dissolution itself is the rate-limiting step, but performance can be sensitive to gastrointestinal conditions [1,13].

6.3 Osmotically controlled systems

Osmotic pumps use water influx through a semipermeable membrane to generate pressure that drives drug release. Their main advantage is relatively predictable delivery that is less sensitive to gastrointestinal pH, agitation, and food than many conventional systems [14,15]. Push-pull designs extend the approach to poorly soluble drugs. Important limitations include the need for precise membrane manufacture and an accurately formed delivery orifice.

6.4 Swelling- and relaxation-controlled systems

Hydrophilic polymers such as HPMC, HPC, PEO, sodium alginate, xanthan gum, and carbomer hydrate after contact with gastrointestinal fluid. The resulting gel layer controls water penetration, drug diffusion, and polymer erosion. The relative contribution of diffusion and erosion depends on drug solubility, polymer properties, loading, and hydration conditions [33,35].

6.5 Erosion- and chemically controlled systems

Biodegradable polymers may release drug as the matrix undergoes bulk or surface erosion. PLGA is widely used for long-acting delivery, although its degradation can create an acidic microenvironment and may cause an initial burst or complex release profile [23,38-40]. Surface-eroding materials such as polyanhydrides can provide more predictable release under appropriate conditions. Chemically controlled systems may also attach the drug to a polymer through bonds that are cleaved by hydrolysis or enzymes.

6.6 Ion-exchange and gastroretentive systems

Ion-exchange resins bind ionizable drugs reversibly and can regulate release as the formulation encounters changing ionic conditions. Gastroretentive systems are useful when a drug is absorbed mainly in the upper gastrointestinal tract or has a narrow absorption window. Approaches include floating, mucoadhesive, swelling, and other retention mechanisms. Site-specific systems must remain intact until they reach the intended region, making physiological variability an important design consideration.

The practical choice of mechanism therefore depends on the desired release profile, drug properties, route, manufacturing capability, and acceptable risk. No single architecture is suitable for all drugs.

7. PRACTICAL ASPECTS OF CONTROLLED-RELEASE DOSAGE FORM DESIGN

Candidate selection is the first major decision. A drug is more likely to benefit when controlled release can meaningfully improve its pharmacokinetic profile, reduce dosing frequency, or limit peak-related exposure. Very short or very long half-lives, large doses, narrow absorption windows, and extensive first-pass loss may make conventional controlled release unsuitable [5,33].

Once a candidate is selected, the target release profile should be derived from pharmacokinetic requirements. The formulation should then be built around an appropriate polymer or rate-controlling mechanism. Drug loading, polymer fraction, particle size, membrane thickness, porosity, and geometry can all influence release. In hydrophilic matrices, excipients that increase or decrease pore formation and hydration can shift the release rate.

Burst release and dose dumping remain major safety concerns. Burst release may result from drug located near the formulation surface, membrane partitioning during manufacture or storage, pores formed during processing, or rapid hydration. Multiparticulate systems can reduce the consequences of failure because the dose is distributed among many individual units rather than concentrated in one structure.

Dissolution testing should be designed to detect meaningful differences between formulations. The choice of apparatus and medium should reflect the dosage form and expected biological environment. Biorelevant gastric and intestinal media can be valuable for poorly soluble or lipid-based systems, while long-acting parenterals may require specialized or accelerated methods [31,40].

Manufacturing and scale-up are closely linked to release performance. Coating uniformity, spray conditions, drying, particle strength, mixing, and other process variables can change the final release profile. Quality-by-design principles can help identify critical material attributes and process parameters and establish a suitable design space [70]. Stability testing is also essential because polymer ageing, moisture uptake,

recrystallization, residual solvent, and polymer degradation may alter release during storage. Sterility and biocompatibility become especially important for implants and injectable depots. Sterilization can alter biodegradable polymers, while residual processing agents may create toxicity concerns. The foreign-body response can also change local drug transport. These issues must be considered together with the intended duration of treatment and the need for safe removal or biodegradation.

Table 03: Practical design considerations and common risks in controlled-release development.

Consideration	Potential risk	Practical approach
Candidate selection	No meaningful pharmacokinetic advantage	Screen half-life, dose, solubility, absorption window, and therapeutic index
Drug loading	Too-rapid release or incomplete release	Determine suitable loading and polymer fraction experimentally
Dose dumping	Acute excessive exposure	Use robustness testing and appropriate dissolution challenges
Dissolution method	Important differences are missed	Use a discriminating method and, when appropriate, biorelevant media
Scale-up	Release profile changes at commercial scale	Apply quality-by-design and identify critical process parameters
Stability	Release changes during storage	Monitor polymer ageing, moisture.

8. BIOMATERIALS IN CONTROLLED DELIVERY

Material behaviour is at the centre of controlled drug delivery. Hydration, swelling, mechanical properties, degradation, permeability, and interactions with the biological environment determine how a formulation releases its payload [41,42,45]. An appropriate biomaterial should be biocompatible for its intended

route, chemically compatible with the drug, processable using the chosen manufacturing method, mechanically suitable, and stable for the required shelf life. If degradation is part of the design, its rate and products must also be acceptable. These requirements can be difficult to satisfy simultaneously, particularly for proteins and other sensitive biological molecules [41,67].

Natural polymers such as alginate, chitosan, hyaluronic acid, gelatin, collagen, albumin, silk fibroin, and cellulose derivatives offer useful biological and formulation properties. Alginate forms gels in the presence of calcium, chitosan provides mucoadhesion and can influence epithelial permeability, and cellulose derivatives such as HPMC are widely used in commercial controlled-release matrices [33,41-44].

Synthetic biodegradable polymers provide greater control over degradation and mechanical properties. PLGA is one of the most widely used materials for parenteral controlled release and has an established clinical history. PLA and PCL can provide longer degradation periods, while polyanhydrides and poly(ortho esters) offer surface-erosion mechanisms that can support more controlled release [23,36-40]. PEG is widely used to increase hydrophilicity and circulation time, although anti-PEG responses have encouraged investigation of alternatives [47,48]. Hydrogels are three-dimensional networks that absorb large amounts of water and can provide a tissue-like environment. Their mesh size, crosslink density, swelling, and degradation influence the movement of the drug. Crosslinking can be covalent, physical, or self-assembled, allowing hydrogels to be designed for injectable or in situ delivery [35,45].

Inorganic and hybrid materials, including mesoporous silica, calcium phosphate, bioactive glass, layered double hydroxides, magnetic materials, and metal-organic frameworks, provide additional options for high loading, local delivery, or stimulus-triggered release. Their long-term safety and toxicology, however, require careful evaluation before broad clinical use [47,50,53].

9. NANOCARRIERS FOR CONTROLLED AND TARGETED DRUG DELIVERY

Nanocarriers extend controlled delivery from temporal regulation toward spatial control. Their size, shape, surface charge, composition, and surface chemistry influence circulation, protein adsorption, cellular uptake, tissue penetration, and clearance [46,47,65]. Particle size is important because very small particles can undergo rapid renal clearance, whereas larger particles are more readily captured by organs of the mononuclear phagocyte system. Shape also affects cellular uptake and circulation. Surface charge influences protein adsorption and cell interaction; strongly positive surfaces can improve cellular binding but may also increase toxicity and rapid clearance. The protein corona that forms on nanoparticles can alter

their biological identity and may obscure targeting ligands, which helps explain why promising in vitro targeting does not always translate in vivo [47,48].

Liposomes are among the most clinically established nanocarriers. They can encapsulate both hydrophilic and lipophilic drugs and can be modified through lipid composition and surface chemistry. PEGylated liposomal doxorubicin demonstrated that changing drug distribution and pharmacokinetics can reduce toxicity while maintaining therapeutic activity [49,50]. Liposomal systems have since been developed for several anticancer, antifungal, and other therapeutics. Lipid nanoparticles are distinct from conventional liposomes and have become important for nucleic-acid delivery. Their ionisable lipids remain relatively neutral at physiological pH but become protonated in acidic endosomes, helping disrupt the endosomal membrane and release the payload into the cytoplasm. The clinical translation of siRNA and mRNA delivery has demonstrated the value of this platform [54,55]. Endosomal escape remains an important limitation, while formulation stability and reproducible manufacturing continue to influence performance. Microfluidic manufacturing addresses some of the reproducibility problems associated with conventional nanoparticle preparation. By controlling mixing and flow on a small scale, microfluidic devices can produce narrower particle-size distributions and more consistent encapsulation. Parallelisation can then be used to scale production while maintaining similar mixing conditions, making the approach relevant to translational manufacturing [57].

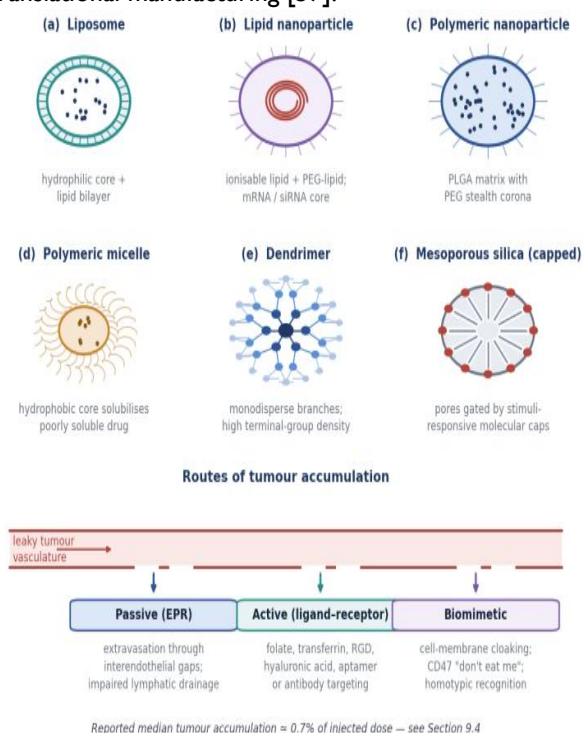


Figure 03: Representative nanocarrier architectures and targeting approaches relevant to controlled and targeted drug delivery.

10. EMERGING AND INTELLIGENT DELIVERY TECHNOLOGIES

Controlled delivery is increasingly moving toward programmable and patient-specific systems. Stimuli-responsive materials can be designed to react to internal signals such as pH, enzymes, redox conditions, or temperature, or to external triggers such as light, magnetic fields, and ultrasound [53,58-64]. The intended benefit is to release the drug when a particular biological or physical condition is present rather than continuously. Microneedles provide another route for controlled delivery. By creating microscopic pathways through the stratum corneum, they can improve access across the skin while remaining minimally invasive. Different microneedle designs can support rapid, sustained, or stimulus-responsive delivery. Important development issues include drug loading, mechanical strength, skin-to-skin variability, manufacturing consistency, and long-term stability [17]. Three-dimensional printing can produce dosage forms with customised geometry, internal structure, and drug distribution. This makes it possible to explore programmable release profiles and patient-specific dosage forms. Microfluidic platforms similarly support precise manufacture of nanoparticles and can be combined with organ-on-chip models to study delivery under more physiologically relevant conditions [52,57].

Artificial intelligence and machine learning are emerging as supporting tools rather than replacements for pharmaceutical experimentation. They can help identify relationships between formulation variables and release behaviour, predict promising compositions, and optimise experimental designs. Their value depends on the quality of the training data, external validation, interpretability, and integration with pharmaceutical quality systems. These approaches are promising, but their outputs still require experimental and clinical confirmation.

11. CHALLENGES, CLINICAL TRANSLATION AND FUTURE DIRECTIONS

Despite substantial progress, controlled drug delivery remains difficult to translate from an attractive laboratory formulation into a robust pharmaceutical product. The first challenge is reproducibility. Small changes in polymer properties, particle size, membrane thickness, drug loading, mixing, or drying can alter release behaviour. This problem becomes more significant as formulations become structurally complex. Safety is another major consideration. Dose dumping, local inflammation, degradation products, nanoparticle accumulation, immune responses, and unexpected interactions with biological systems must be assessed according to the route and duration of exposure. For implants and injectable depots, sterilization and foreign-body responses can influence both safety and release. Scale-up is closely connected to reproducibility. A formulation that performs well in a small laboratory batch may behave differently during

commercial manufacturing because mixing, heat transfer, coating, drying, and shear conditions change with scale. Quality-by-design approaches, well-defined critical quality attributes, and validated analytical methods are therefore important for controlling these differences [70]. Regulatory assessment can also become more demanding when a system combines several mechanisms, materials, devices, or external triggers. A clinically useful formulation must demonstrate not only a desirable release profile but also consistent manufacturing, stability, safety, and therapeutic performance. Future research is likely to focus on simpler but more reliable combinations of established technologies rather than increasing complexity for its own sake. Important directions include long-acting injectable systems, targeted and responsive nanocarriers, improved microneedles, programmable and printed dosage forms, microfluidic manufacturing, and data-driven formulation development. The most useful advances will be those that connect material properties and release mechanisms with clinically meaningful pharmacokinetic and therapeutic outcomes.

12. CONCLUSION

Controlled drug delivery has developed from relatively simple sustained-release matrices into a broad field that can regulate the timing, location, and conditions of drug release. Pharmacokinetic principles remain the foundation: the formulation must be designed around the drug's half-life, absorption behaviour, distribution, clearance, therapeutic window, and clinical objective. Release-kinetic models then help explain and compare the behaviour of the selected system. Conventional matrices, reservoir systems, osmotic pumps, biodegradable polymers, hydrogels, transdermal systems, and gastroretentive approaches remain important because their mechanisms are comparatively well understood. Nanocarriers, stimuli-responsive materials, microneedles, microfluidics, three-dimensional printing, and AI-assisted formulation are expanding the possibilities for targeted and personalised delivery. The major challenge is no longer simply demonstrating that a sophisticated delivery system can release a drug in a controlled way. The larger task is showing that the system can be manufactured reproducibly, remain stable, be safe, meet regulatory requirements, and provide a meaningful clinical benefit. Future progress will therefore depend on integrating pharmacokinetics, materials science, manufacturing, modelling, and patient-specific design. The most successful systems will be those that offer precise control without unnecessary complexity and that can be translated reliably from laboratory development to routine clinical use.

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15. CONFLICT OF INTEREST

Nil

16. INFORMED CONSENT

Not applicable

17. ETHICAL STATEMENT

Not Applicable.

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