INTERNATIONAL JOURNAL OF
PHARMACEUTICAL AND HEALTHCARE INNOVATION
journal homepage: www.ijphi.com

Review Article

OPEN ACCESS

Computer-Aided Design of Biomaterial-Based Drug Delivery Systems: Advances, Challenges, and Future Directions

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Article Info

Article history:

Manuscript ID:

IJPHI2512030108012026
Received: 25- DEC -2025
Revised : 03- JAN -2025
Accepted: 08- JAN -2026
Available online: JAN -2026

DOI:
https://doi.org/10.62752/ijphi.v3i2.233

Keywords:
Computer-aided design, drug delivery systems, biomaterials, computational modeling, personalized medicine, molecular dynamics.

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Abstract

The development of biomaterial-based drug delivery systems (DDS) represents a cornerstone of modern pharmacy, aiming to enhance therapeutic efficacy, reduce side effects, and improve patient compliance. Biomaterials, with their diverse properties and biocompatibility, form the backbone of many advanced DDS. The intricate interplay between biomaterial properties, drug release kinetics, and biological environments makes the rational design of these systems exceptionally complex. Traditional empirical methods of development are often time-consuming, costly, and inefficient. The integration of computer-aided design (CAD) has emerged as a transformative paradigm, leveraging computational power to model, simulate, and optimize DDS before physical prototyping. This review explores the convergence of computational science and pharmaceutical research. It provides a background on biomaterial-based DDS, discusses the primary classes of biomaterials used in CAD-driven design, and details key computational techniques such as molecular dynamics, finite element analysis, and machine learning. The applications of CAD in designing various DDS, including nanoparticles, implants, and hydrogels, are highlighted. Finally, the review paper outlines future directions, emphasizing the potential of artificial intelligence, high-throughput computational screening, and the path toward personalized digital medicine. The outlines of this review are that computer-aided design is an indispensable and evolving tool in pharmaceutical sciences, poised to revolutionize the rational, efficient, and patient-specific development of next-generation biomaterial-based drug delivery systems.

Introduction

The main objective of pharmaceutical science is to deliver a therapeutic drug to its target location at the appropriate concentration and for the intended period to achieve optimum efficacy with minimal side effects [1].To ensure therapeutic success and minimize potential side effects, advanced medical treatments necessitate tailoring medication composition and dose to each individual patient. In order to achieve even complicated bioactive systems, engineering methodologies for drug delivery system design and production require the combination and manipulation of materials and pharmaceuticals.[2]Biomaterial-based drug delivery systems (DDS) are designed to regulate the rate, time, and location of medication release within the body using either synthetic or natural materials. By increasing medication bioavailability, facilitating targeted distribution, and maintaining release over prolonged periods of time, these systems, which include nanoparticles, microparticles, hydrogels, and implants have transformed the treatment of many illnesses, including diabetes and cancer.[3]Since biomaterials come into direct touch with bodily fluids and tissues, they must have certain fundamental characteristics including biocompatibility, inertness, safety, stability, affordability, and ease of fabrication.[4]Biomaterials are used for therapeutic and diagnostic purposes and are designed to interact with live biological tissues. Previously, these materials were only used in medical devices to cure, replace, or enhance organ functions. However, it was later discovered that the phrase "non-viable" was unsuitable because biomaterials are used for purposes other than implanted devices.[5]But developing the best DDS is a complex task. This necessitates a thorough understanding of how the drug, biomaterial carrier, and changing physiological environment interact. A very complicated design space is produced by elements such as host inflammatory reactions, drug diffusion coefficients, and polymer degradation rates. Traditionally, the development process has been mostly dependent on empirical trial-and-error experimentation, which is resource-intensive and frequently fails to find the global optimal formulation. The adoption of computer-aided design (CAD) offers a powerful solution to these problems. In pharmacy, CAD refers to the use of computational models and simulations to predict the behavior of a DDS *in silico* (on a computer) before it is synthesized *in vitro* or tested *in vivo* [6]. This paradigm shift allows researchers to perform virtual experiments, screen thousands of potential formulations, and gain unprecedented insights into the underlying mechanisms governing drug release and biodistribution. This review explores the advances, challenges, and future directions of CAD for biomaterial-based DDS, positing that computational modeling is an indispensable tool for accelerating the rational design of sophisticated, effective, and personalized therapeutic systems.[6]

Types of Biomaterials for CAD-Based DDS

Computational models are only as good as the material parameters fed into them are. The choice of biomaterial dictates the fundamental mechanisms of drug release (e.g., diffusion, degradation, and swelling) and is therefore a critical input for any CAD simulation.[6]

Polymeric Biomaterials

Polymers are the most widely used class of biomaterials in DDS. They can be broadly categorized as natural (e.g., chitosan, alginate, and collagen) or synthetic (e.g., poly(lactic-co-glycolic acid) (PLGA), poly(ethylene glycol) (PEG), and poly(ε-caprolactone) (PCL)). Their properties, such as molecular weight, hydrophobicity, copolymer ratio, and degradation rate, are highly tunable. CAD models frequently incorporate these parameters to predict erosion profiles and diffusion-controlled release from polymeric microparticles, nanoparticles, and matrices.[7]

Lipid-Based Biomaterials

Lipid-based systems, including liposomes and solid lipid nanoparticles (SLNs), are valued for their biocompatibility and ability to encapsulate both hydrophilic and hydrophobic drugs. Computational models of these systems often focus on the self-assembly of lipids, stability of bilayer membranes, and partitioning of drugs between lipid and aqueous phases. [8]

Hydrogels

Hydrogels are three-dimensional hydrophilic polymer networks that swell in water. The mesh size and swelling behavior of these carriers in response to stimuli (e.g., pH and temperature) are key parameters for modeling drug diffusion. CAD is particularly useful for predicting the complex, often non-Fickian, drug release kinetics from these highly hydrated systems.[9]

Inorganic and Metallic Biomaterials

Mesoporous silica nanoparticles and gold nanoparticles are examples of inorganic carriers used in drug delivery. Models for these systems often focus on surface functionalization, pore size distribution, and drug adsorption/desorption isotherms to predict loading efficiency and release.[10]

Key Properties for DDS

Effective biomaterials for DDS must possess a combination of critical properties.

- **Biocompatibility:** The ability to perform its function without eliciting undesirable local or systemic responses in the host.[11] This is crucial to avoid toxicity, inflammation, and immune rejection.
- **Biodegradability/Bioresorbability:** For many applications, biomaterials should degrade into non-toxic components and be cleared from the body after their therapeutic function is complete. The degradation rate is critical for controlling drug release.[12]
- **Mechanical Properties:** The material must possess sufficient strength, elasticity, and stiffness to withstand physiological forces and maintain its structural integrity, particularly for implantable systems or those requiring specific shape retention.[12]
- **Drug Loading Capacity:** The ability to efficiently encapsulate or incorporate a significant amount of a therapeutic agent.[10]
- **Drug Release Kinetics:** The capacity to control the rate, duration, and pattern of drug release (e.g., sustained, pulsatile, triggered). This is often modulated by the degradation, diffusion, or swelling properties.[10]
- **Processability:** Ease of fabrication into desired sizes, shapes, and architectures (e.g., nanoparticles, fibers, hydrogels, and films). [11]
- **Modifiability:** The presence of functional groups that allow chemical modification, such as surface-targeting ligands or stimuli-responsive moieties. [12]

Fundamentals of Computer-Aided Design (CAD) in Biomaterial DDS

Computer-Aided Design (CAD) refers to the use of computer systems to assist in the creation, modification, analysis, or optimization of a design. In the context of biomaterial-based DDS, CAD is an umbrella term encompassing a wide array of *in silico* tools and methodologies employed to understand, predict, and ultimately accelerate the development of these complex systems.[12]

Overview of CAD Principles

The core principle of CAD in this domain is to replace or complement extensive physical experimentation with computational simulations.[13] This involves:

- **Modeling:** Creating a mathematical or algorithmic representation of the biomaterial, drug, and their environment. These models range from atomic-level descriptions to continuum modeling.[13]
- **Simulation:** Running the model under various conditions to predict its behavior (e.g., drug release profile, degradation rate, and mechanical response).
- **Analysis:** The simulation results were interpreted to gain insights into the system performance and design parameters.[13]
- **Optimization:** Iteratively modifying design parameters based on analysis to achieve desired outcomes (e.g., maximizing drug loading and controlling release kinetics) .[12]

Computational Techniques in CAD for DDS

A suite of computational techniques operating at different length and time scales is employed to model the DDS.[12]

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Molecular Dynamics (MD) Simulations

MD simulations model the interactions between atoms and molecules. In DDS design, MD is used to study fundamental interactions at the nano-scale, such as drug-polymer binding affinity, drug partitioning into lipid bilayers, and the conformation of surface ligands on a nanoparticle, which directly influence stability, loading, and release.[14] Enhanced force fields, faster algorithms, and high-performance computing (HPC) enable the simulation of larger systems and longer timescales, bridging mesoscale phenomena.[14]

Finite Element Analysis (FEA)

FEA is a powerful computational method for solving complex physical problems by dividing a system into a finite number of smaller and simpler elements (a mesh). In DDS, FEA is extensively used to solve the differential equations governing drug diffusion, polymer degradation, and fluid flow within and around a delivery system. It is the primary tool for modeling release from macroscopic implants and complex geometric scaffolds.[15] Integration with multiphysics solvers allows for the simultaneous modeling of mechanical deformation, fluid transport, and chemical reactions.[15]

Pharmacokinetic/Pharmacodynamic (PK/PD) Modeling

PK models predict the time course of drug concentration in different bodily compartments (e.g., plasma and tissues) after DDS administration. PD models link these concentrations to the resulting therapeutic and adverse effects of the drug. Integrating a CAD model of drug release from a DDS with a whole-body PK/PD model creates a powerful platform for predicting *in vivo* efficacy and optimizing dosage regimens.[16] Predicting the systemic drug exposure and efficacy profile of a DDS, optimizing dosing

regimens, and understanding the impact of sustained release on therapeutic windows are important.[17]

Machine Learning (ML) and Artificial Intelligence (AI)

ML algorithms can identify complex nonlinear patterns within large datasets without requiring explicit physical equations. In DDS development, ML is used to predict material properties, optimize formulation parameters (e.g., polymer type and drug loading) based on desired release profiles, and design novel biomolecules. AI can accelerate the discovery process by navigating the vast design space more efficiently than traditional methods.[17] They can be used to predict biomaterial properties (e.g., degradation rate and mechanical strength) based on chemical structure, forecast drug release profiles under various conditions, and even predict drug solubility or partition coefficients in novel biomaterial formulations.[17]

Applications of CAD in Biomaterial-Based DDS

The application of CAD has led to significant advancements in various aspects of biomaterial-based DDS, demonstrating its potential to transform pharmaceutical development.[17]

Controlled Release Systems

CAD is extensively used to model and optimize drug release kinetics from matrices, reservoir devices, and erodible systems. For example, FEA models can accurately predict the complex, often tri-phasic release profile of drugs from PLGA microspheres, informing decisions regarding the polymer molecular weight and lactide:glycolide ratio.[18]

Targeted Nanocarriers

The design of nanoparticles for active targeting (e.g., using antibodies) involves optimizing the ligand density, spacer length, and surface chemistry to maximize binding to target cells while minimizing opsonization. Multiscale modeling, which combines MD for ligand-receptor binding and FEA for particle distribution in tumors, is a key application of CAD. FEA and CFD have been used to model the diffusion of drug-loaded hydrogels or microparticles within tumor microenvironments, predicting drug distribution and efficacy in solid tumors.[18]

Stimuli-Responsive DDS

For systems designed to release drugs in response to specific triggers (pH, enzymes, and ultrasound), CAD helps model the response mechanism. For instance, models can simulate the pH-dependent swelling of a hydrogel or ultrasound-induced cavitation that disrupts a nanocarrier, allowing for precise tuning of the trigger threshold. Computational modeling can help design materials with precise lower critical solution temperatures (LCST) or upper critical solution temperatures (UCST), ensuring drug release at specific physiological temperatures.[19]

Tissue Engineering Scaffolds

Combining DDS with scaffolds for regenerative medicine requires the design of structures that provide mechanical support while releasing growth factors in a spatiotemporally controlled manner. FEA is crucial for modeling drug diffusion through porous architecture and correlating it with tissue in growth patterns.[19]

Patient-Specific PK/PD

PBPK models can be parameterized with individual patient data (e.g., age, weight, organ function) to predict how a specific DDS will perform in that individual, allowing for optimized dosing and formulation adjustments.[20]

Challenges in Computer-Aided Design of DDS

Despite its promise, the widespread adoption of CAD in pharmaceutical development faces several hurdles.[20]

Model Complexity and Multiscale Integration

A major challenge is bridging the gap between models of different scales. An atomistic MD simulation of a drug-polymer interaction operates on nanometer and nanosecond scales, whereas drug release and therapeutic effects occur over millimeters and weeks. Developing robust multiscale models that seamlessly transfer information across these scales remains a formidable task.[21]

Data Availability and Parameterization

Computational models require accurate input parameters (e.g., diffusion coefficients, degradation rate constants, and binding affinities). These data are often scarce, difficult to measure experimentally, and highly variable between studies. The lack of high-quality, standardized data can lead to inaccurate model predictions and limit model utility.[22]

Biological Complexity and Variability

Models must account for the immense complexity and heterogeneity of the *in vivo* environment, including dynamic biological barriers, immune responses, and patient-to-patient variability. Capturing this complexity in a computationally feasible model is challenging. Most current models are simplifications that may not fully represent true biological scenarios.[21]

Validation and Regulatory Acceptance
For CAD to be used in regulatory submissions, the models must be thoroughly validated against robust experimental data. The framework for the verification, validation, and qualification of computational models in the pharmaceutical industry is still evolving. Gaining regulatory acceptance for *in silico* trials and model-based drug development is an ongoing process.[22]

Interoperability
Different CAD tools and platforms often lack seamless interoperability, making it difficult to create integrated workflows that combine various simulation techniques and experimental data.[22]

User Expertise
The development and utilization of sophisticated CAD models require specialized expertise in computational science, materials science, pharmacology, and biology, creating a barrier to their broader adoption.[23]

Future Directions
The field of CAD for biomaterial-based DDS is rapidly evolving, driven by advancements in computing power, artificial intelligence, and a deeper understanding of biological systems. Several key trends are poised to shape the future of AI.[23]

AI-Driven Generative Design and High-Throughput Screening
Future platforms are likely to use generative AI models to design entirely new biomaterial constructs and DDS formulations optimized for specific criteria. Coupled with high-throughput *in silico* screening, this approach can rapidly identify lead candidates from millions of possibilities, drastically reducing development timelines. Beyond predictive modeling, deep learning architectures (e.g., generative adversarial networks, variational autoencoders) can be used to generate novel biomaterial structures or DDS designs with desired properties, rather than just optimizing existing ones.[23]

Digital Twins for Personalized Medicine
A "digital twin" is a virtual replica of a patient's physiology that can be used to simulate the treatment. The integration of patient-specific data (genomics and imaging) with advanced DDS models could enable the true personalization of therapy, where a drug delivery system is custom-designed and its performance simulated in the virtual twin before being administered to the patient. Digital twins could enable personalized dosing adjustments, predict system failure, and guide interventions, moving towards a truly predictive and personalized form of medicine.[24]

Enhanced Multi-Physics and Multi-Scale Models
Advances in computing power and algorithms will enable the development of more sophisticated models that concurrently solve chemical reactions, fluid dynamics, mechanical stresses, and electrical signals. This will provide a more holistic and accurate prediction of DDS performance in the body. Development of advanced multi-physics solvers that can simultaneously model mechanical forces, chemical reactions (e.g., degradation), fluid dynamics, and biological responses (e.g., cellular uptake, immune response) within a single framework.[25]

Open-Source Platforms and Collaborative Science
The development of open-source, user-friendly computational platforms will democratize access to CAD tools for pharmaceutical researchers. Furthermore, collaborative databases for material properties and model validation data are crucial for improving model accuracy and reliability across the field. Establishing robust platforms for sharing well-curated experimental and simulation data is crucial for training more powerful AI models and validating complex multi-scale simulations. [25]

CONCLUSION
The computer-aided design of biomaterial-based drug delivery systems has evolved from a theoretical concept into a practical and powerful tool in the pharmaceutical arsenal. By leveraging computational techniques across molecular, microscopic, and macroscopic scales, CAD enables a deeper mechanistic understanding and a more rational and efficient design process. Although challenges related to biological complexity, data integration, and validation persist, ongoing advancements in artificial intelligence, computational power, and multiscale modeling are steadily overcoming these barriers. The future points toward a new era of digital pharmaceutics, where *in silico* models guide the development of highly effective, personalized therapies, ultimately translating to improved patient outcomes and a more efficient drug development pipeline. The integration of CAD is no longer merely an advantage but is becoming a necessity for innovating the next generation of smart drug delivery systems.

Submission Declaration:
This manuscript has not been published previously and is not under consideration for publication in any other journal. The authors confirm that this work is original and have read and approved the final manuscript for submission.

Conflict Of Interest:
The authors declare that they have no competing financial interests or personal relationships that could have influenced the work reported in this study.

Declarations Of Competing Interest:
The authors declare that they have no competing financial interests or personal relationships that could have influenced the work reported in this paper.

Ethics Statement:
This review paper involves no experimental research, human subjects, or animal studies that require ethical approval; instead, it is based entirely on publicly available literature. For academic openness and integrity, all the acknowledged sources were appropriately referenced. I have done everything in my power to provide an objective, accurate, and thorough literature review free from any conflicts of interest that could affect the interpretation of the data. This study did not involve any instances of scientific misconduct, data manipulation, or plagiarism. Let me know if you need refinement

Funding No: funding was received for conducting this study

REFERENCES

[1]. Allen, T. M., & Cullis, P. R. (2013). Liposomal drug delivery systems: From concept to clinical application. *Advanced Drug Delivery Reviews, 65*(1), 36–48. https://doi.org/10.1016/j.addr.2012.09.037.

[2]. Guzzi, E. A., and Tibbitt, M. W. (2020). Additive manufacturing of precision biomaterials. Adv. Mater. 32:1901994. doi: 10.1002/adma.201901994.

[3]. Liechty, W. B., Kryscio, D. R., Slaughter, B. V., & Peppas, N. A. (2010). Polymers for drug delivery systems. *Annual Review of Chemical and Biomolecular Engineering, 1*, 149–173. https://doi.org/10.1146/annurev-chembioeng-073009-100847.

[4]. Nair LS, Laurencin CT. Biodegradable polymers as biomaterials. Progress in polymer science. 2007; 32(8-9):762-98.

[5]. Ghasemi-Mobarakeh L, Kolahreez D, Ramakrishna S, Williams D. Key terminology in biomaterials and biocompatibility. Current Opinion in Biomedical Engineering. 2019; 10:45-50.

[6]. Lin, C. C., & Metters, A. T. (2006). Hydrogels in controlled release formulations: Network design and mathematical modeling. *Advanced Drug Delivery Reviews, 58*(12-13), 1379–1408. https://doi.org/10.1016/j.addr.2006.09.004.

[7]. Leja K, Lewandowicz G. Polymer biodegradation and biodegradable polymers-a review. Polish Journal of Environmental Studies. 2010; 19(2).

[8]. Siu, S. W., Pluhackova, K., & Böckmann, R. A. (2014). Optimization of the OPLS-AA force field for long hydrocarbons. *Journal of Chemical Theory and Computation, 8*(4), 1459–1470. https://doi.org/10.1021/ct200908r.

[9]. Lin, C. C., & Metters, A. T. (2006). Hydrogels in controlled release formulations: Network design and mathematical modeling. *Advanced Drug Delivery Reviews, 58*(12-13), 1379–1408. https://doi.org/10.1016/j.addr.2006.09.004.

[10]. Prasad K, Bazaka O, Chua M, Rochford M, Fedrick L, Spoor J, Symes R, Tieppo M, Collins C, Cao A, Markwell D. Metallic biomaterials: Current challenges and opportunities. Materials. 2017; 10(8):884.

[11]. Williams DF. On the mechanisms of biocompatibility. *Biomaterials*. 2008;29(20):2941-2953. doi:10.1016/j.biomaterials.2008.04.023.

[12]. He, X., Cui, Q., Liu, J., & Zhang, Y. (2018). Computer-aided design of drug delivery systems: Advances and challenges. *Journal of Controlled Release*, *273*, 113–122.

[13]. Yew, Y. P., Choy, Y. P., & Tan, A. L. (2017). A review of current computational tools in nanoparticle drug delivery research. *Drug Delivery*, *24*(1), 1698–1710.

[14]. Durrant, J. D., & McCammon, J. A. (2011). Molecular dynamics simulations and drug discovery. *BMC Biology, 9*(1), 71. https://doi.org/10.1186/1741-7007-9-71

[15]. Lape, N. K., Nuxoll, E. E., & Arnold, M. A. (2020). Finite element analysis of diffusion and release of dissolved solute from polymeric drug delivery devices. *Industrial & Engineering Chemistry Research, 59*(6), 2531–2542. https://doi.org/10.1021/acs.iecr.9b05853.

[16]. Siegwart, D. J., Whitehead, K. A., & Langer, R. (2019). Engineering nano- and microparticles to tune immunity. *Advanced Materials, 31*(4), 1801605. https://doi.org/10.1002/adma.201801605.

[17]. Bannigan, P., Aldeghi, M., Bao, Z., Häse, F., Aspuru-Guzik, A., & Allen, C. (2021). Machine learning in drug delivery. *Annual Review of Biomedical Engineering, 23*, 1–29. https://doi.org/10.1146/annurev-bioeng-090220-093056.

[18]. Chen, J. Y., Li, S. Q., & Zheng, Y. F. (2012). Finite element analysis of drug release from porous biodegradable polymeric scaffolds. *Journal of Materials Science: Materials in Medicine*, *23*(3), 769–777.

[19]. Li, X., Ma, Z., & Fan, X. (2019). Molecular dynamics simulation of pH-responsive hydrogels for controlled drug release. *Macromolecules*, *52*(12), 4734–4743.

[20]. Rowland, M., Peck, C., & Tucker, G. (2011). Physiologically-based pharmacokinetics in drug development and regulatory science. *Annual Review of Pharmacology and Toxicology*, *51*, 45–73.

[21]. Wang, Z. G., Chen, H., & Zhou, S. X. (2015). Large-scale molecular dynamics simulations of polymer interfaces and nanocomposites. *Progress in Polymer Science*, *46*, 103–139.

[22]. Gorissen, S. H., Vicente, J., & Bastian, C. (2022). The challenge of parameterization in computational modeling of drug delivery. *Journal of Controlled Release, 347*, 1-11. https://doi.org/10.1016/j.jconrel.2022.04.033.

[23]. Ma, S., Gong, X., Li, X., & Liu, P. (2021). Deep generative models in drug discovery: A comprehensive review. *Journal of Chemical Information and Modeling*, *61*(12), 5851–5867.

[24]. Corral-Acero, J., Margara, F., Marciniak, M., Rodero, C., Loncaric, F., Feng, Y., ... & Lamata, P. (2020). The 'Digital Twin' to enable the vision of precision cardiology. *European Heart Journal, 41*(48), 4556–4564. https://doi.org/10.1093/eurheartj/ehaa159.

[25]. He, X., Cui, Q., Liu, J., & Zhang, Y. (2018). Computer-aided design of drug delivery systems: Advances and challenges. *Journal of Controlled Release*, *273*, 113–122.