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Integration of AI-Driven QSAR Modelling and Organ-on-Chip Technology in Ophthalmic Medicine

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1. Abstract

AI-driven pharmacology in ophthalmology addresses critical challenges in drug discovery for ocular diseases like age-related macular degeneration (AMD) and diabetic retinopathy, where physiological barriers and complex biomarkers hinder traditional methods. This review outlines AI's role in accelerating target identification, lead optimization, and clinical translation to enhance precision medicine and reduce development timelines.

1.1. Design/Methodology/Approach

A systematic analysis of recent literature integrates machine learning models (e.g., deep docking, QSAR), generative AI for novel compound design, and multi-omics data with organ-on-chip simulations. Key platforms like Panda Omics prioritize druggable targets, while predictive modelling evaluates pharmacokinetics and toxicity in preclinical ocular models.

1.2. Findings

AI shortens drug development from years to months, as in the 18-month INS018_055 fibrosis candidate adaptable to ophthalmic fibrosis. Applications include VEGF inhibitors for AMD via binding predictions and peptide designs for bacterial keratitis. Clinical trials benefit from AI-optimized patient stratification using multimodal imaging biomarkers, improving efficacy forecasts and minimizing failures. It advances ophthalmic pharmacology by bridging computational innovation with real-world barriers, guiding future research toward personalized therapies.

2. Introduction

The increasing prevalence of ocular diseases such as age-related macular degeneration (AMD), diabetic retinopathy, glaucoma, and infectious keratitis presents significant challenges for effective therapy development. The eye's unique anatomy, comprising

multiple protective barriers like the corneal epithelium, conjunctiva, and blood-retinal barrier, limits the bioavailability and penetration of pharmacological agents [1]. Traditional experimental approaches in drug development are time-consuming, costly, and often yield insufficient translational success due to interspecies differences in animal models and oversimplified in vitro systems. Artificial intelligence (AI) offers transformative potential in pharmacology by enabling high-throughput virtual screening, mechanistic modelling, and personalized medicine. Among AI tools, quantitative structure-activity relationship (QSAR) modelling employs computational predictions based on molecular descriptors to estimate biological activities, facilitating rapid lead optimization [2]. Meanwhile, organ-on-chip (OoC) technology replicates human ocular microenvironments within microfluidic systems, closely mimicking physiological and pathological conditions, thereby enhancing preclinical testing relevance. This review explores the current state of AI-driven QSAR and OoC platforms in ophthalmic pharmacology, highlighting key methodologies, breakthroughs in drug discovery, translational implications, and existing barriers to clinical implementation [3].

3. Methodology

An extensive systematic literature review was conducted, covering peer-reviewed publications, patents, and clinical trial databases until 2025, focusing on AI applications in ophthalmic drug development. Key search terms included "QSAR modelling," "organon chip," "ophthalmology pharmacology," and "AI-driven drug discovery." Data extraction concentrated on QSAR model types (2D, 3D, machine learning-based), descriptor calculations (physicochemical, topological, electrostatic), and validation strategies (internal cross-validation, external test sets) [4]. QSAR modelling has matured to incorporate a diverse array of computational techniques aimed at enhancing prediction accuracy and applicability. Classic QSAR methods rely on linear regression models correlating selected molecular descriptors with biological activity; however, their limitations in capturing com-

plex molecular interactions have spurred adoption of machine learning (ML) and deep learning (DL) approaches. Popular ML algorithms in QSAR include Random Forests, Support Vector Machines (SVM), Gradient Boosting, and Artificial Neural Networks (ANN), each offering strengths in handling nonlinear data patterns and multivariate descriptor spaces. Deep learning, particularly convolutional neural networks (CNNs) and graph neural networks (GNNs), enables automatic feature extraction from molecular graphs, improving lead optimization by

identifying subtle structure-activity relationships that manual descriptor calculation may overlook. Importantly, these models undergo rigorous validation schemes including k-fold cross-validation, external validation on blind test sets, and applicability domain assessments to ensure reliability. Explainable AI (XAI) techniques are increasingly integrated to decipher model decisions, thus improving interpretability crucial for regulatory acceptance. In ophthalmology, these sophisticated QSAR models drive iterative design of VEGF inhibitors and novel peptides, guiding synthesis of molecules with optimized efficacy and minimized toxicity profiles [5].

For OoC systems, studies were selected based on their demonstration of microfluidic platforms replicating corneal, retinal, or vitreous body physiology, with emphasis on integration with AI for image and multi-omics data analytics. Special attention was afforded to studies offering translational insights, including pharmacokinetic modeling, toxicity predictions, and personalized therapy simulations. The synthesized review aims to provide an interdisciplinary perspective bridging computational, engineering, and clinical ophthalmology domains.

Organ-on-chip platforms in ophthalmic research emulate key anatomical and physiological features of eye tissues via microfabricated devices incorporating living cells and extracellular matrix components. Cornea-on-chip systems typically consist of epithelial and endothelial cell layers separated by a membrane, exposed to dynamic fluid flow simulating tear film dynamics and blinking. These devices enable real-time monitoring of drug permeability, barrier integrity, and inflammatory responses. Retina-on-chip models integrate retinal pigment epithelial cells, photoreceptors, and microvascular endothelial cells within microfluidic chambers mimicking choroidal blood flow and oxygen gradients, crucial for studying retinal diseases and evaluating anti-angiogenic therapies. Vitreous body-on-chip designs incorporate gel-like matrices to replicate vitreous humor's viscoelastic properties, facilitating drug diffusion studies. Advanced OoC systems embed sensors for pH, oxygen, and mechanical forces, yielding multidimensional data streams. Integration with AI algorithms for image analysis and pattern recognition enhances the interpretive value of experiments, allowing for dynamic pharmacodynamic modeling and identification of subtle drug-induced changes at cellular and tissue levels [6].

3.1. Case Studies in Ophthalmic Drug Development

A notable case involves the AI-assisted design of INS018_055, an anti-fibrotic agent first developed for pulmonary fibrosis, which was adapted for ocular fibrosis therapy using QSAR-guided lead optimization and OoC validation. QSAR models predicted structure modifications that improved binding affinity to fibrotic mediators, while OoC systems mimicked fibrotic retinal microenvironments for efficacy and toxicity assays, enabling a preclinical development timeline reduction from 3–5 years to approximately 18 months. Similarly, VEGF inhibitors targeting neovascular AMD have been optimized using deep learning QSAR models that screened virtual libraries of small molecules and peptides, with promising candidates validated on retina-on-chip platforms simulating choroidal neovascularization. Peptide therapeutics designed against bacterial keratitis pathogens benefited from AI-augmented QSAR predicting antimicrobial potency, complemented by cornea-on-chip platforms replicating infection dynamics under tear flow, reducing animal testing needs. These case studies illustrate how the synergy of QSAR and OoC, empowered by AI, enhances drug discovery efficiency and translational fidelity in ophthalmology [7].

4. Results and Discussion

QSAR modelling has evolved from simple linear regression approaches to complex machine learning and deep learning frameworks capable of capturing nonlinear molecular interactions. Modern QSAR leverages large chemical datasets and advanced feature selection to generate predictive models that estimate drug binding affinities, ADMET (absorption, distribution, metabolism, excretion, and toxicity) profiles, and off-target interactions with higher precision. In the context of ophthalmology, QSAR models have been used to optimize inhibitors targeting pathological angiogenesis via VEGF pathways, a leading cause of vision loss in AMD. Furthermore, peptide therapeutics against ocular infections have benefited from in silico design iterations, substantially reducing experimental burdens. Nevertheless, challenges such as model interpretability and transferability remain critical areas for improvement.

Organ-on-chip technologies represent a paradigm shift in preclinical ophthalmic research. These microfluidic devices simulate dynamic physiological conditions including shear stress, oxygen gradients, and nutrient supply, which are crucial for maintaining native tissue function and response. OoC platforms have successfully modeled ocular barriers, enabling robust pharmacokinetic and toxicity testing of novel compounds with significantly improved human relevancy compared to static cell cultures or animal models. AI techniques enhance OoC utility by automating high-content image analysis, pattern recognition, and real-time monitoring, thereby refining drug effect assessment and facilitating personalized medicine approaches [8]. Despite their promise, the integration of QSAR and OoC presents

hurdles such as the need for standardization in chip fabrication, harmonization of experimental protocols, and effective data integration frameworks combining heterogeneous datasets. Regulatory considerations also pose challenges for clinical adoption. Collaborative efforts amongst academia, industry, and regulatory bodies are essential to advance these technologies from bench to bedside, potentially transforming ophthalmic drug discovery and therapeutic development [9,10].

References

1. Cheng H. Ophthalmic drug discovery and development using artificial intelligence. Expert Opin Drug Discov. 2025.
2. Brown EE. Physics-informed deep generative learning for quantitative structure–activity relationship modeling in retinal pharmacology. Preprint. 2024.
3. EyesOpen. 3D-QSAR machine learning for binding affinity prediction in ocular targets. Science Brief. 2025.
4. Integrating QSAR modelling and deep learning in drug discovery. Nat Rev Drug Discov. 2024.
5. Artificial intelligence for ophthalmic drug discovery and development. Artif Intell Health. 2024.
6. AI techniques in inherited retinal diseases: A review. arXiv. 2024.
7. Kravchenko SV. Application of organ-on-a-chip in experimental ophthalmology. PubMed. 2023.
8. Deng S. Organ-on-a-chip meets artificial intelligence in drug evaluation. Theranostics. 2023.
9. Li J. An overview of organs-on-chips based on deep learning. SPJ Sci. 2022.
10. AI-assisted diagnosis of ocular surface diseases with OoC validation. Front Cell Dev Biol. 2023.