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Article

Design Thinking and its Application to Healthcare Innovation: An AI-Enhanced Framework for Drug Discovery

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All Researchers Contributed Equally

Abstract: The drug discovery process of new pharmaceuticals is costly, time-consuming and lacks patient-centered innovation. Artificial intelligence (AI) has accelerated elements of drug development such as compound identification and toxicity screenings. However, it lacks adaptability and often detaches from users' needs. Design thinking, a human-centered approach emphasizing empathy and ideation, can bridge this gap by reframing drug development challenges with patient needs in mind. The aim of this study involves integrating AI with design thinking as it optimizes efficiency while ensuring innovative and user-focused pharmaceutical solutions. By analyzing results from incorporating design thinking principles into prompt engineering with three AI models: ChatGPT, Gemini, and DeepSeek, this study explores how combining AI's speed and predictive modeling with design thinking's iterative approach can enhance drug discovery. The responses demonstrated a deeper understanding of the user's needs through the "Empathize" step and became more dynamic through the "Ideation" step. This research proposes a hybrid framework leveraging AI and the design thinking process ensures drugs are developed efficiently while prioritizing patient-centered care, ultimately leading to more effective and diverse pharmaceutical innovation.

Keywords: design thinking; user-centered design; artificial intelligence; large language models; drug discovery; healthcare

1. Introduction

Design Thinking is a human-centered problem-solving approach that emphasizes empathy, creativity, and iterative learning to develop innovative solutions[1-2]. Rooted in the 1950s with early contributions from Herbert A. Simon, the methodology gained widespread recognition through Stanford's D.School, which played a crucial role in formalizing and teaching Design Thinking as a structured process[3]. The Design Thinking framework consists of five key stages: Empathize, Define, Ideate, Prototype, and Implement. The process begins with the Empathize phase, where researchers engage with and observe users to understand their needs and challenges. In the Define stage, these insights are synthesized into a clear and actionable problem statement. During the Ideate phase, teams brainstorm a wide range of potential solutions. The Prototype stage involves creating preliminary versions of ideas for early testing. Finally, in the Test phase, feedback is gathered to refine and improve the solution[4]. These five stages ultimately aim to understand user needs, generate creative ideas, and redefine solutions through rapid prototyping and feedback[5]. This approach fosters collaboration, reduces risks by validating ideas early, and is effective in creating user-friendly products[6]. The iterative nature of design thinking enables rapid testing and immediate feedback.

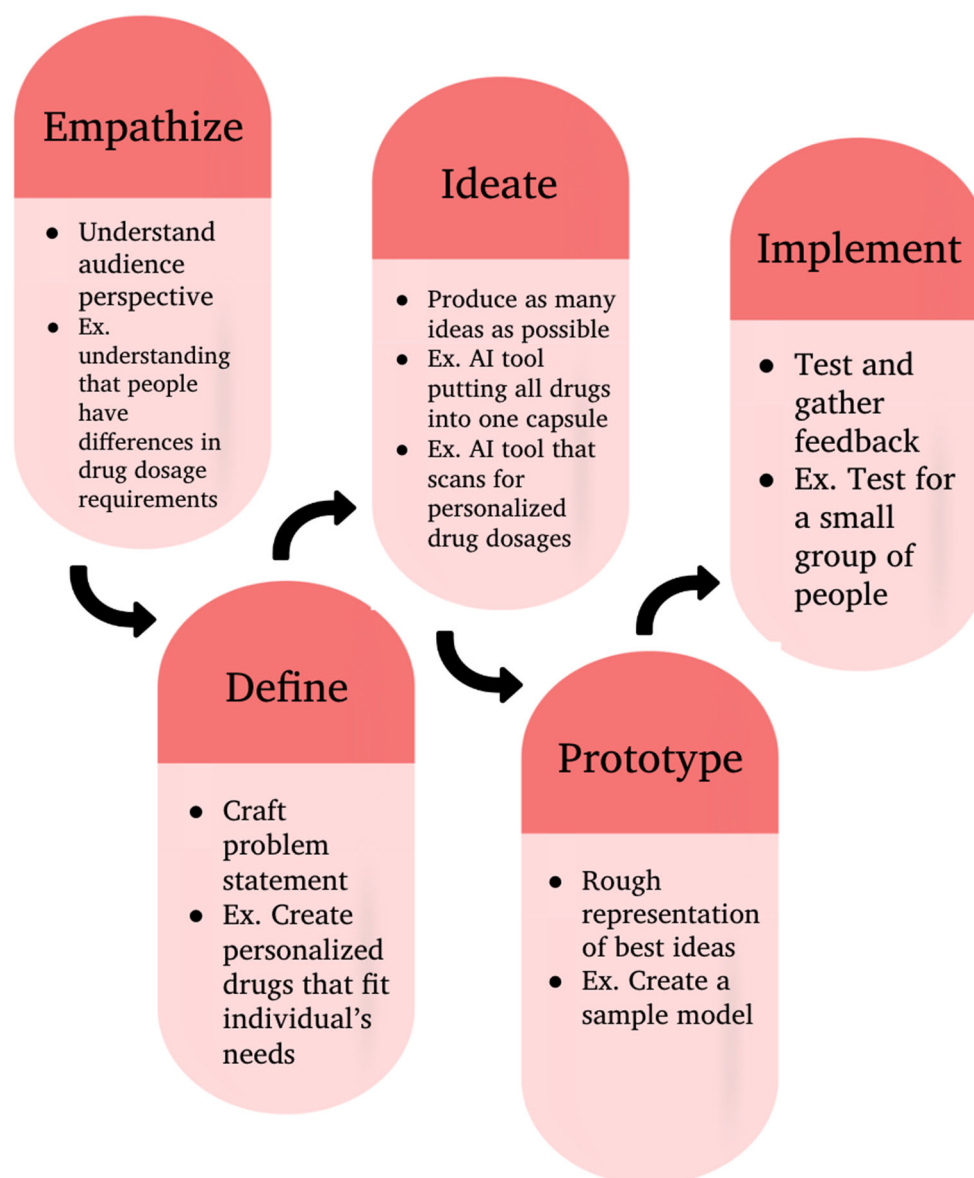


Figure 1. Design thinking methodology.

Design thinking has been applied in healthcare settings to improve patient care, redesign system processes, and streamline drug discovery[7]. By offering human centered approaches to reframing issues in healthcare organization, design thinking allows researchers to focus on efficiency and patient care[8]. For example, by using design thinking principles, an emergency department implemented patient advocates to open up communication between the providers and patients. This led to greater patient satisfaction and efficient wait times[9]. Design thinking in high-stress areas like the ICU has led healthcare innovators to target operational inefficiencies, such as redesigning layouts of medical supplies and equipment for optimized patient care. Another example of design thinking is its application in radiology. By analyzing patient needs, innovators were able to redesign X-ray spaces to create a less intimidating atmosphere. By using design thinking to reframe healthcare issues, innovators are able to focus on patient needs and understand the overall perspective of the issue.

As technology advances, there is more potential for drug discovery to improve. Drug discovery is defined as “a complex and time-consuming process that involves identifying molecules that can interact with specific molecular targets in the body to treat diseases[10]”. However, drug discovery

is not centered around what a specific user needs. Many times drugs are tailored towards those who took part in the study, who, due to historical bias, tend to be white males[11]. This means many drugs were not tested enough on minorities and women, which leads to 1 in 5 patients experiencing adverse drug reactions (ADR) to drugs that were not tailored enough[12]. Without diversity in sample sizes, the study may not represent the entire population and can lead to serious side effects, such as ADR. The preferences of users are not addressed in the creation of drugs. In fact, 50% of patients do not take their medications[13] because the schedules prescribed to them do not work. Many patients face polypharmacy, the use of over medications at the same time[14]. With patients taking multiple medications, dangers like adverse drug effects, unexpected drug interactions, and prescribing cascades can occur. Drug candidates go through several stages including discovery and development, preclinical research, and clinical trials before a select few make it to FDA review. As of right now, the drug discovery pipeline is a slow and inefficient process, taking on average between 10 and 15 years to develop a drug. Costing \$2.6 billion to reach the marketing approval state with only 14% of drugs gaining FDA approval, the drug discovery process is an ineffective process[15-16]. Many drugs fail because of the technology utilized in the drug discovery process[17]. Some examples of such technologies are organ-on-chips model, QSAR modeling, and De Novo Molecular Design. While these technologies are meant to improve the drug discovery processes, they are often inaccurate or lengthy.

Design thinking has helped shape drug discovery by streamlining the lengthy process, implementing AI for optimization, and focusing on patient satisfaction. By implementing design thinking, healthcare professionals can solve issues using human-centered strategies and focusing on user experience. This ensures that developed medicines and therapies focus on patients' needs, and make the system more efficient. Furthermore, integrating AI into areas such as the identification of novel compounds and lead identification has accelerated the drug discovery process. Models such as QSAR, De novo molecular design, and protein targets can be enhanced using design thinking trained AI. Additionally, AI's repetitive iterative nature, similar to design thinking, allows models to efficiently identify drug compounds[18]. This allows the model to run through compounds faster as they have a large database of previous knowledge.

Traditionally, the pharmaceutical industry has relied on small bioavailable molecules around "druggable" targets, guided by Lipinski's Rule of Five (Ro5). It predicts permeation if a molecule exceeds specific parameters when identifying molecular targets. However, the industry calls for exploration beyond traditional small molecules and Ro5. Advances like artificial intelligence (AI) and machine learning (ML) are transforming drug design by addressing challenges in peptide synthesis, structure-based and ligand-based virtual screening, toxicity prediction and pharmacophore modeling, quantitative structure-activity relationship (QSAR) and drug repositioning and poly-pharmacology[19].

The de novo method, a traditional approach to drug design, faces challenges such as complex synthesis pathways and difficulties in predicting biological effects in compounds. With AI, these challenges can be addressed by enabling efficient compound creation[20]. AI models have efficient compound generation, cost reduction, and faster lead identification compared to the de novo method. Generative models like Reinforced Adversarial Neural Computer (RANC) and other generative frameworks can generate molecular structures based on specific chemical properties and offer innovative solutions by optimizing molecular diversity while maintaining structural feasibility[21]. AI-driven frameworks like Long Short-Term Memory (LSTM) networks are used to generate libraries of potential drug compounds.

Pharmacovigilance is crucial in detecting and preventing adverse drug reactions (ADRs) and highlights the role of AI in addressing emerging challenges like polypharmacy and patient diversity. The pharmaceutical industry faces many challenges concerning drug safety. The high attrition rate of drugs due to unexpected toxicities, structural limitations in clinical trials, and post-marketing challenges like underreporting of ADRs contribute to these challenges[22]. Traditional methods of QSAR modeling as a foundational approach in predicting drug toxicity and the use of animal studies

and their constraints are outdated when compared to the emergence of advanced AI techniques that are less problematic in fields of cost, ethics, and time[23]. AI's ability to process vast datasets from electronic health records (EHRs) and other medical databases limits the further potential of human error and increases clinical efficiency[24]. In post-marketing surveillance, where drugs are monitored for ADRs, AI can address bias in spontaneous reporting systems and improve the detection of rare events and drug-drug interactions.

Compared to traditional methods, AI excels in rapidly generating responses due to its iterative nature and identifying limiting factors in current drug discovery. However, AI falls short in producing the creative responses necessary for innovation in the field of healthcare. This gap presents an opportunity to implement design thinking to further foster creativity in problem-solving and enhance innovation. Through integrating the precision of AI and empathetic problem-solving elements of design thinking, more efficient and cost-effective approaches to healthcare challenges in drug discovery can be developed and hold the potential to revolutionize the innovation process of the pharmaceutical industry. Considering the above information, in this research article we aimed to integrate Design Thinking in Drug Discovery. Furthermore, by generating broader solutions without original innovation, AI generates solutions that are detached from the user. This allows for iterative, empathetic, and varying solutions. In our study, we aim to address the gap through the implementation of design thinking using a Large Language Model (LLM), through which the models can reframe their perspective to be more patient-centered while prioritizing efficiency and empathy. Our research opens a new era of applying generative AI to address the Drug Discovery pipeline.

2. Background

Design thinking differs from traditional problem-solving by emphasizing empathy, iteration, and efficiency over linear, data-driven analysis[25]. Unlike conventional methods that follow a structured, rigid process to identify a single solution, Design Thinking focuses on deeply understanding user needs through research, observation, and empathy, allowing for more creative and unconventional solutions. A key distinction is the use of rapid prototyping, a concept that addresses the critical gap in innovation that only about 10% of new products or services effectively meet user needs, while the remaining 90% result in wasted resources. By integrating rapid prototyping, Design Thinking allows teams to test multiple ideas early, minimizing risk and allowing for continuous ideation. This reduces the risk of failure by ensuring that solutions are continuously improved before large-scale implementation. By focusing on user needs, experimentation, and adaptability, Design Thinking is particularly effective for solving complex, innovation-driven challenges across fields[26].

Generative artificial intelligence is a subset of deep learning models that can be trained using large amounts of data to perform certain tasks[27]. Large Language Models (LLMs) are a type of generative artificial intelligence with the ability to respond to text[28]. LLM is trained on large quantities of data through the processes of self-supervised, supervised, and reinforced learning[29-30]. These models can perform a variety of tasks including summarizing and answering questions.

Our study focuses on three main LLM models. A prominent one is ChatGPT, a chatbot trained to interact with humans and produce text using a large dataset[31]. It was designed by OpenAI to generate human-like text responses, assist with writing, answer questions, and perform various tasks. Another AI model is Google DeepMind's Gemini, formerly known as Bard, which is designed to handle complex reasoning, multimodal inputs (text, images, and audio), and real-time information retrieval. Gemini integrates with Google's ecosystem, enhancing applications like Search, Docs, and Assistant. Another emerging AI model, DeepSeek, developed by a Chinese AI research team, focuses on natural language understanding, coding, and multilingual capabilities, with an emphasis on high-performance AI for enterprise and research applications.

As a user-centered problem-solving approach, Design Thinking has applications in a variety of fields, from education to farming and much more.

Invented by David Kelley, a professor at Stanford University, the Design Thinking method is a way to come up with ideas[32]. He states that to work with complex projects, the prototyping and implementing of inventions is a fundamental step. Through recent collaboration, the Hasso Institute of Design and the Stanford Institute for Human Centered Design have been working on combining the design thinking approach with the use of artificial intelligence. The projects aim to improve research on AI systems that are human-centered. They have projects on AI-assisted privacy, human-human interaction, fabrication tools, and social computing systems[33].

Design Thinking implementation in media management education has been examined through a structured university course designed to train students, especially those with technical backgrounds, in user-centered innovation. Conducted by the EMMi Lab at Tampere University of Technology in Finland, the course blended the traditional Design Thinking phases with additional self-learning and business planning stages. It emphasized active, problem-based learning, requiring students to participate in interdisciplinary teamwork, understand consumer needs, and iteratively refine their solutions. The course was structured as a hands-on experience in an innovation lab setting, ensuring a creative, open environment that encouraged exploration. A major focus was to overcome common educational limitations by teaching students how to navigate “wicked problems”—problems that are complex and ill-defined—in media innovation, encouraging integrative thinking, experimentation, and collaboration. Students engaged in real-world challenges, developing practical prototypes and business plans, therefore bridging the gap between theoretical knowledge and practical application. Ultimately, the course demonstrated how Design Thinking can be effectively adapted and applied to business management education, equipping students with the skills necessary to approach complex problems creatively and strategically[34].

Design Thinking further has applications in improving healthcare delivery intensive care units (ICUs), specifically in aligning life-sustaining treatment with patient values. In a study by Kristyn A Krolikowski et al., Design Thinking principles were applied to develop more patient-centered approaches in critical care[35]. While Design Thinking provided practical tools for engaging multiple perspectives, it also posed challenges, such as the risk of overgeneralization and the absence of standardized evaluation criteria. To address these limitations, qualitative research methods were used to create structured evaluation techniques. The study highlights the potential of Design Thinking in healthcare while emphasizing the need to complement it with established evaluation methodologies. Ultimately, Design Thinking can enhance healthcare delivery in the ICU by fostering meaningful collaboration between clinicians, patients, and families[36].

This paper aims to further apply Design Thinking to the context of drug discovery by using the problem-solving process to address the following issues within the drug discovery process:

Induced pluripotent stem cells or iPSCs are differentiated into various cell types that model human diseases in vitro, providing a valuable alternative to traditional animal models in drug discovery. Somatic cells of patients can be reprogrammed to their pluripotent state form to be able to derive the disease genotype[37]. In vitro cell-based models of neural lineage cells of diseases hold promise for monitoring disease progression and can improve drug testing on patient-derived cells, limiting unexpected side effects[38]. The implementation of iPSCs holds a new strategy to model human cancer as they have characteristics similar to embryonic stem cells and can provide a valuable tool in understanding the pathogenesis of familial cancer early on to identify additional genetic alterations[39]. However, the potential of iPSCs is unstable and limits their effectiveness for clinical and research applications. They have unpredictable changes in their DNA and gene regulation during or after reprogramming[40]. These changes could lead to harmful effects like cancer or reduced functionality.

These computational methods of drug discovery have also improved in recent years, such as machine learning, molecular docking, and quantitative structure-activity relationship (QSAR) modeling. The use of artificial intelligence in drug discovery enhances molecular design, drug repurposing, and toxicity prediction. These methods can model how a drug might interact with the target, but they often struggle with issues like overfitting and predicting accidental interactions with

other proteins. They also have issues of high costs, time consumption, and low efficacy, and require much improvement before they can be used regularly for drug design[41].

Animal testing, procedures performed on animals[42], is one approach used to test drugs. However, animal testing has very high failure rates, with 9 out of 10 such as high failure rates, inaccurate representations of humans, and ethical concerns. One technology used in drug discovery is the organ-on-chips model, cultures of engineered miniature human tissue systems developing in microfluidic chips[43]. The organ-on-chips system was formed to create an accurate model to test drugs on instead of using animals to test treatments. However, this model has a lot of room for improvement. The main issue with human organs-on-chips for disease modeling and drug development is the difficulty in fully replicating the complexity of human physiology, including inter-organ interactions, immune responses, and disease-specific factors, while also ensuring scalability, reproducibility, and regulatory acceptance.

De novo molecular design involves generating novel chemical structures that meet specific objectives, such as biological effectiveness, safety, and synthesis feasibility[44]. A key challenge is balancing these factors, as highly effective molecules may be difficult to synthesize or pose safety risks, while simpler molecules may lack potency[45]. While generative models and computational methods can explore chemical space more efficiently than traditional approaches, they still struggle to predict the real-world feasibility of molecules[46]. As a result, de novo design often fails to generate compounds that optimize the trade-offs between these competing needs, limiting its effectiveness in drug discovery. The iterative nature of design thinking can improve de novo molecular design, allowing it to rapidly test different compounds.

QSAR (Quantitative Structure-Activity Relationship) correlates the biological activity of compounds to chemical structures[47]. It has a crucial role in drug discovery as it lets researchers evaluate drugs without a long and expensive process[48]. QSAR looks at separate molecular features and correlates them with the actual biological effect, which allows researchers to predict the effects of a certain drug or compound. It has been used for years throughout the drug discovery pipeline and rapidly streamlined the screening of chemical libraries. AI can also be implemented in QSAR, improving its accuracy and solidifying its critical role in modern drug discovery[49]. A design thinking trained Large Language Model can also be implemented in QSAR, improving its accuracy and solidifying its critical role in modern drug discovery.

Protein targets are considered druggable if they can bind to small drug-like molecules and produce a desired therapeutic effect. A protein is considered undruggable if it is difficult to target for drug development. Some contributing factors which may make a protein target undruggable are if it has flat functional interfaces without defined pockets for ligand interactions, is involved in several other protein-protein interactions, or is an intracellular protein rather than an extracellular protein. As of today, about 85% of proteins are considered undruggable, translating to about 60% of drug discovery projects failing due to undruggable targets. Implementing protein targets to increase the accuracy of drug development and streamline the pipeline can save time and money. Furthermore, machine learning can enhance the accuracy of druggable proteins.

Considering all the above applications of DT in medicine and healthcare, our study tries to understand how each LLM (ChatGPT, Gemini, & Deepseek) will further help to address these drug discovery challenges in a systematic approach like multiple iterations and testing to discover an optimized drug.

3. Methodology

This study examines AI-driven design thinking in healthcare, particularly in the drug discovery pipeline. AI is being increasingly implemented in problem-solving, making it crucial to examine how AI models, such as Chat-GPT, Deepseek, and Gemini compare to human creativity when addressing healthcare challenges. By implementing design thinking principles of repeated iterations and user-centric solutions, this research compares the different design thinking trained AI models, and human ingenuity to discover the strengths and limitations of each approach.

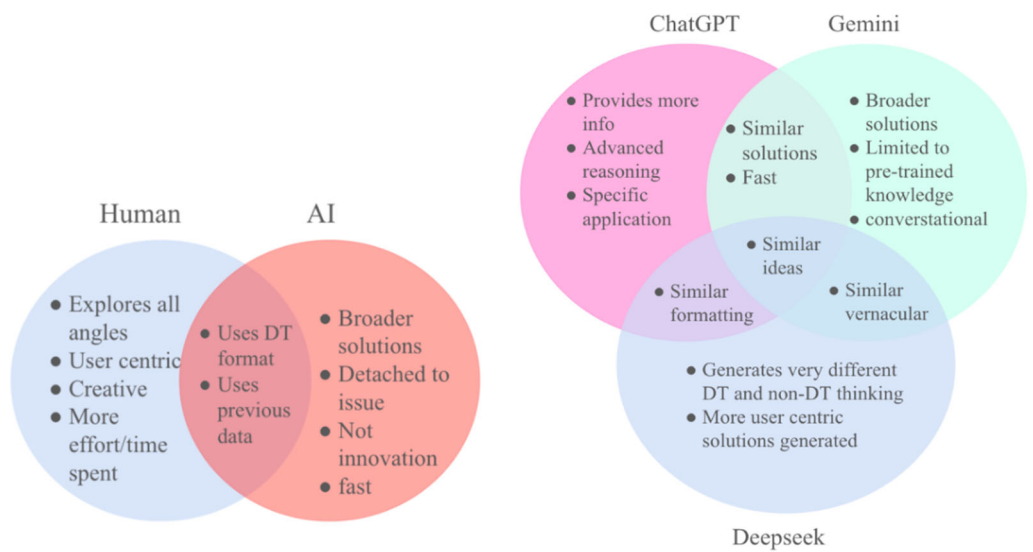


Figure 2. A comparison of Human vs. AI and ChatGPT vs. Gemini in addressing problems using design thinking.

Thorough literature reviews were conducted on numerous topics, including design thinking in healthcare, AI-driven problem-solving in drug discovery and medicine, and pharmaceutical problems relating to drug discovery. Reviews were utilized to identify major challenges in the pharmaceutical industry and recognize the potential of the Stanford design thinking process in drug discovery as a more patient-centered framework. Six main problems were identified surrounding the risks of implementing iPSCs, challenges with computer modeling molecules, organs-on-chips, druggable proteins, de Novo molecular design, and QSAR.

A qualitative comparison was done to select a large Language model (AI generative models) that would be used to conduct the study. The research was conducted using the ChatGPT, Gemini, and Deepseek models to create applicable solutions for major problems found in the pharmaceutical industry. To be able to accurately distinguish the benefit of applying design thinking in the drug discovery and design process, a second set of trials were conducted asking both models to create solutions to the same set of problems with the Stanford design thinking process. A description of the process was provided to assist the accuracy of the model's response. The prompt required the model's response to follow each core stage of the process including empathize, define, ideate, prototype, and test.

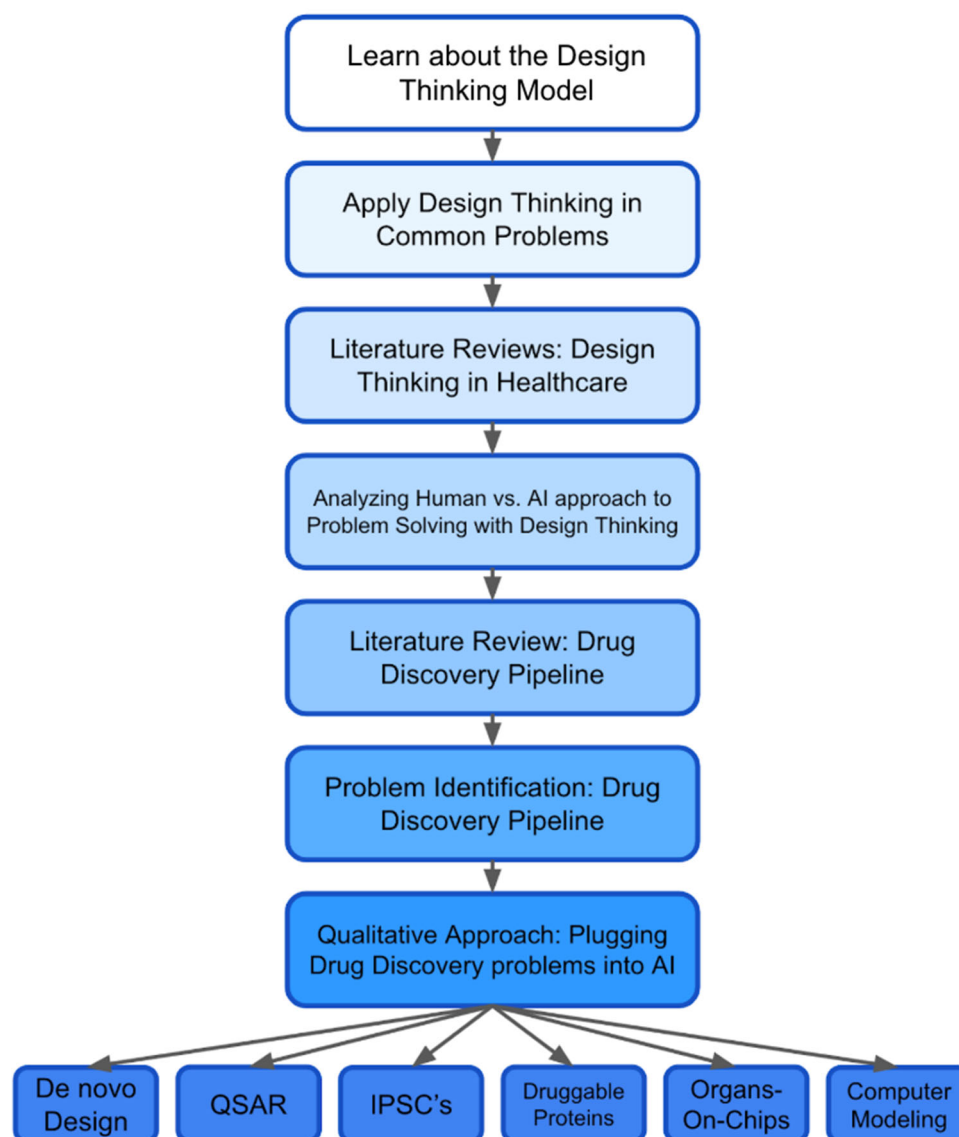


Figure 3. Methodology pipeline.

This pipeline refers to the methodology of the study and outlines the integration of design thinking into drug discovery. It begins with the applications of design thinking to common problems and also details on the qualitative approach taken to assess the incorporation of AI in our novel design.

The study was conducted through a structured process that involved selecting a review article, defining a problem statement, and obtaining AI-generated responses both with and without the application of the design thinking methodology. Initially, the AI was provided with a reference abstract and prompted to identify a relevant problem related to the study's focus. For example, it was asked: "What are some problems concerning organs-on-chips for drug development and personalized medicine? Here is an abstract for reference: [abstract]." The AI responded by identifying the primary challenge as the difficulty in fully replicating the complexity of human physiology—specifically inter-organ interactions, immune responses, and disease-specific factors—while also ensuring scalability, reproducibility, and regulatory acceptance.

Subsequently, the AI was asked to propose solutions to the identified problem while referencing the same abstract. To enhance its domain-specific knowledge, it was provided with a reference paper

covering key topics such as 1)organ-on-chip models, induced 2) pluripotent stem cells (iPSCs), computational modeling, 3) druggable proteins, 4) de novo molecular design, and 5) quantitative structure-activity relationship (QSAR) analysis. A sample prompt included: *“Use the following information to generate solutions for this problem concerning human organs-on-chips modeling: Question: [problem statement]. Information: [abstract].”*

Following this, the same problem-solving process was repeated using the design thinking methodology. The AI was prompted to apply this framework by structuring its response through stages such as empathizing with users, defining the problem, ideating potential solutions, prototyping, and testing. An example prompt was: *“Use the following information to generate solutions to this problem regarding human organs-on-chips modeling using the design thinking problem-solving methodology: Question: [problem statement]. Information: [abstract].”*

The responses obtained through both approaches were systematically compared and analyzed to identify similarities and differences. This analysis aimed to assess the impact of explicitly training an AI model to use design thinking versus allowing it to solve the problem without a structured methodology.

Finally, both results were compared to find the similarities and differences when training an LLM to use design thinking as opposed to simply asking it to solve the problem. In the final phase, the characteristics of each model were analyzed and compared. By evaluating factors such as creativity, effective use of design thinking, and adaptability, a chart was created to compare the three models. These similarities and differences were transferred to a Venn diagram. This diagram plotted the strengths and weaknesses of each model which allows for classification of areas where AI does well and areas where human ideas may still be needed.

4. Results

To assess AI’s ability to implement Design Thinking in the various aforementioned problems, we prompted each LLM with problem statements paired with a review article abstract about the specific topic to contextualize. Summarized example LLM responses with and without the Design Thinking methodology regarding the human organs-on-chips for disease modeling and drug development are provided below. A [secondary document](#) containing the full list of problems, prompts, and responses can be accessed for further demonstration.

1. Organ-on-chip

Problem	Organ-on-chips
Prompt	<p>The main issue with human organs-on-chips for disease modeling and drug development is the difficulty in fully replicating the complexity of human physiology, including inter-organ interactions, immune responses, and disease-specific factors, while also ensuring scalability, reproducibility, and regulatory acceptance.</p> <p><u>Background Information:</u></p> <p>Abstract</p>

ChatGPT Response with Design Thinking :	<p>In the ideation phase, we brainstorm potential solutions. These solutions should aim to address the identified pain points. Here are a few ideas:</p> <p>a. Enhancing Physiological Complexity</p> <ul style="list-style-type: none">• Multi-Organ Chips: Develop systems that combine multiple organ chips (e.g., liver, heart, kidney, brain, gut) into interconnected models to mimic inter-organ interactions and responses. This could better reflect the complexity of human systems and disease pathways.• Immune Cell Integration: Integrate immune cells (e.g., macrophages, T-cells) into organ-on-chip models to study immune responses in disease and drug testing, such as cancer immunotherapy.• Personalized Chips: Use patient-derived cells to create "living avatars" for personalized medicine. This would involve modeling genetic and disease-specific factors to predict how individual patients might respond to treatments. <p>b. Improving Scalability and Reproducibility</p> <ul style="list-style-type: none">• Standardized Platforms: Develop a standardized, modular organ-on-chip platform that allows for easy customization. Standardization would improve scalability (e.g., for high-throughput drug screening) and ensure reproducibility across different labs.• Automated Culture Systems: Integrate AI and robotics for automating cell culture processes, fluid flow control, and data analysis to reduce human error and improve consistency across experiments. <p>c. Ensuring Regulatory Acceptance</p> <ul style="list-style-type: none">• Regulatory Compliance Framework: Establish a clear framework for organ-on-chip devices to meet regulatory standards, collaborating with regulatory agencies like the FDA. This may include standardized protocols for cell sourcing, chip construction, and validation testing.• Validation Studies: Conduct large-scale validation studies comparing organ-on-chip responses with known human clinical responses to establish credibility with regulatory bodies.
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ChatGPT Response without Design Thinking :	<div><div>1.Multi-Organ-on-a-Chip Systems</div><div><div>◦ Solution: Integrating multiple organs (e.g., liver, heart, kidney) into a single microfluidic system to study inter-organ interactions.</div><div>◦ Benefit: Provides realistic insights into diseases and drug effects across multiple systems.</div></div><div>2.Immune System Integration</div><div><div>◦ Solution: Incorporating immune cells to simulate inflammation, autoimmune responses, and tumor-immune interactions.</div><div>◦ Benefit: Enhances disease modeling for immune-related conditions like cancer and infections.</div></div><div>3.Personalized Medicine Using Patient-Derived Cells</div><div><div>◦ Solution: Using patient-specific cells to create personalized organ models for drug testing.</div><div>◦ Benefit: Reduces reliance on animal models and improves individualized treatment predictions.</div></div></div>
ChatGPT Response without Design Thinking (cont.):	<div><div>4.Advanced Cell Culture Techniques</div><div><div>◦ Solution: Utilizing 3D cell culture, tissue engineering, and bioprinting for more functional tissue models.</div><div>◦ Benefit: Enhances physiological relevance, making organ chips more accurate for drug development.</div></div><div>5.Improving Scalability and Automation</div><div><div>◦ Solution: Implementing automated microfluidic platforms for high-throughput drug screening.</div><div>◦ Benefit: Increases efficiency, reduces costs, and improves reproducibility.</div></div><div>6.Standardization and Regulatory Framework</div><div><div>◦ Solution: Develop standardized protocols and collaborate with regulatory agencies.</div><div>◦ Benefit: Ensures reproducibility and accelerates acceptance as an alternative to animal models.</div></div><div>7.Incorporating Disease-Specific Factors</div><div><div>◦ Solution: Using genetic engineering (e.g., CRISPR) to model specific diseases like Alzheimer's or cancer.</div><div>◦ Benefit: Improves disease modeling for more targeted drug testing.</div></div><div>8.Enhancing Vascularization and Fluid Dynamics</div><div><div>◦ Solution: Improving blood flow simulation and capillary networks within organ chips.</div></div></div>

	<ul style="list-style-type: none">◦ Benefit: Enhances organ function and supports long-term drug testing. <p>These advancements collectively push organ-on-a-chip technology toward more accurate, scalable, and personalized disease modeling and drug testing.</p>
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As shown above, the Design Thinking response from ChatGPT provided a clear implementation plan and realistic solutions. Similar results were found for several other problems in the healthcare and drug discovery sector. The following table provides an example response generated by Gemini for the same problem regarding the organ-on-chips.

LLM	Gemini
Problem	Organ-on-chips
Prompt	<p>The main issue with human organs-on-chips for disease modeling and drug development is the difficulty in fully replicating the complexity of human physiology, including inter-organ interactions, immune responses, and disease-specific factors, while also ensuring scalability, reproducibility, and regulatory acceptance.</p> <p><u>Background Information:</u></p> <p>Abstract</p>

Gemini Response with Design Thinking:	<p>1. Empathize – Understand Users' Needs</p> <p>Users: Researchers, pharmaceutical companies, regulatory agencies, clinicians, and patients.</p> <p>Needs:</p> <ul style="list-style-type: none">• Researchers need reliable models for disease study and drug testing.• Pharmaceutical companies seek efficient, cost-effective drug development tools.• Regulatory agencies require robust, reproducible data.• Clinicians need personalized medicine approaches.• Patients need safe, effective treatments.
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Gemini Response with Design Thinking (cont.):	<ul style="list-style-type: none">• Challenges: Limited physiological complexity, scalability, reproducibility, regulatory acceptance, and high costs.• Learning Methods: Literature reviews, expert interviews, lab visits, case study analysis, and conferences. <p>2. Define – Clarify the Problem</p> <p>Problem Statement: Organs-on-chips struggle with replicating human physiology, ensuring scalability, reproducibility, and gaining regulatory approval, limiting their adoption.</p> <p>Specific Needs:</p> <ul style="list-style-type: none">• Improved physiological accuracy (inter-organ interactions, immune responses, disease-specific factors).• Scalable and reproducible systems for high-throughput screening.• Regulatory-compliant data generation.• Cost-effective, accessible technology. <p>User Insights: Researchers need realistic models, pharma companies need efficient tools, regulators need strong data, clinicians need personalized approaches, and patients need better treatments.</p> <p>3. Ideate – Generate Solutions</p> <p>Key Ideas:</p> <ul style="list-style-type: none">• Enhancing Complexity: Multi-organ chips, immune system integration, perfusable vascular networks, iPSCs, ECM, dynamic microenvironments, microbiome incorporation.• Improving Scalability & Reproducibility: Automation, standardized protocols, optimized microfluidic designs, advanced data analytics.• Achieving Regulatory Acceptance: Validation studies, collaboration with regulators, standardized reporting, focusing on key applications (e.g., drug toxicity testing).• Reducing Cost & Increasing Accessibility: Economies of scale, open-source platforms, training programs. <p>"How Might We" Questions:</p> <ul style="list-style-type: none">• How might we design multi-organ chips that accurately mimic inter-organ communication?• How might we integrate immune responses?
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- How might we automate high-throughput organ-on-chip experiments?
- How might we standardize protocols for reproducibility?
- How might we collaborate with regulators to set guidelines?
- How might we lower costs for broader accessibility?

4. Prototype – Develop & Test Solutions

Prioritization: Select solutions based on feasibility and impact (e.g., developing a multi-organ chip for a specific disease).

Prototyping Approaches:

- Designing and fabricating a multi-organ system (e.g., liver-gut-on-a-chip).
- Creating automated systems for cell seeding and perfusion.
- Developing standardized protocols for liver toxicity assessment.

Iteration & Testing: Prototype, test, refine based on experimental results, compare with traditional models (e.g., animal studies) for validation, and optimize culture conditions and microfluidics.

By following this **human-centered approach**, organs-on-chips can evolve into more **accurate, scalable, and widely accepted** tools for **disease modeling, drug discovery, and personalized medicine**.

Gemini Response without Design Thinking:	<p>The main challenge in human organs-on-chips is balancing physiological complexity with scalability, reproducibility, and regulatory acceptance. Key solutions include:</p> <ol style="list-style-type: none">Enhancing Physiological Complexity<ul style="list-style-type: none">Multi-Organ Chips: Connect different organ types to study systemic effects.Immune System Integration: Incorporate immune cells to analyze immune responses.Perfusable Blood Vessels: Improve nutrient delivery, waste removal, and immune interactions.Patient-Derived Cells (iPSCs): Personalize organ chips for individualized medicine.3D Culture & ECM: Create realistic cell environments for better function.Dynamic Microenvironment Control: Regulate flow, oxygen, and nutrients for precise experiments.Microbiome Integration: Study host-microbiome interactions, especially in gut-on-a-chip models.Improving Scalability & Reproducibility<ul style="list-style-type: none">Automation & High-Throughput Screening: Enable mass production and testing.Standardized Protocols: Ensure consistency across labs.Optimized Microfluidic Design: Enhance device reliability and usability.Advanced Data Management: Use AI and machine learning for meaningful insights.Gaining Regulatory Acceptance<ul style="list-style-type: none">Validation Studies: Compare results with animal models and clinical trials.Collaboration with Regulators: Define clear validation guidelines.Reproducibility & Transparency: Ensure well-documented methods and data sharing.Targeted Applications: Focus first on drug toxicity testing and rare disease modeling.Reducing Costs & Increasing Accessibility<ul style="list-style-type: none">Economies of Scale: Lower costs as adoption grows.
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	<ul style="list-style-type: none">• Open-Source Platforms: Facilitate wider adoption and innovation.• Training & Education: Expand knowledge and usability across research fields. <p>By advancing engineering, biology, and medicine, researchers can develop more sophisticated organ-on-a-chip systems, improving drug development, disease modeling, and personalized medicine.</p>
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The following table provides an example response generated by Deepseek for the same problem regarding the organ-on-chips.

LLM	Deepseek
Problem	Organ-on-chips

Prompt	<p>The main issue with human organs-on-chips for disease modeling and drug development is the difficulty in fully replicating the complexity of human physiology, including inter-organ interactions, immune responses, and disease-specific factors, while also ensuring scalability, reproducibility, and regulatory acceptance.</p> <p><u>Background Information:</u></p> <p>Abstract</p>
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Deepseek Response with Design Thinking:	<p>Applying the Stanford Design Thinking Model to human organs-on-chips (OoCs) can help address key challenges and accelerate adoption.</p> <ol style="list-style-type: none">1. Empathize – Engage stakeholders (researchers, pharmaceutical companies, regulators, and patients) to identify pain points such as reproducibility, scalability, cost, and regulatory acceptance.2. Define – Reframe challenges as opportunities, such as improving multi-organ integration, standardizing protocols, and reducing costs.3. Ideate – Brainstorm solutions like modular OoC systems, AI-driven automation, 3D bioprinting, immune system integration, and low-cost fabrication materials.<ol style="list-style-type: none">1. Multi-Organ Integration: Develop modular OoC systems that allow for plug-and-play integration of different organ chips.2. Use microfluidic networks to simulate blood flow and inter-organ communication.3. Scalability and High-Throughput Screening: Automate OoC fabrication and operation using robotics and AI-driven systems.4. Create standardized, disposable OoC cartridges for high-throughput applications.5. Biological Fidelity: Use 3D bioprinting to create more realistic tissue structures.6. Incorporate primary cells or advanced iPSC differentiation protocols to improve cell source reliability.7. Add immune cells and endothelial layers to mimic vasculature and immune responses.8. Standardization and Reproducibility: Develop universal protocols for OoC design, fabrication, and operation through industry-wide collaboration.9. Use machine learning to optimize and standardize cell culture conditions and fluid dynamics.10. Regulatory and Industry Acceptance: Conduct large-scale validation studies comparing OoC results to clinical data.11. Collaborate with regulatory agencies to establish guidelines for OoC use in drug development.12. Cost and Accessibility: Use low-cost, biocompatible materials for chip fabrication.13. Develop open-source OoC designs to democratize access.
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14. Ethical and Social Considerations: Establish clear guidelines for the ethical use of human-derived cells and patient data.

15. Implement robust data privacy and security measures for personalized medicine applications.

16. Long-Term Viability: Develop advanced cell culture media and conditions to extend the lifespan of OoC cultures.

17. Incorporate self-renewing cell types or bioreactors to maintain cell functionality.

18. Disease Modeling: Create multi-tissue OoC models to capture the complexity of multifactorial diseases.

19. Integrate patient-specific cells for personalized disease modeling.

20. Integration with Omics Technologies: Develop interfaces for seamless integration of OoCs with genomics, proteomics, and metabolomics platforms.

Deepseek Response with Design Thinking (cont.):	<div>1.</div> <div><div>4. Prototype – Develop and test modular systems, automated platforms, and models with immune and vascular components through rapid prototyping and iterative testing.</div><div>5. Test – Conduct validation studies, compare results to clinical data, and collaborate with regulatory agencies to ensure reliability and approval.</div><div>6. Implement – Scale solutions through industry partnerships, regulatory collaboration, and commercialization while training researchers in OoC technology.</div><div>7. Iterate – Continuously refine OoC designs and protocols based on stakeholder feedback and technological advancements.</div></div> <div>By using this structured approach, OoCs can evolve into a transformative tool for disease modeling, drug development, and personalized medicine, ensuring practicality, efficiency, and broad</div>
Deepseek Response without Design Thinking:	<div>Organs-on-chips (OoCs) hold great promise for disease modeling, drug development, and personalized medicine, but several challenges must be addressed for widespread adoption. Key issues include:</div> <div><div>1. Complexity and Scalability – Integrating multiple organs to mimic whole-body physiology remains difficult, and scaling up for high-throughput drug screening is a challenge.</div><div>2. Biological Fidelity – Variability in cell sources and the lack of immune and vascular components limit accuracy in replicating human physiology.</div><div>3. Standardization and Reproducibility – The absence of universal protocols and inconsistencies in chip materials and conditions affect comparability and reliability.</div><div>4. Regulatory and Industry Acceptance – Extensive validation against clinical data is needed, and the pharmaceutical industry may resist transitioning from traditional models.</div><div>5. Technical and Engineering Challenges – Material limitations and the complexity of mimicking human fluid dynamics hinder precise modeling.</div><div>6. Cost and Accessibility – High costs and the need for specialized expertise restrict broader adoption.</div><div>7. Ethical and Social Considerations – Issues related to human cell use, consent, and data privacy must be addressed.</div><div>8. Limited Long-Term Viability – Short culture lifespans limit studies on chronic diseases and long-term drug effects.</div></div>

	<div><div><div><div><div><div></div><div>9. Incomplete Disease Modeling – Many chips fail to capture the full complexity of multifactorial diseases.</div></div></div><div><div><div></div><div>10. Integration with Other Technologies – Combining OoCs with omics technologies for comprehensive analysis is still developing.</div></div></div></div></div><div><p>Advancements in engineering, biology, and regulatory collaboration are essential to overcoming these hurdles and unlocking the full potential of organ-on-chip technology.</p></div></div>
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Some of the other main issues in drug discovery that the AI models aimed to solve are iPSCs, Druggable Proteins, De novo molecular design, and QSAR.

Induced pluripotent stem cells (iPSCs) face major limitations due to genetic and epigenetic instability introduced during the reprogramming process, potentially leading to tumor formation or inconsistent results. When analyzed through a Design Thinking (DT) framework, all LLMs emphasized a more human-centered, iterative, and interdisciplinary approach. The ChatGPT-generated response offered a higher-level conceptual understanding of Design Thinking and traditional methods, emphasizing empathy, iterative refinement, and long-term scalability. It was more abstract and lighter on technical detail. Gemini's response, on the other hand, was more technically dense and specific, offering a wide array of concrete solutions across both DT and non-DT frameworks, including parthenogenesis, microRNA modulation, and machine learning. Gemini's DT response did not have clear applications of the Design Thinking framework. DeepSeek emphasized user needs and suggested genome editing tools such as CRISPR-Cas9 and AI-drive quality control in its DT section. Its non-DT section focused on technical solutions like epigenetic modulators. Gemini provided richer technical content and broader solution spaces, which would benefit a reader with a scientific background. Deep Seek provided a cohesive overview of scientific and human-centered strategies. However, ChatGPT better captured the process of Design Thinking, making it more suitable for implementation in drug development.

The main challenge with druggable proteins is that only a small amount of proteins have specific protein pockets that can bind to small drug-like molecules, which render them druggable. This means that around 85% of proteins in the human body are undruggable, making the drug discovery lengthy and risky, with a reduced potential for clinical applications. Future advances in protein technology are necessary to increase the number of proteins that can be targeted by drugs. The LLMs focusing

on analysis through a Design Thinking framework brought forth creative solutions such as using special peptides, PROTACs, and AI in order to identify new binding spots and to design more effective molecules. The non-design thinking model was more analytical, direct, and technology-driven, and presented solutions without a structured iterative process. The LLMs using Design Thinking overall had more user centered and feasible ideas generated than the LLMs with non Design Thinking analysis.

The process of de novo molecular design involves creating new molecules; however, the method struggles with creating molecules that balance the needs of effectiveness, safety, and ease of synthesis. If the models created by this method don't have the expected impact, it can be dangerous in clinical applications and difficult to manufacture and distribute. These challenges limit the usefulness of de novo molecular design in drug discovery. The design thinking AI models broke the problem into challenges faced by each stakeholder. It prioritized collaboration, transparency, and interactive AI tools. The non-design thinking AI was technical and structured solutions around scientific and algorithmic improvements.

Organ on chip models entail creating cell cultures on plates. These models commonly face issues regarding ethics and high failure rates. Large language models such as ChatGPT, Gemini, and Deepseek when asked to solve the organs on chips problem rarely take the user and their needs into consideration. When the three AI models mentioned above were trained to use the Design Thinking approach to solve the same problem, they provided more detailed solutions. These solutions were more creative and also had more empathy for the user. Some solutions the models gave when using design thinking were on reducing cost and increasing accessibility, with critical questions that validated the user's interests. These solutions compared much better than solutions without the use of Design Thinking.

Computational models often face challenges such as overfitting, poor generability, high costs, and time consuming processes. AI models that are not trained on design thinking address these issues by using specific technical solutions such as expanding databases and integrating data. However, these solutions do not consider stakeholders in the healthcare system, such as patients, providers, and researchers. When trained on design thinking, the AI models gave more comprehensive solutions by being more user oriented and identifying root causes such as not enough patient data, broken validation systems, and lack of collaboration. The design thinking trained models proposed solutions like using pharmacogenomics data and validating the model's predictions with real world data.

QSAR modeling faces challenges with overfitting. Since the model performs well on training data, it becomes accustomed to the training data and struggles with generalizing to new compounds. The QSAR model learns irrelevant patterns in the training data such as noise, which reduces its predictive accuracy for new datasets, which limits its application in drug discovery. The AI models trained to use design thinking identified the different needs of drug developers, patients, and researchers in off-target drug effects and came up with a range of solutions. Some examples include using AI in lab testing and implementing simulations. ChatGPT provided extensive solutions presented in the design thinking format, while Gemini's answer when using design thinking was significantly shorter. The non-design thinking model for all the LLMs gave a longer list of quick and technical solutions.

The comparisons made in ChatGPT, Gemini, and Deepseek, which compare design thinking and non-design thinking approaches, explore the ways in which AI can use design thinking methodology to improve the drug discovery industry. ChatGPT's responses with and without design thinking highlight the importance of using a design thinking model. The design thinking approach demonstrates well-thought-out solutions and a clear path to follow. The solutions provided empathize well with the people, encouraging the drug discovery industry to be more customer-centered.

Additionally, Gemini provides detailed responses using design thinking methodology, providing specific needs, follow-up questions, and detailed explanations. The combination of Gemini and the design thinking method can help to clear the process going into drug discovery.

When DeepSeek used the design thinking method, it provided a long list of ideas during the prototype stage. The vast quantity of solutions provided can help speed up the drug discovery process through the process of rapid iteration. The combination of Deepseek and the design thinking process creates the potential to improve the healthcare industry.

These findings create the foundation for the healthcare implications, which will be explored in the discussion section.

5. Discussion

AI and human cognition each offer distinct advantages in problem-solving. AI excels in processing vast amounts of data, recognizing patterns, and optimizing predictive models with unparalleled speed and efficiency. However, it lacks contextual understanding, ethical considerations, and the ability to incorporate patient-centered needs. Human researchers, on the other hand, contribute experiential knowledge, creativity, and ethical reasoning, which are essential for developing innovative and practical solutions.

The integration of Design Thinking with AI combines AI's analytical capabilities with a structured, iterative approach that prioritizes user needs and interdisciplinary collaboration. Traditional problem-solving in pharmaceutical research often follows a rigid, linear model, potentially overlooking critical patient-centric factors. Design Thinking introduces flexibility through continuous feedback, rapid prototyping, and iterative refinement, ensuring that technological advancements are both scientifically robust and practically relevant. By leveraging AI within a Design Thinking framework, pharmaceutical research can achieve both efficiency and adaptability, leading to more effective and patient-focused outcomes.

Design Thinking offers substantial benefits across various aspects of pharmaceutical research and development. By incorporating stakeholder engagement from the early stage spanning researchers, clinicians, and regulatory agencies, Design Thinking facilitates the development of more biologically relevant models, improving drug testing reliability and reducing dependence on animal models. Another significant application is in personalized medicine. Conventional clinical trials often fail to adequately represent diverse populations, leading to variations in drug efficacy and safety. Design Thinking ensures that patient demographics and genetic variability are integral to the development process.

AI can analyze large datasets to identify patterns in genetic markers and disease mechanisms, while human experts refine these findings to enhance clinical applicability. Furthermore, AI-driven drug discovery benefits from Design Thinking by enhancing the interpretability and relevance of computational models. While AI can rapidly generate and test molecular structures, the iterative nature of Design Thinking ensures that these models are continuously refined based on experimental validation and real-world clinical insights. This approach enhances the success rate of drug candidates progressing through the development pipeline.

6. Conclusions

The traditional drug discovery pipeline is extremely inefficient, with average development for a single drug taking over 10 years and \$2 billion, and less than 15% of drugs gaining FDA approval. Additionally, a lack of diversity in drug development studies leads to increased ADRs (adverse drug reactions) in minorities and women, as the majority of the participants in trials are white males. As patients grow older, they encounter more health problems, and this can lead to the prescription of several non-tailored drugs at once - polypharmacy - and can increase the risk of ADRs.

Using the design thinking framework for drug discovery allows for continued innovation in the field, and emphasizes a patient-centered approach. The use of AI cultivates new ways to advance pharmaceutical development. This method can foster further advancements to improve efficiency, equity, and safety in the field of drug discovery.

Since many new drugs are not tested on minorities and women, 1 in 5 patients experience adverse drug reactions (ADR) to drugs that were not tailored enough⁴⁶. The integration of AI and design thinking has efficiently improved pharmaceutical system efficiency and fixed operational challenges. The repetitive nature of AI combined with the design thinking process for streamlining development ensures that developed medicines and therapies are human-centered. By focusing deeply on understanding user needs, design thinking allows for more systematic and unconventional solutions. Design thinking also minimizes risk by testing multiple ideas early on in the process, an attribute valuable in patient care.

As our study suggests, incorporating design thinking principles into the prompt engineering with three AI models: ChatGPT, Gemini, and DeepSeek, significantly improved their ability to provide a user-centric and innovative solution to critical issues in the pharmaceutical industry. The responses demonstrated a deeper understanding of the user's needs through the "Empathize" step and incorporated more adaptable solutions. The static and insipid responses that were outputted without design thinking often lacked practicality and feasibility. By leveraging the "ideation" step, responses become more dynamic and diverse. Integrating the design thinking process with LLMs fostered an actionable and creative AI system.

As pharmaceutical research continues to evolve, the integration of AI and Design Thinking will be instrumental in shaping the future of drug development and innovation. This approach ensures that medical advancements remain scientifically robust, ethically sound, and focused on improving patient outcomes, ultimately driving meaningful progress in healthcare.

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Abbreviations

The following abbreviations are used in this manuscript:

QSAR Quantitative structure-activity relationship

iPSCs Induced Pluripotent Stem Cells

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