ISSN Print: 2664-6536
ISSN Online: 2664-6544
Impact Factor: RJIF **5.4**
IJBB 2025; SP-7(2): 43-47
www.biosciencejournal.net
Received: 22-04-2025
Accepted: 27-05-2025

Ruchil Joshi
Department of Zoology,
Government College Kota,
Kota, Rajasthan, India

Corresponding Author:
Ruchil Joshi
Department of Zoology,
Government College Kota,
Kota, Rajasthan, India

Two-Days National Conference on Multidisciplinary Approaches for Innovation and Sustainability: Global solution for contemporary Challenges-NCMIS (DPG Degree College: 17 th-18th 2025)

Drug discovery and development process: An evolving scientific journey

Ruchil Joshi

DOI: https://www.doi.org/10.33545/26646536.2025.v7.i2a.129

Abstract
The process of drug discovery and development (DDD) is a critical pathway in modern medicine, aiming to identify and bring new therapeutic agents to the market. It typically begins with target identification, followed by hit discovery, lead optimization, preclinical studies, and multiple phases of clinical trials. The field of drug discovery and development is undergoing a profound transformation, driven by innovations in AI, gene editing, and human-relevant models.
The integration of emerging technologies such as Artificial Intelligence (AI), CRISPR based gene editing, Organ-on-a-Chip Models mRNA & Biologics (mRNA vaccines) and Nanotechnology is transforming drug development by improving target selection, reducing failure rates, and accelerating clinical translation. However, high costs, regulatory hurdles, low success rates, lengthy clinical trials and ethical concerns pose significant challenges. Advances in precision medicine, AI-driven drug screening, and biologics have the potential to enhance the efficiency of drug discovery while reducing costs, ensuring faster and safer drug availability for patients worldwide.

Keywords: CRISPR, lead optimization, hit discovery, organ on chip model

1. Introduction
Drug discovery is the process by which drugs are discovered and designed. It is a process which aims at identifying chemical entities that have the potential to become therapeutic agents useful in curing & treating disease. Drug discovery and development is a complex, multi-phase, highly intricate and resource-intensive process, involving multiple phases from target identification to regulatory approval.

Objective
This paper explores the key stages, modern innovations, and ongoing challenges in the field of drug development and discovery, with a focus on how emerging technologies are reshaping the future of medicine.

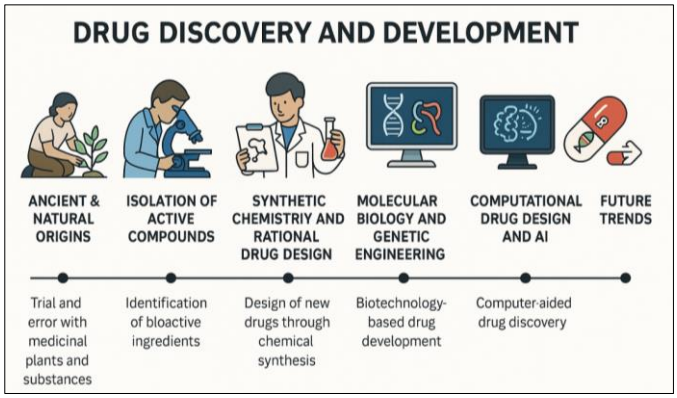


Fig 1: Show drug discovery and development

Drug discovery and Development

The process of drug discovery and development has undergone a significant evolution over centuries.

Early history of medicine

- **(Before 500 CE):** Relied heavily on observation, trial and error, and traditional knowledge passed down through generations. Early treatments often used plant and animal extracts.
- **Ayurveda in India:** Codified by sages like Charaka and Sushruta, emphasizing plant-based medicine and holistic treatment.
- **Greek & Roman Medicine:** Hippocrates and Galen promote observation and classification of diseases; use of opium, wine, and willow bark (early aspirin).

Industrial Revolution & Modern Pharmacology (1800-1900)

- **Quinine:** Derived from the bark of the cinchona tree, quinine was used to treat malaria.
- **Aspirin:** Extracted from the bark of willow tree, aspirin was used for the treatment of fever.
- **Mercury:** This was used to treat syphilis.

20th Century the golden age of drug discovery

Early 1900s-1940s

Aspirin (1899) becomes mass-produced.
Insulin (1921) revolutionizes diabetes treatment.
Penicillin (1928, mass-produced in 1940s): First true antibiotic.

- **Sulpha drugs:** First broad-spectrum antibacterials.
- **1950s-1980s:** Expansion of Drug Classes
- **Antibiotics boom:** Streptomycin, tetracycline, etc.

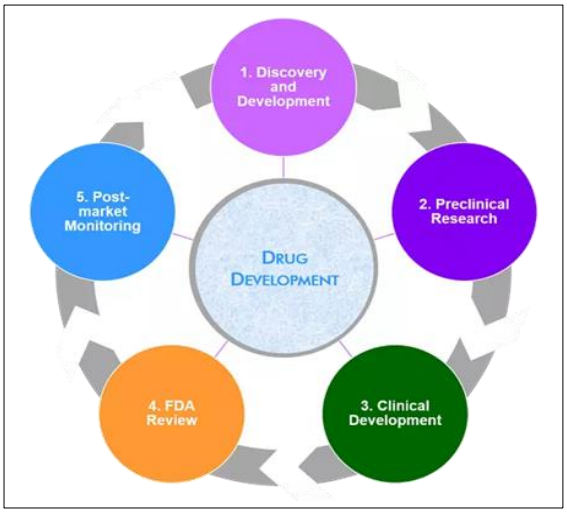
AI-Driven Drug Discovery (2010s present)

Modern drug discovery incorporates a variety of approaches, including small molecule and gene therapies. It also leverages advancements in technologies like genomics, proteomics, and AI to identify new drug targets and accelerate the drug development process.

Stages of drug development and modern techniques in drug discovery

The process of drug discovery and development is complex and involves multiple stages, from identifying potential drug candidates to bringing a safe and effective product to market. It typically takes 10-15 years and costs billions of dollars to develop a single drug. The process consists of the following key phases, drug discovery, preclinical testing, clinical trials, and regulatory approval.

2. Drug Discovery Process



2.1 Target Identification and Validation

The first step in drug discovery is identifying a biological target usually a protein, gene, or receptor that plays a key role in disease progression. The target must be validated to ensure that modifying it will have a therapeutic benefit. Techniques like genomic analysis, proteomics, and high-throughput screening are used to identify and validate these targets.

2.2 Hit Discovery and Lead Optimization

Hit Identification (Screening of Compounds): A hit compound is a molecule that exhibits activity at the target of interest during an HTS (High-Throughput Screening).

Lead Optimization

Promising hits (lead compounds) are modified to improve their efficacy, selectivity, solubility, and metabolic stability while reducing toxicity.

Lead Identification: Finding compounds that show promise in preclinical studies and have the potential to become drug candidates.

In vitro (cell-based) and *in vivo* (animal-based) models are used to test the optimized compounds.

2.3 Preclinical Testing

Before human trials, the drug undergoes extensive in vitro (e.g., cell cultures) and in vivo (animal models), to evaluate their pharmacological and toxicological profiles. The focus is on "ADMET" characteristics Absorption, Distribution, Metabolism, Excretion, and Toxicity which help predict the behaviour of the compound in the human body. Only compounds with acceptable safety margins and pharmacokinetic profiles progress to human testing.

Regulatory Submission (IND-Investigational New Drug Application): If results are promising, an IND is submitted to regulatory agencies (e.g., FDA, EMA, DCGI) for approval to start human trials.

3. Clinical Trials (Human Testing)

Phase 1 (Safety & Dosage) 6 months to 1 year

- **Participants:** 20-100 healthy volunteers or patients.
- **Objective:** Test for safety, dosage, and side effects.

Phase 2 (Efficacy & Side Effects) 1 to 2 years

Participants: 100-500 patients.

Objective: Evaluate effectiveness and short-term side effects.

Phase 3 (Large-scale Testing) 3 to 5 years

- **Participants:** 1,000-5,000 patients across multiple sites.
- **Objective:** Confirm efficacy, monitor side effects, and compare with existing treatments.

  If successful, a New Drug Application (NDA) is submitted to regulatory agencies for approval.

Phase IV

Post-marketing surveillance after regulatory approval to track long-term safety and real-world effectiveness.

4. Regulatory Approval

The FDA, EMA, or DCGI (depending on the country) reviews clinical data to approve the drug. These bodies rigorously evaluate the evidence for safety, efficacy, and manufacturing quality before granting market authorization.

Recent advancements in drug discovery

1. **Artificial Intelligence (AI) & Machine Learning:** Used for drug repurposing and predictive modelling.
2. **CRISPR & Gene Editing:** Developing gene-based therapies.
3. **mRNA & Biologics:** mRNA vaccines (like COVID-19 vaccines) and monoclonal antibodies are revolutionizing medicine.
4. **Organs-on-Chips:** Lab-grown microenvironments mimicking human organs for better drug testing.
5. **Nanotechnology:** Targeted drug delivery using nanoparticle.

What is CRISPR-Cas9?

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats: CRISPR-Cas9 is a powerful and precise gene-editing technology that allows scientists to modify DNA within living organisms. Originally discovered as a natural defence system in bacteria, CRISPR works alongside the Cas9 protein, which acts like molecular scissors to cut DNA at specific locations. By designing a guide RNA that matches a target DNA sequence, researchers can direct the Cas9 enzyme to that exact spot in the genome. Once the DNA is cut, the cell repairs the break either by joining the ends together often causing mutations or by inserting a new, desired sequence using a repair template.

2. Applications of CRISPR in gene-based therapies

(a) Treating Genetic Disorders

CRISPR is being used to correct mutations responsible for inherited diseases such as:

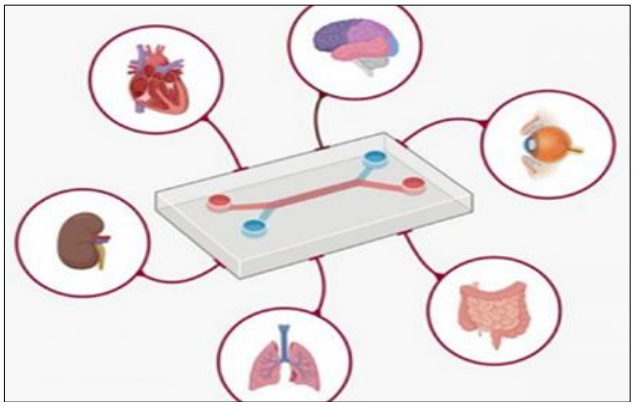
- Sickle cell disease & beta-thalassemia
- Cystic Fibrosis
- Duchenne Muscular Dystrophy (DMD)
- Cancer Immunotherapy
- Neurological Disorders: Eg: Huntington's disease.

3. Ethical & Regulatory Challenges: Despite its potential, CRISPR raises significant ethical concerns:

- **Germline Editing:** Editing embryos could lead to unintended genetic consequences for future generations (e.g., the controversial "CRISPR babies" case in China).
- **Off-Target Effects:** Unintended mutations may introduce new health risks.
- **More CRISPR-Based** Medicines: Expansion into new disease areas, including cardiovascular diseases and metabolic disorders.

1. Improving Crop Traits: CRISPR technology holds significant promise for revolutionizing agriculture by enabling precise and efficient genome editing in crops. This technology can be used to enhance various traits, including nutritional value, disease resistance, drought tolerance, and improved post-harvest quality, while also reducing the need for chemical pesticides.

2. Organs-on-Chips



Organs-on-chips are systems containing engineered or natural miniature tissues grown inside microfluidic chips. The goal for organ-on-a-chip is to develop human tissue models for disease modelling and drug testing.

These are tiny, see-through computer chip, but instead of wires and circuits, it contains living human cells that act like mini-organs. It's about the size of a USB stick, and inside, it mimics how organs like the lung, heart, or liver actually work-including how blood flows and how tissues react.

Organ on Chips are small, flexible chips, typically made from polydimethylsiloxane (PDMS) or other biocompatible materials. These chips contain micro scale channels lined with human cells, allowing researchers to replicate:

Applications of organs-on-chips:

1. **Reducing Animal Testing:** OoCs offer a humane and more accurate alternative to animal models, aligning with the 3Rs principle (Replacement, Reduction, and Refinement).
2. **Drug Discovery & Testing**

- **More accurate preclinical testing:** OoCs provide human-relevant responses, reducing the reliance on animal models.
- **Personalized medicine:** Patient-derived cells can be used to test drug responses before prescribing treatments.
- **Toxicity screening:** Helps predict drug-induced liver, kidney, or heart toxicity before human trials.

3. **Studying Organ Interactions:** Multi-organ-on-a-chip systems can simulate how different organs interact in response to drugs, toxins, or diseases
4. **Disease Modelling:** Researchers can replicate diseases like cancer, Alzheimer's, or respiratory infections on chips, allowing them to test potential therapies in a controlled environment.

Examples of Organ-on-a-Chip Models: Several models using different organs such as lungs on a chip, liver on a chip, kidney on a chip, heart on a chip, intestine on a chip and skin on a chip have been successfully developed.

- **Lung-on-a-Chip:** Simulates breathing by stretching lung cells; used for respiratory disease research.
- **Brain-on-a-Chip:** Mimics the blood-brain barrier; helps study neurological diseases like Alzheimer's.
- **Heart-on-a-Chip:** Uses beating cardiac cells to test drug effects on the heart.
- **Retina-on-a-Chip:** Studies eye diseases and potential treatments.

4. Advantages of Organs-on-Chips

- **Human-relevant responses:** Mimic actual human physiology better than animal models.
- **Real-time monitoring:** Researchers can track cellular responses to drugs in real-time.
- **Cost-effective:** Reduces the need for expensive and lengthy clinical trials.
- **Customizable:** Can be tailored for specific diseases or patient samples.

5. Challenges & Future Directions

- **Scalability:** Mass-producing these chips for widespread adoption remains a challenge.
- **Integration with AI:** AI-driven data analysis can enhance prediction accuracy for drug responses.
- **Multi-Organ Systems:** Developing a "Human-on-a-Chip" by connecting multiple organ systems for holistic drug testing.

Case studies in drug development and discovery

- **mRNA Vaccines for COVID-19:** Pfizer-BioNTech and Moderna developed mRNA vaccines within a year using lipid nanoparticles, genomics, and AI-supported trial management.
- **Drug Repurposing:** Thalidomide and Remdesivir. Thalidomide was repurposed for multiple myeloma; remdesivir, initially for Ebola, was repurposed for COVID-19.

5. Conclusion

Drug development is a cornerstone of modern healthcare, playing a critical role in the prevention, management, and treatment of diseases. It not only improves patient outcomes and quality of life but also supports healthcare systems by reducing the burden of long-term treatments, hospitalizations, and surgical interventions. With the rise of chronic diseases, antibiotic resistance, and global pandemics, the demand for safe, effective, and accessible medications has never been greater. Thus, by continuing to integrate these cutting edge technologies the pharmaceutical industry can accelerate the development of novel therapies and address unmet medical needs more effectively.

"Behind every drug is a patient waiting for hope. Our work in drug discovery isn't just about science it's about changing lives. Let’s continue striving to make that difference”.

6. References

1. Mullard A. AI in drug discovery: Where are we now? Nat Rev Drug Discov. 2020;19(8):491-492.
2. Doudna JA, Charpentier E. The new frontier of CRISPR gene editing. Science. 2014;346(6213):1258096.
3. Zhang B, *et al*. Organ on a chip models for drug testing. Nat Biotechnol. 2021;39(3):273-283.
4. PhRMA. The Cost of developing a new drug. Pharmaceutical Research and Manufacturers of America; 2020.
5. DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: New estimates of R&D costs. J Health Econ. 2016;47:20-33.
6. Paul SM, *et al.* How to improve R&D productivity: The pharmaceutical industry's grand challenge. Nat Rev Drug Discov. 2010;9(3):203-214.
7. Pushpakom S, *et al.* Drug repurposing: Progress, challenges and recommendations. Nat Rev Drug Discov. 2019;18(1):41-58.
8. Charpentier E, Doudna JA. Rewriting a genome. A perspective piece summarizing their CRISPR, Nature. 2013;495(7440):50-51. [Perspective Piece].