IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Drug Discovery

Satyansh Kumar Singh, Piyush Yadav, Priyanshu Mishra, Asgar Shameem, Deepak Kumar Yadav.

Department of pharmacy, Prasad institute of technology, jaunpur, (Uttar Pradesh), india.

Abstract: The process of drug development is very expensive process due to high costs of R&D and human clinical tests. At present a new approach is being tried to understand how disease and infection are controlled at the molecular and physiological level and to target specific entities based on the knowledge. The drugs discoveries are based on molecular biological targets and improve the therapy for disease, wide ranging dosages of the compounds are introduced to the cell line or animal in order to obtain preliminary efficacy and pharmacokinetic information. The process of drug discovery involves the identification of candidates, synthesis, characterization, screening & assay for therapeutic efficacy. Once a compound has shown its value in these tests, it will begin the process of drug development prior to clinical trials.

Keywords: Drug discovery: introduction, history of drug discovery, drug discoveries overview, steps in modern drug discovery, advantages and disadvantages of drugs discovery, conclusion.

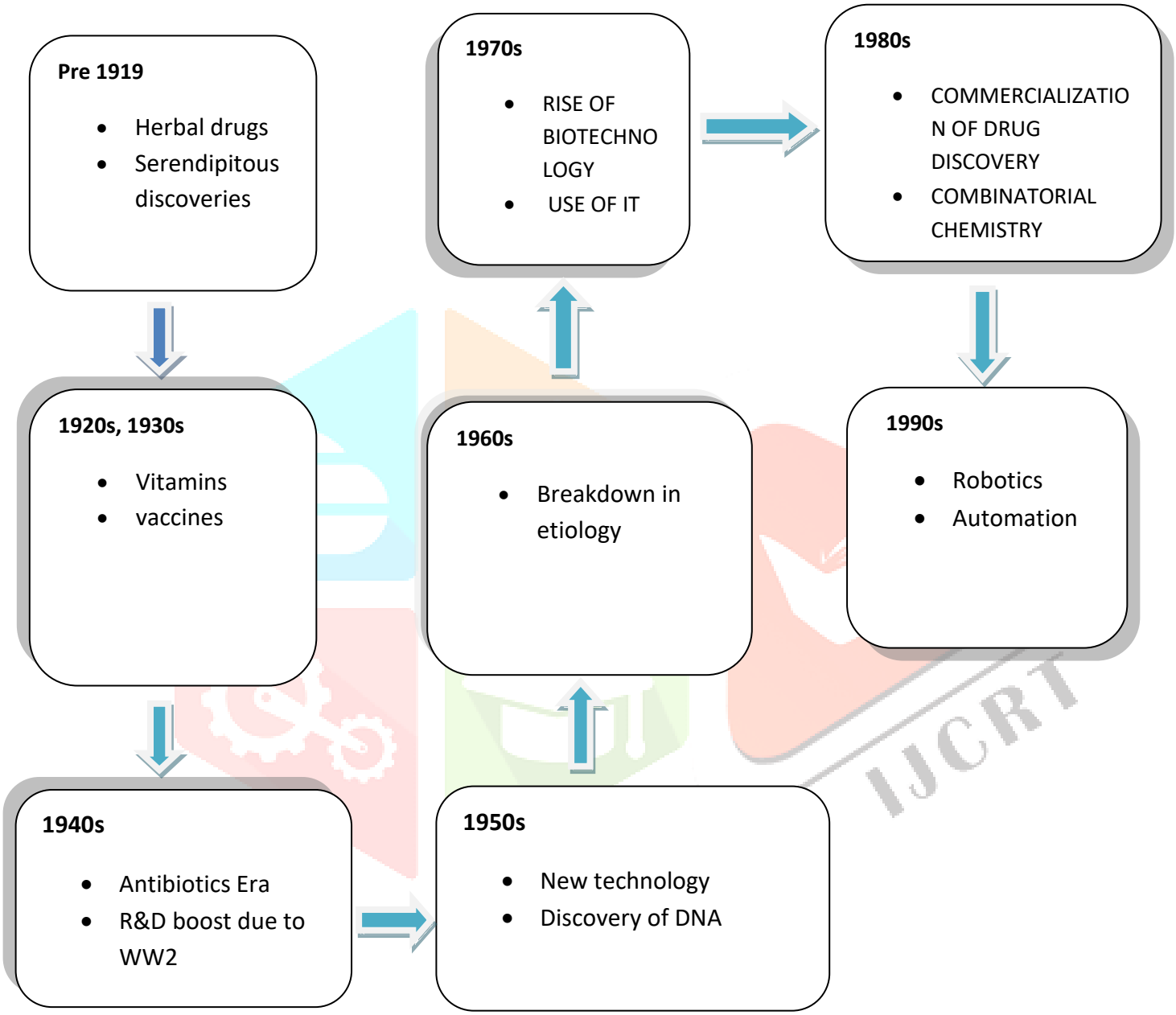
Introduction- "**Drugs discovery is the process through which potential new medicines are identified. It involves a wide range of scientific disciplines, including biology, chemistry and pharmacology**". In the most drugs have been discovered either by identifying the active ingredient from traditional remedies or by serendipitous discovery, but we know the disease controlled by the molecular and physiological level and shape of molecule at atomic level is well understood. The drugs discovery process mainly involves for the identification of candidates, characterization, screening and assay for therapeutic efficacy. The process of drug development is very expensive process due to high costs of R&D and human clinical tests. The average total cost for only drug development is varies from USD 897 million to USD 1.9 billion. The typical development time is 10-15 years. The past most drugs have been discovered

either by identifying the active ingredients from traditional remedies or by serendipitous discovery. At present a new approach is being tried to understand how disease and infection are controlled at the molecular and physiological level and to target specific entities based on the knowledge.

History- Occasionally new drugs are found by accident. The discovery of new pharmaceutical agents has gone through an evolution over the years and has been adding new technologies to this increasingly complex process. More frequently they are developed as part of organized efforts to discover new ways to treat specific disease. The drugs discoveries is based on molecular biological targets and improve the therapy for disease, example captoprilis is leader of angiotensin-converting enzyme (ACE) - inhibitors used for treatment of essential hypertension. Alternative and complementary treatments for hypertension involve use of angiotension 2 receptor antagonists, losartan was the first compound in this class and was followed by several additional molecules. Treatment of hypertension by these mechanism provided physicians with additional options to consider as part of combination therapy or when other possibilities such as diuretics and/or beta-blockers are unsatisfactory.

Discovered In 1976 – Captoprils
Discovered in 1986 - Valmasartan, telmisartan, and irbesartan
Discovered 1989 - discovered in 1989 M1 and M3 receptor
Discovered 1992 - Imatinib (treatment of myeloid leukemia)
Discovered 2001 - Sitagliptin

HISTORY OF DRUG DISCOVERY



Drug Discovery Overview

- Drugs discovery effort addresses **a biological target** that been shown to play a role in the development of the disease or starts from **a molecule with intresting biological activities**
  1. Identification of a new potential drug target
  2. Rational drug design
  3. Modification of an existing drug/potential drug
  4. Screening of chemical/macromolecule/organic chemical libraries
  5. Biotechnical approaches using the human genome.
  6. Combination of known drugs to obtain aided or synergistic effects[5].

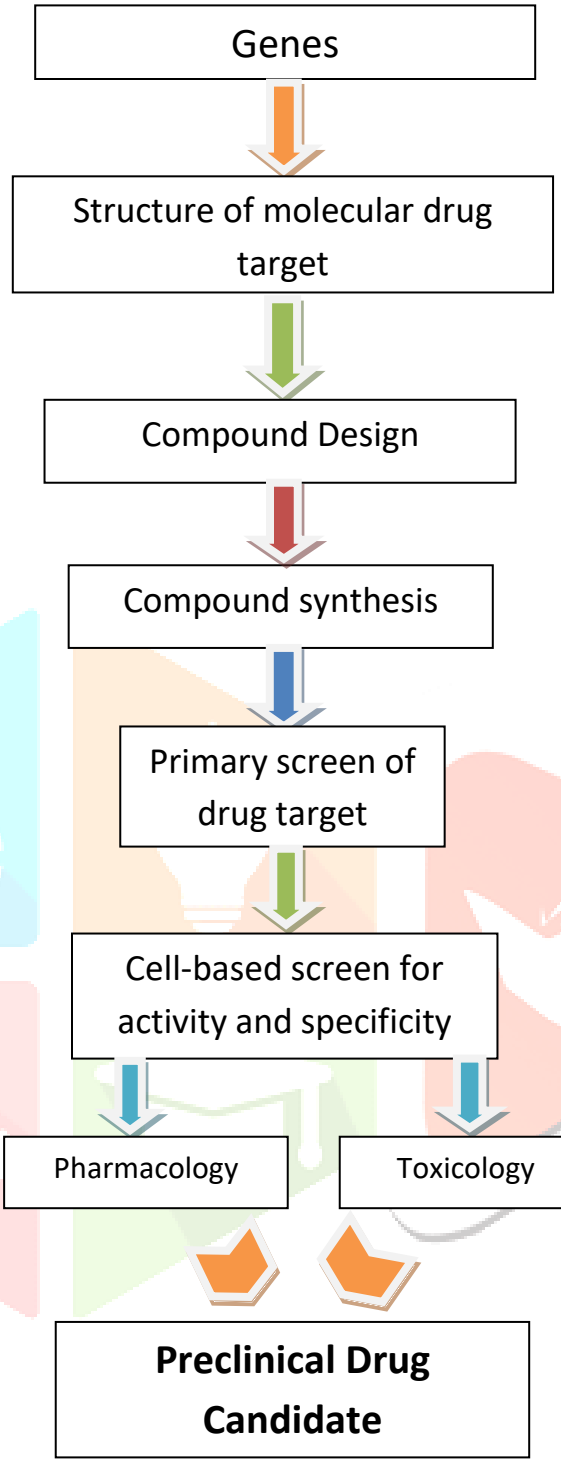
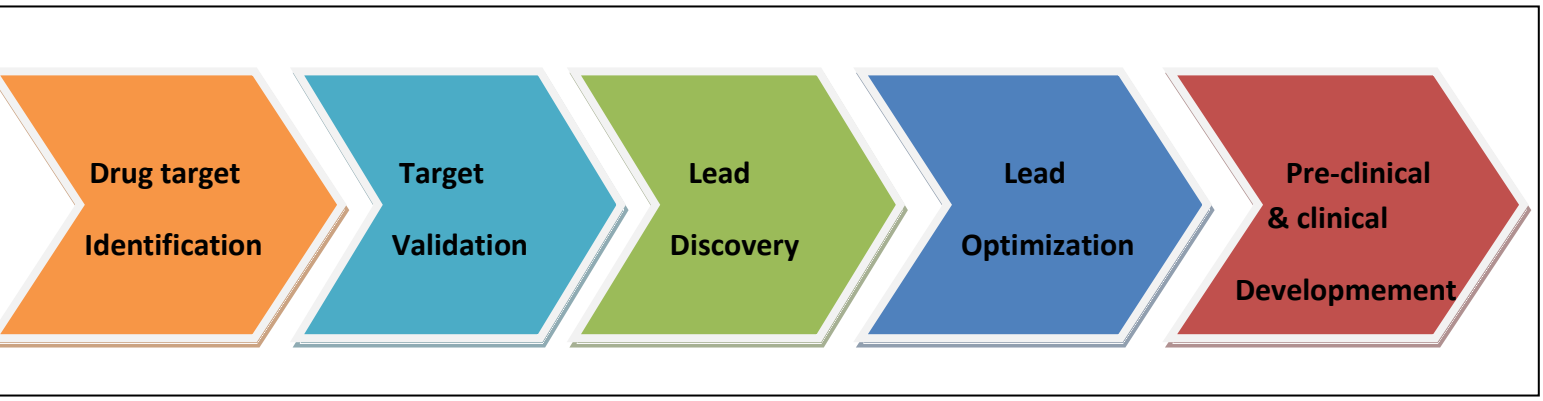


Fig: Drug discovery

Steps in Modern Drug Discovery



Step 1: Target identification

Target identification is the first key stage in the drug discovery pipeline. Generally speaking, a drug target is the specific binding site of a drug *in vivo* through which the drug exerts its action[6]. The process is a chemistry based. Which mean produce compounds for screening. Approach of identification includes protein expression structural and functional studies and study of biochemical pathways. For these modes of identification, recently several methods are available-

1. Sequence Analysis
2. Positional cloning
3. cDNA library generation

Therefore process helps to find a huge number of target identification[7]. A bio molecule may be involved in a disease process, but to be a drug target it has to be validated. In other words shown to be critical in the disease process useful technique available are to validate a target such as gene knockout and RNA interference.

STEP 2: Target validation

New target validation is the basis of completely new drug exploration and the initial step of drug discovery.

Research scientists can they identify compounds that have an effect on the target selected. Test are conducted to confirms that interaction with the drugs target are associated with a desired change in the behaviour of diseased cells, researcher analyze and compare each drug target to other based on their association with a specific disease and their ability to regulate

biological and chemical compounds in the body[8]. New drug research and development but also provide more insight into the pathogenesis of target related disease. Basically, the target validation process might include six steps:

1. Discovering a molecule of interest.
2. Evaluating its potential as a target.
3. Designing a bioassay to measure biological activity.
4. Constructing a high-through put screen.
5. Performing screening to find hits.
6. Evaluating the hits.

Basic research into understanding the fundamentals, essential processes for signalling within and between cells and their perturbation in condition has been the basic approach for establishing potential targets suitable for drug intervention[9].

STEP3: Lead discovery

This is accomplished primarily with knock-out or knock-in animal models; small molecular target *in vitro* usually precedes the validation of the therapeutic concept *in vivo;* together this defines in clinical potential. Validation involve studies in molecular target *in vitro* usually proceeds with the target protein and modulate its activity[10]. Synthetic chemicals, peptides, natural or engineered protein, or antibodies are exposed to the target in a manners that will detect and isolate those members of the library that interact with and preferably have an effect on the target[11]. For example, if the goal is to inhibit a protein that is involved in activating the expression of a particular gene or set of genes, the assay can include readout to determine if the expression of the gene is reduced by the compound. The assay can be cell-based, but more often they are enzymatic assay that can be performed in a high-throughput manner.

STEP 4: Lead optimization

A **lead compound** is a compound from a series of related compounds that has some of a desired biological activity. Leads compounds that survive the initial screening are then "optimized'" or altered to make them more effective and safer. By changing the structure of a compound, scientists can give it different properties. For example, they can make it less likely to interact with other chemical pathway in the body, thus reducing the potential for side effects.

Researchers begin to think about how the drug will be made, considering formulation (the recipe for making a drug, including inactive ingredient used to hold it together and allow to

dissolve at the right time), delivery mechanism (the way the drug is taken – by mouth, injection, inhaler) and large-scale manufacturing (how you make the drug in large in large quantities)[12].

STEP 5: Pre-clinical and clinical and development

Pre-clinical development: the pre-clinical development includes the following develop large scale synthesis; animal safety studies; carcinogenicity tests; drug delivery; elimination and metabolism studies; drug formulation experiments; dose-ranging studies in animals. Wide ranging dosages of the compounds are introduced to the cell line or animal in order to obtain preliminary efficacy and pharmacokinetic information.

Clinical development

The NH organizes clinical trial in to 5 different types:

- Treatment trials: test experimental treatments or a new combination of drugs.
- Prevention trials: look for ways to prevent a disease or prevent it from returning.
- Diagnostic trials: find better test or procedures for diagnosing a disease.
- Screening trials: test methods of detecting disease.
- Quality of life trials: explore way to improve comforts & quality of life for individuals with a chronic illness

Pharmaceutical clinical trials are commonly classified into 4 phases.

1. **Phase** 0/**Micro dosing**-
    - To obtain prelimary data pharmacokinetics data.
    - Sub acute toxicity study in one species by two routes of administration.
2. **Phase 1 –**
    - 20-25 healthy volunteers; duration 6-12 months.
    - The aim of a phase 1 trial is to determines the maximum tolerated dose (MTD) of the new treatment.
3. **PHASE 2-**
    - New action of a marketed drug, start with phase 2.
    - Designed to study efficacy and assess dosing requirements

4. **Phase 3 –**
    - Its a therapeutics confirmatory trial.
    - Target population: several 100 are to 3000 patients.
    - Duration: takes a long time, up to 5 years.
5. **Phase 4-**
    - Post marketing surveillance (PMS).
    - Confirms the efficacy and safety profiles in large population during practice.
    - The ADR can be reported to a formal reporting system such as:
        - WHO international system
        - USFDA- medwatch
        - UK- yellow card system
        - India- national pharmacovigilance programme (CDSCO)

Advantages -

1. Patients receive optimal pharmaceutical therapy.
2. Allows for improved availability of medicine because of consistent and known usage patterns.
3. Enables consistent and predictable treatment from all levels of providers and at all locations.
4. Helps provide good outcomes because patients are receiving the best treatment regimen available.

Disadvantages –

1. Guidelines development and maintenance takes much time and effort.
2. STGs may give false of security and discourage ongoing critical thinking.
3. Inaccurate guidelines will provide the wrong information. Often guidelines are based on existing practices rather than evidenced-based medicine.

Conclusion

The drugs discovery is a time consuming and expensive process, the top twenty pharmaceutical companies spent – $16 billion on research and development every year, but recent discovery technologies and strategies have reduced the bottleneck in discovering high affinity ligand for therapeutic targets. Well designed and effectively executed clinical trials form the base of therapeutic decisions. The availability of biologics reagents, new methods,

technologies and computational tools is revolutionizing the way we do biological discovery and is enabling new approaches to identify noval targets drug discovery and development.

Reference-

1. https://www.slideshare.net/mobile/sabaahmed56/drug-discovery-53678448.
2. Gien sefen H, hilgenfield R, hillisich A (2003) modern method of drug discovery institute of molecular biotechnology, beutenbergster germany 1:109-155.
3. Propst C, modern technologies for the discovery of new pharmaceuticals in the world biotech report – USA, Vol. 2 online publication, new York, PP- 283-289.
4. Joel C. Barrish, Percy H. Carter, Peter T.W. Cheng and Robert Zahler, Accounts in Drug Discovery case study in medicinal chemistry RSC Publishing U.k page no.- 1-5.
5. Drews J (2000) Drug discovery a historical in perspective science 287:1960-1963.
6. https://www.slideshare.net/mobile/Brittosamuel/drug-discovery-65551415.
7. Wang s, sim TB kim ys chang YT (2004) tools for target identification & validation curr opin Chem Biol 271-377.
8. DUGH (2004) evaluation & validation of drug targets acta pharmacol Sin 25:1566.
9. www.nlm.nih.gov/services/ctphases.html
10. Shayne Z(G 2006) Introduction : drug discovery in the 21ST century drug diecovery Handbook Wiley Press.
11. Jens Eckstein ISOA/ARF Drug development tutorial, Alzhemir Research forum 1-18.