New Drug Discovery and Development

Definitions -

Drug: A chemical substance of known structure, other than a nutrient or an essential dietary ingredient, which, when administered to a living organism, produces a biological effect.

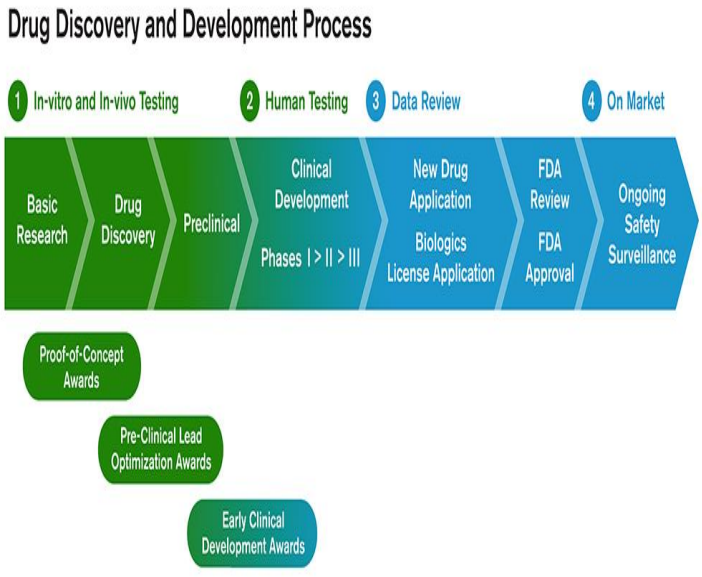
Discovery Phase: Identification of new chemical entity as a potential therapeutic agent.

Development Phase: Compound is tested for safety and efficacy for one or more clinical indications, and in suitable formulations and dosage form.

New Drug Definition (CDSCO) According to rule 122E: A new substance of chemical, biological, or biotechnological origin in bulk or prepared dosage form used for prevention, diagnosis or treatment of disease in man or animal which except during local clinical trial, has not been used in country to any significant extent and which except during local clinical trials, has not been recognized in the country as effective and safe for the proposed claim.

Stages of the New Drug Synthesis:

- Drug Discovery: Candidate molecules are chosen on the basis of their pharmacological properties.
- Preclinical Development: Non-human studies (e.g., toxicity testing, pharmacokinetic analysis and formulation) are performed.
- Clinical Development: The selected compound is tested for efficacy, side effects and potential dangers. Drug development is the process of bringing a new pharmaceutical drug in market once a lead compound has been identified through the process of drug discovery. It includes preclinical research o microorganism and animals, filing for regulatory status, such as via the United States Food and Drug Administration for an investigational new drug to initiate clinical trials on human and may include the steps of obtaining regulatory approval with new drug application to market the drug.



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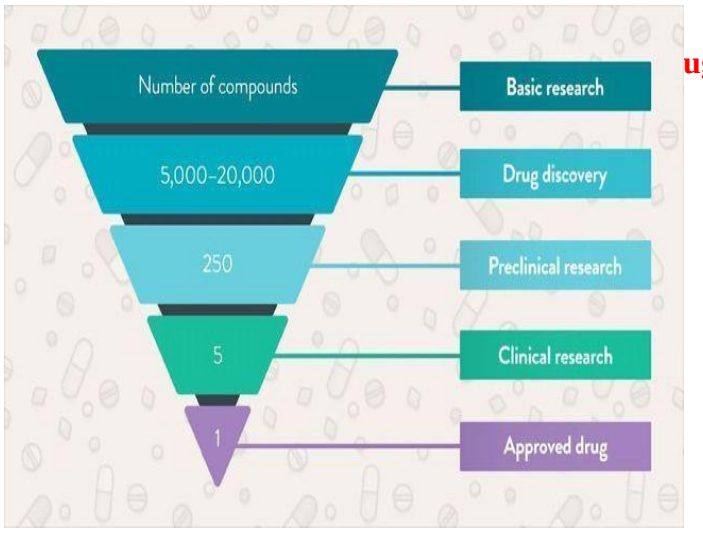
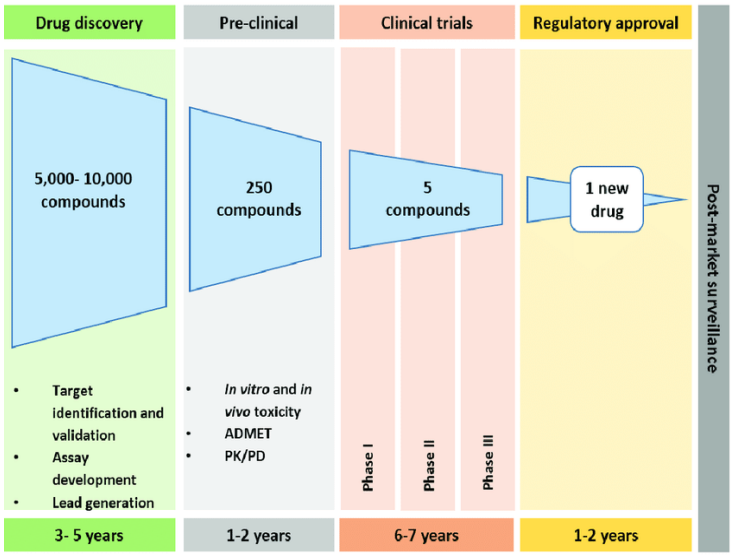
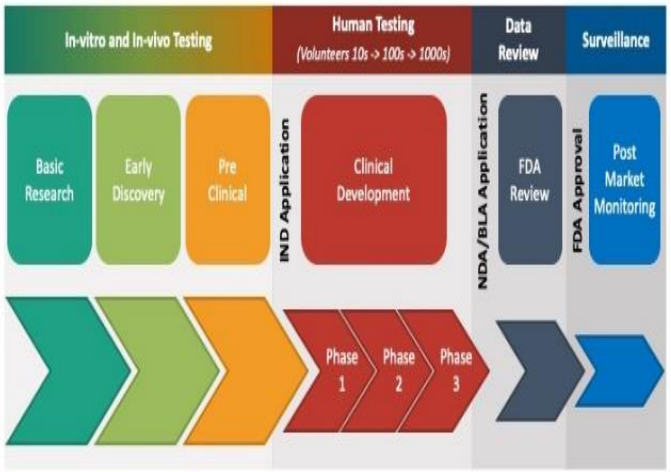


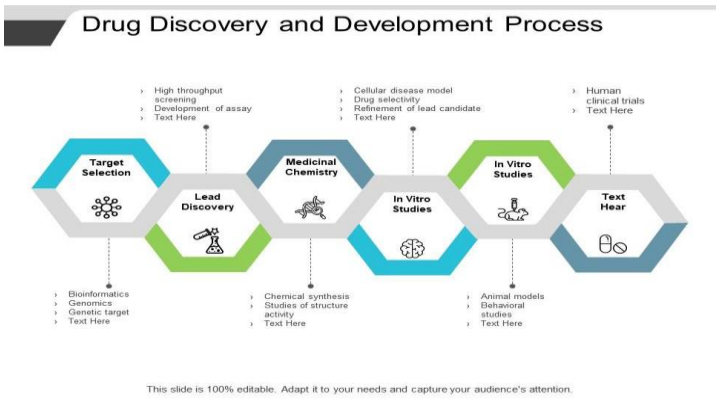
ug Discovery and Development Timeline:





Procedure for Drug Discovery:

1. Random **screening:** in this procedure new chemical entities are subject to battery of screening test designed to determine different type of biological activity.
2. **Molecular manipulation:** In this procedure analogous of existing drugs are synthesized and tested for their biological activity.
3. **Molecular designing:** In its simplest form this may involve the synthesis of naturally occurring substance, hormone, a vitamin of a precursor of neurotransmitter.



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4. **Metabolites of drug**: sometimes active metabolites of drug are found to possess therapeutic advantages over parent compound.
5. **5.Serendipity:** it means "happy observation by chance" and has led to introduction of many remedies in the past.

❖ **Steps Involved in Drug Development:**

➢ Preclinical synthesis and physiochemical analysis

⬇

Preliminary biological evaluation

⬇

Secondary and specific biological evaluation

⬇

Rang finding toxicological studies

⬇

Target organ toxicological studies

⬇

Acute and subacute toxicological studies

⬇

Metabolic studies.

➢ Synthesis and quality control of bulk Materials

⬇

Phase 1 clinical evaluation

⬇

Final formulation and final physiochemical analysis

⬇

Phase 2 clinical evaluation

⬇

Phase 3 clinical evaluation

⬇

Phase 4 clinical evaluation

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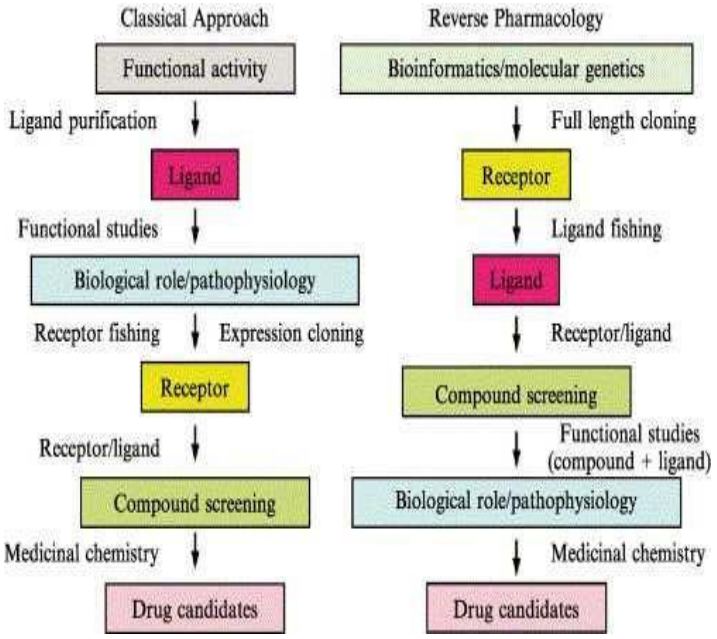

Target Identification Strategies:

- Gene Expression Profiling**:** Genomics
- Focused Proteomics
- Metabolic Pathway Analysis: Molecular Biology
- Phenotype Analysis
- Genetic association

Approaches to the new drug molecule

Newer Technique:

I. Molecular modelling:

- AKA rational drug designing.
- Added by 3-dimensional computer graphics.
- Allows design of structure based on new and non-molecule.
- Highly selective targeted compounds are created by enhancing desired properties of known molecule.

II. Combinatorial chemistry:

It is systematic and repetitive covalent connection of set of different building blocks of varying structures to each other to yield a large array of diverse molecule entities.

III. Biotechnology: Therapeutic agents produced by biotechnology rather than conventional synthetic chemistry are called biopharmaceuticals.

Involve the use of recombinant DNA technology/ genetic engineering.

IV. Genetic medicine:

Transfer of genetic materials

I. A single gene which is typical for gene therapy.

II. Fragments of coding sequences (as in RNA modification therapy- MC being anti sense oligonucleotide strategy).

III. Entire genome (as in the case of SSC and ESC therapy).

V. Immunopharmacology:

Deals with finding the biological immuno-modifier or immune-modulating agent that cause selective up regulation or down regulation specific immune response.

❖ What After Preclinical Phase?

- Once the preclinical trial is over sponsors are required to submit the "investigational new drug " application.

- It contains information:

- 1. Preclinical data: PK, PD and toxicological

- 2. Manufacturing data: composition, manufacturing process, stability and shelf life.

- 3. Protocol of clinical trials.

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