DRUG DESIGN

Worked By
Mr. Khatal Sushant Suryabhan

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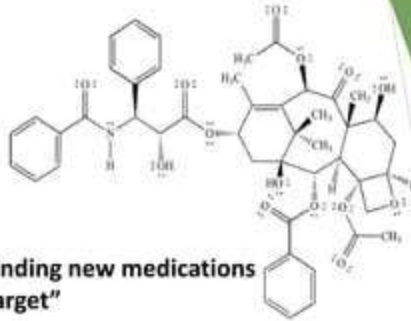
DRUG DESIGN



- Drug design is **"the inventive process of finding new medications based on the knowledge of a biological target"**
- Drug design in which develop a new drug by molecular modification of lead compound for optimization of desired effect and minimization of side effect
- It is the process to find out the new medicine base on the knowledge of target.
- The main aim to find out or develop drug with high therapeutic value.

OBJECTIVE

- Therapeutic Target Identification
- Study the method Minimization of Adverse Effects
- Understanding the Enhancement of Drug Bioavailability
- Understanding the Prevention of Drug Resistance
- Reading the process Validation through Preclinical Studies
- Reading Clinical Efficacy and Safety Assessment
- Reading the steps involved in the Regulatory Approval and Market Access
- Study the ways to Reduce the wastage of material during physical invention
- Study of source of drug
- Study of combinatorial chemistry

❖ Type of Drug Design:

- Ligand base drug design
- Structure base drug design

❖ Various approaches in drug design:

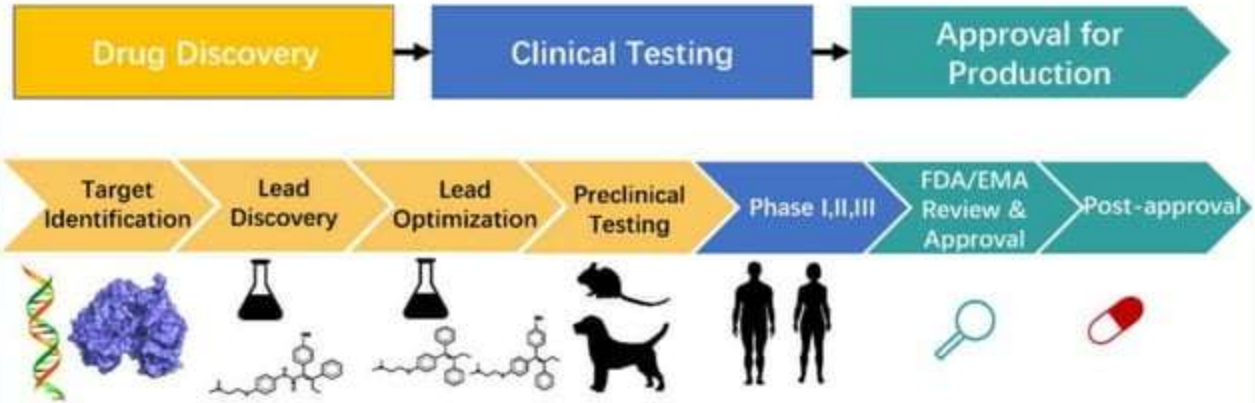
1) Design of analogue
2) Design of pro drug
3) Design of lead compound
4) Rational approaches

DRUG DISCOVERY

"It is a process by which new candidate medication are discovered"

- Following some of the important method which can be used for lead discovery:
  1) Random screening
  2) Non-Random screening
  3) Drug metabolism study
  4) Clinical observation

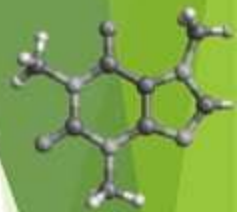
- Drug discovery involves identification, synthesis, characterization, screening and assay for therapeutic efficacy


Drug Discovery
Clinical Testing
Approval for Production
Target Identification
Lead Discovery
Lead Optimization
Preclinical Testing
Phase I,II,III
FDA/EMA Review & Approval
Post-approval

LIMITATION OF DRUG DESIGN

- Incomplete knowledge of disease mechanisms
- Limited target drug ability
- High development cost and time consuming process
- Unpredictable clinical outcome
- Diversity in patient population
- Complexity of biological system

QSAR QUANTATIVE STRUCTURAL ACTIVITY REALATIONSHIP



- QSAR is developed by hansch in 1969
- QSAR is a **"computational or mathematical modeling method to reveal relationships between biological activities and the structural properties of chemical compounds"**

- QSAR is a computational modeling technique used in chemistry, pharmacology and toxicology to predict the biological activity or properties of chemical compound based on their chemical structure
- The generated QSAR model are used to predict and classify the biological activities of new chemical compound

SEVERAL PARAMETER AND CONCEPT OF QSAR ESSENTIAL FOR ANALYSIS

- Molecular Descriptor
- Biological Activity

MOLECULAR DESCRIPTOR:

Molecular descriptors are essential QSAR parameters that quantify various structural and physicochemical properties of chemical compounds.

These descriptors play a crucial role in building QSAR models as they provide the quantitative information needed to relate a compound's structure to its biological or chemical activity

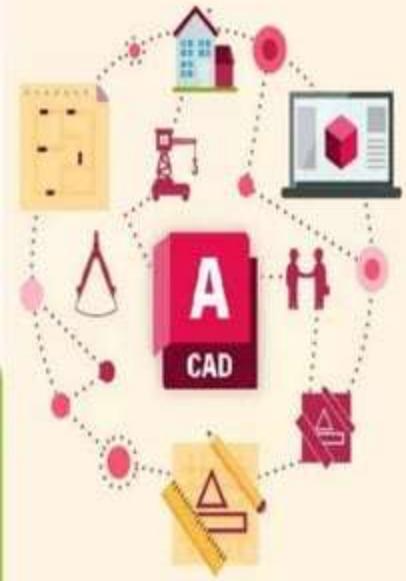
Topological descriptor
Geometrical descriptor
Electronic descriptor
Physicochemical descriptor
Spectral descriptor
Shape descriptor
Constitutional descriptor

BIOLOGICAL ACTIVITY:

Biological activity parameters used in Quantitative Structure-Activity Relationship (QSAR) modeling are crucial for predicting how chemical compounds interact with biological systems

Inhibitory Concentration 50 (IC50)
Effective Concentration 50 (EC50)
Lethal Dose 50 (LD50)
Effective Dose 50 (ED50)
Minimum Inhibitory Concentration (MIC)
Inhibition Constant (Ki)
Half Life

INTRODUCTION TO CADD

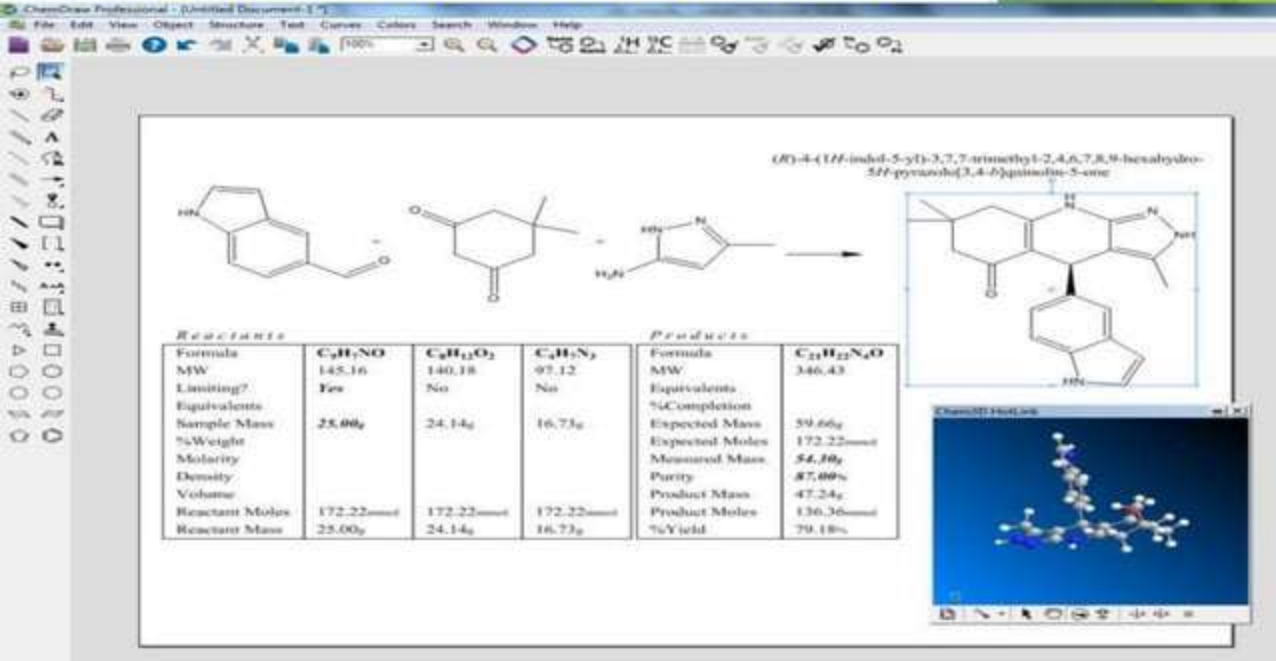


- Computer-Aided Design, commonly known as CAD, is a software commonly use in pharmacy use to creating, modifying, and analysing 2D and 3D designs of compound

- Some benefit of CAD Software
  - 2D 3D modeling
  - Accuracy
  - Efficiency
  - Collaboration
  - Simulation & Analysis

- Uses of CAD in Pharmacy
  - Drug Formulation & Development
  - Chemical structure analysis
  - Pharmaceutical Packaging Design
  - Lab equipment Design
  - Quality control & Validation

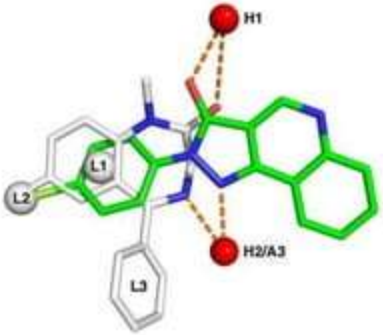
CHEMICAL STRUCTURE DRAWING



PHARMACOPHORE

- A pharmacophore is a three-dimensional arrangement of chemical features within a molecule that are responsible for its biological activity.
- The original concept of pharmacophore is developed by Paul Ehrlich
- These features can include atoms, functional groups, and their spatial relationships.
- The primary goal of pharmacophore modeling is to identify and define the specific structural and chemical elements that are necessary for a molecule to bind to its target
- Pharmacophores help in bridge the gap between the chemical properties of a drug and its biological activity

- It is define the important group is involved in binding
- It is define the relative position of the binding group

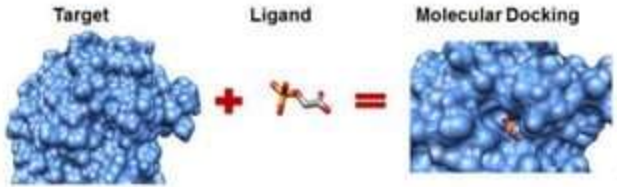


example of a pharmacophore model of the benzodiazepine binding site on the $GABA_A$ receptor.

White sticks represent the carbon atoms of the benzodiazepine
green represents carbon atoms of the nonbenzodiazepine
Red and blue sticks are oxygen and nitrogen atoms
The red spheres labeled H1 and H2/A3 are, respectively, hydrogen bond donating and accepting sites in the receptor, while L1, L2, and L3 denote lipophilic binding sites

DOCKING

- Molecular docking is a computational technique used in the field of structural biology and drug discovery.
- The primary goal of molecular docking is to simulate and analyse how a ligand can bind to a specific receptor, & understand the binding affinity and interactions between them.
- Docking Software
  - Autodock Tools
  - Autodock Vina



USES OF DOCKING IN PHARAMACY

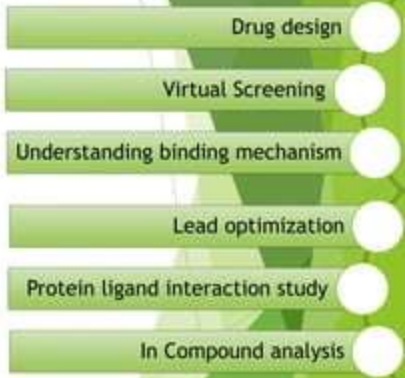
- Drug Design:
  Molecular docking helps in the design and optimization of new drug candidates.

- Virtual Screening:
  Docking can be used to virtually screen a large database of compounds to identify potential drug candidates that may bind to a particular target

- Understanding Binding Mechanisms:
  Understanding the mechanism of action of drugs and other biomolecular interactions.

- Lead Optimization:
  Suggest modification and help in optimization

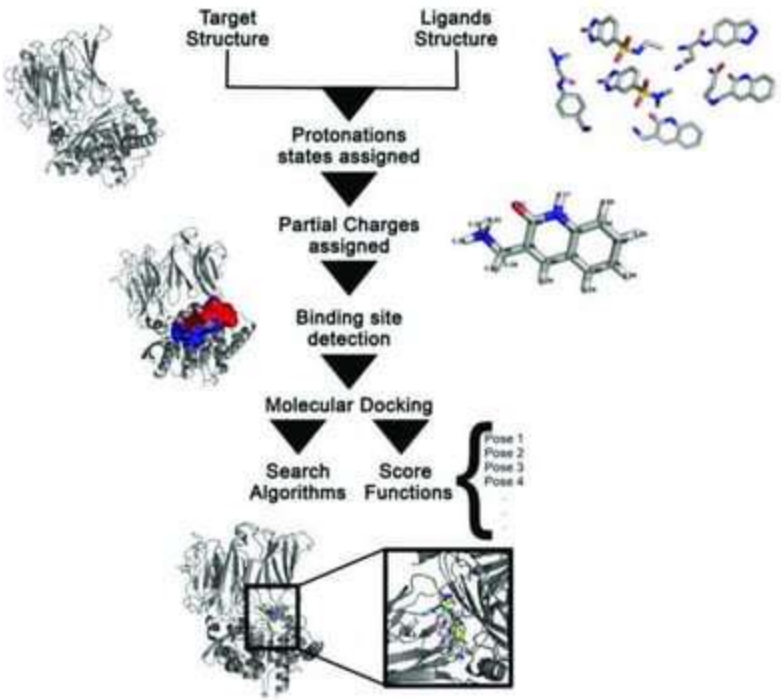
- Protein-Ligand Interaction Studies:
  Researchers use docking to study the interactions between various ligands and proteins



DOCKING ANALYSIS

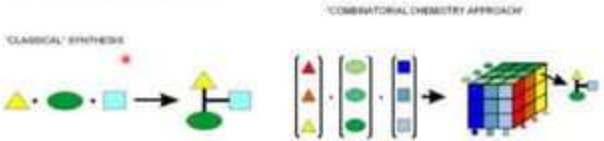
- Docking analysis is a computational technique used in molecular biology and drug discovery to predict the binding interactions between molecules, such as a ligand and a target protein.
- It involves simulating the binding process to understand how well a ligand can fit into the binding site of a protein and how strong the interaction
- Docking Score is found out by Visualization tool in Pymol software

PyMOL
System software


Target Structure
Ligands Structure
Protonations states assigned
Partial Charges assigned
Binding site detection
Molecular Docking
Search Algorithms
Score Functions
Pose 1
Pose 2
Pose 3
Pose 4

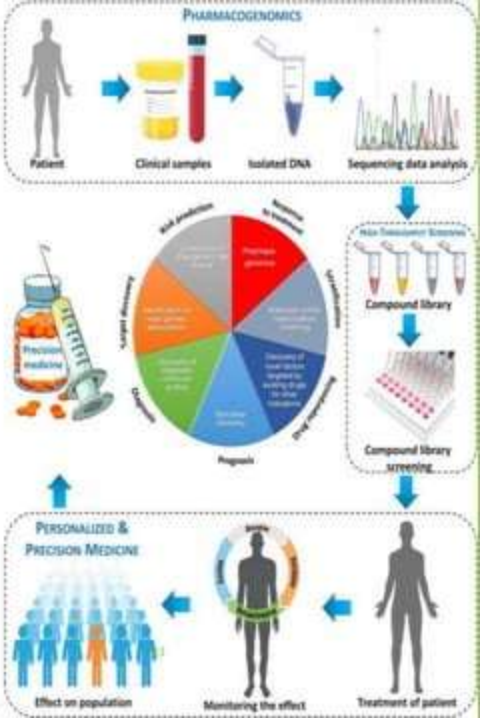
COMBINATORIAL CHEMISTRY

- This is a method used to create a large number of chemical compounds rapidly by combining various building blocks and chemical reactions.
- It's a valuable tool in drug development because it allows for the generation of diverse compound libraries
- Combinatorial chemistry is a technique used in the field of chemistry and drug discovery to efficiently create and screen a large number of diverse chemical compounds.
- It involves systematically synthesizing many different compounds by combining various building blocks and chemical reactions.



HIGH THROUGHPUT SCREENING

- HTS is a process where a large number of compounds are tested rapidly to identify those that have a specific biological activity
- It's commonly used in early-stage drug discovery to assess how compounds interact with a particular target, such as a protein associated with a disease.
- HTS is valuable for quickly identifying lead compounds for further development
- It is a drug discovery process widely use in pharmaceutical industry



DRUG FROM NATURAL SOURCES

- Many drugs and pharmaceutical compounds are derived from natural sources, including plants, microorganisms, and animals.
- Natural products have been a valuable source of medicinal compounds for centuries. Here are some examples of drugs and pharmaceuticals that originate from natural sources

DRUG	MEDICAL USE	PLANT SOURCE
Aspirin	Analgesic,Anti inflammatory	Filipendula ulmaria
Atropine	Pupil dilator	Atropa belladona

THANK YOU