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Evolution and Advancements in Drug Design: A Comprehensive Overview

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Abstract: Drug design is the part of pharmaceutical science with the vast history. Drug design in the Indian context has been a sophisticated pharmaceutical science since the late 19th century. Inspired by Emil Fisher's analogy of drug-receptor interaction resembling a key & lock. Over the time, drug design has developed into a disciplined science with a robust theoretical foundation and practical applications. Currently, it stands as the latest & most advanced technique for discovering new drugs with the primary goal of developing effective, specific, innocuous, acceptable and reliable drugs. It integrates the scientific and technological advancements into a diverse range of methodologies and tools. The established knowledge of Quantitative Structural-Activity Relationship (QSAR) knowledge optimistically guides the selection of pharmaceutical targets to the pharmaceutical industries, as they are facing challenges in developing cost effective new molecule. Drug design is currently experiencing rapid advancements, is a forefront area of science, particularly influenced by the integration of artificial intelligence. This overview aims to highlight key milestones in drug design history, outline popular contemporary techniques and present the author's perspective on future directions. However, it acknowledges that it does not claim to comprehensively cover the extensive range of drug design topic

Index Terms - Drug design, QSAR, Computer Aided Drug Design (CADD), artificial intelligence, drug discovery and development.

I. INTRODUCTION

Drug discovery is a complex and costly process , taking several years and billions of dollars to bring a new drug to the market. Despite extensive steps, including target identification, lead molecule optimisation, pre-clinical and clinical trials the success rate is only 13% , often due to issues with pharmacokinetic properties. Computer Aided Drug Design (CADD) has played a crucial role in accelerating this process, reducing costs and mitigating failures in the later stages of development. Computer Aided Drug Design (CADD) plays an crucial role in understanding how drugs interact with target protein. Supercomputing, parallel processing and advanced algorithm have enhanced lead identification in pharmaceutical research. Artificial intelligence and machine learning have also revolutionised and analysis of vast pharmaceutical data. Methods like pharmacophore modelling, QSAR, molecular docking, quantum mechanics and statistical learning aid in finding new drug candidates from chemical database, using either structural and ligand based approaches.

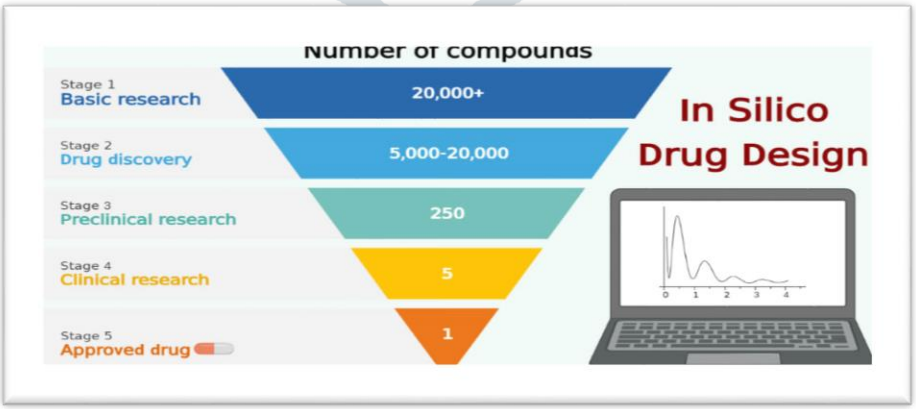

Fig. 1 Drug discovery and development funnel

Drug design is the method of modifying existing chemicals at a molecular level to optimize the intended benefits while minimising undesirable side effects, ultimately creating new and effective medications.

Types of drug design:

1. Drug design based on mechanism
2. Drug design based on structure
3. Ligand-based drug design
4. Drug design based on receptor
5. Drug design based on computer

1.Drug design based on mechanism:
It involves the understanding the biological process they target by identifying specific proteins or pathways related to the disease and creating molecules that interacts with them.
2. Drug Design based on structure:
Drug design based on structure involves creating new medications by considering three dimensional arrangement of molecules. This approach utilizes information about the atomic and molecular structure of biological targets, such as proteins or enzymes to design drugs that fit into specific binding sites with high affinity.
3. Ligand-based drug design:
It focuses on the characteristics of the molecules(ligands) that interact with a biological target. It involves analysing the properties of lingands such as their shape, charge and binding affinity. This approach often employs computational methods and QSAR models to predict and optimize the biological activity of potential drug candidates based on their ligand properties.
4. Drug design based on receptor:
It involves developing medications that specifically interact with and modulate biological receptors. In this approach, the aim is to design drugs that selectively bind to the receptors, either activating or inhibiting their function, to achieve therapeutic effects.
5. Drug design based on computer:
Computer-aided drug design (CADD) utilizes computational methods and algorithms to expedite the drug discovery and design process. This approach involves virtual screening, molecular modelling to predict that how molecules will interact with biological targets. By leveraging powerful computing resources, researchers can analyse large databases of chemical compounds, predict their binding affinity to target proteins and optimize molecular structures for desired properties. CADD accelerates the identification of potential drug candidates, saving time and resources in the early stages of drug development.

QSAR:
Structural- Activity Relationship (SAR) and Quantitative Structural-Activity Relationship (QSAR) are essential methods that connect the structural characteristics of a therapeutic compound with its biological effects. SAR focuses on understanding how changes in the molecular structure impact the compound's activity, while QSAR specifically quantifies these relationships, providing a mathematical model for predicting properties based on structure. These techniques play a crucial role in drug design and optimization by offering insights into the molecular features influencing biological responses. QSAR studies operates on the fundamental principle that alterations in the biological activity of compounds can be associated with corresponding modifications in their molecular structures. This correlation forms the basis for understanding and predicting how changes at a molecular level influence the overall biological response of a compound. QSAR povides a systematic approach to deciphering the relationship between structure and activity, facilitating rational drug design and optimization.

In essence, QSAR aims to establish a robust connection between molecular attributes and biological activity to assess novel compounds. By exploring electronic effects, steric effects and lipophilicity through alterations in the chemical structure of a lead compound, QSAR seeks to enhance therapeutic agents.

Parameters:

1. Lipophilic parameters – Partition coefficient, Molar refractivity
2. Electronic parameters – Hammet's constant
3. Steric parameters – Taft's constant, verloop steric parameter

Partition coefficient:
Lipophilicity, assessed by the partition coefficient (P), measures how a substance distribute between aqueous and non aqueous phases. In the log P range of 1-4, a linear relationship is observed, such as log 1/C = 0.75 log P + 2.30. Graphs stretched to high log P values yield a parabolic curve: log 1/C = (log P)2 + K2 log P + K3. At low P, the impact of log P is prominent. Hydrophobic substituent constants, like substituent constants decrease with large P, dominated by log P squared. Hansch and colleagues introduced the PX constant (Log PX. – Log PH), where a positive value indicates a preference for the organic phase, signalling higher lipophilicity than hydrogen. Conversely, a negative value suggests a preference for the aqueous phase, indicating lower lipophilicity than hydrogen.
Hammet's constant:
The Hammett constant, denoted as σ, is a measure of the electronic effect of substituents in organic compounds. It helps to predict and understand how different substituents influence the reaction rates of organic reactions. The values of Hammett constants are specific to a particular reaction and are determined experimentally. There are two main types of Hammett constants:
σ(sigma) for substituent σ+ (sigma plus): Represents electron-donating effects of substituents.
σ- (sigma minus): Represents electron withdrawing effects of substituents.
ρ (rho) for reaction constants reflects the sensitivity of a reaction rate to changes in substituent.
Taft's constant: tops constant denoted as π, is another parameter used in organic chemistry to quantify the steric effect of substitutes in a molecule. It is a part of the Taft equation, which relates the reactivity of a compound to the electronic and steric properties of its substituents. The value of Taft's constant depend on the type of steric interaction being considered (e.g. van der waals, axial, equatorial), and it is determined experimentally for specific reactions.
Experimental:

A. Introduction to CADD: Computer Aided Drug Design (CADD) is a technology that utilizes software to create, modify, analyse, and optimize designs for various disciplines such as architecture, engineering and manufacturing. It enhances the traditional manual drafting process by providing tools for precise and efficient creation of 2D and 3D models. CADD applications enable professionals to visualise, simulate and document their designs, contributing to improve accuracy and productivity in the design and drafting process.

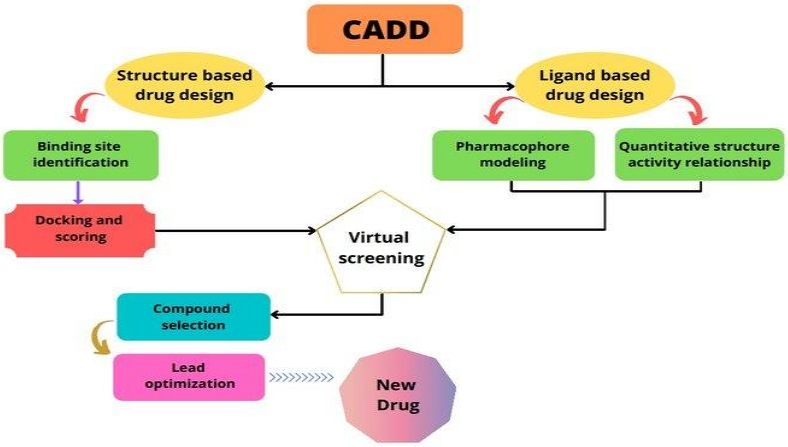

Fig. 2. Classification of CADD

B. Chemical structure drawing: It involves representing the arrangement of atoms and bonds in a molecule. Computer-Aided design tools for chemistry, typically use specialized software like ChemDraw, Marvin Sketch, or ChemSketch. These programs allow you to draw and manipulate molecular structures, depict reactions, and generate chemical formulas. The software often provides range of tools for creating 2D and 3D representations of molecules.

- **ChemDraw:** ChemDraw is a popular chemical drawing software used by chemists and researchers for creating molecular structures, reactions and chemical illustrations. It provides a user-friendly interface with tools for drawing, editing and visualising complex chemical structures. ChemDraw is widely utilised in academia and industry for tasks such as creating publication quality graphics, generating chemical databases, and aiding in the communication of chemical information. It supports various file formats and integrates with other chemistry-related software, making it a versatile tool for professionals in the field. ChemDraw excels in its ability to generate accurate molecular structures from chemical names and provides precise representations conforming to IUPAC nomenclature.
- **Chemdoodle:** Chemdoodle is a powerful tool that enables you to recreate detailed chemical diagrams from molecule photos, even without specific chemical information. It excels in generating intricate illustrations of chemical mechanisms. It has hundreds of chemical characteristics that contribute to creation of visuals of highest calibre.
- **Chemsketch:** Chemsketch is a versatile tool for drawing various chemical structures, including organic, organic, organometallic, and polymers. It goes beyond depiction, offering features for structure identification, calculating molecular parameters like weight and density, cleaning and visualizing both 2D and 3D structures, and predicting logP values.
- **Marvin:** Marvin is a comprehensive chemical editor that allows user to create, modify, publish, render, import and export chemical structures. It supports file conversion between various graphical and chemical formats, making it a fully functional tool for working with chemical data.
- **BKChem:** BKChem is a molecular drawing program preliminary used for creating structural formulas of chemical compounds. It is an open-source software, which means its source code is freely available for users to view, modify and distribute. BKChem provides a variety of drawing tools such as bonds, atoms and functional groups to facilitate the creation of complex molecular structures. Users can edit 2D molecular structures, including moving atoms and bonds, resizing structures, and making other modifications. BKChem allows users to input chemical information, such as elemental composition and molecular weight, providing useful data for the drawn structures.

C) Chemical structure presentation:

- **Benzoic acid:**

  Molecular formula: C_6H_5COOH

  Molecular weight: 122.12g/mol

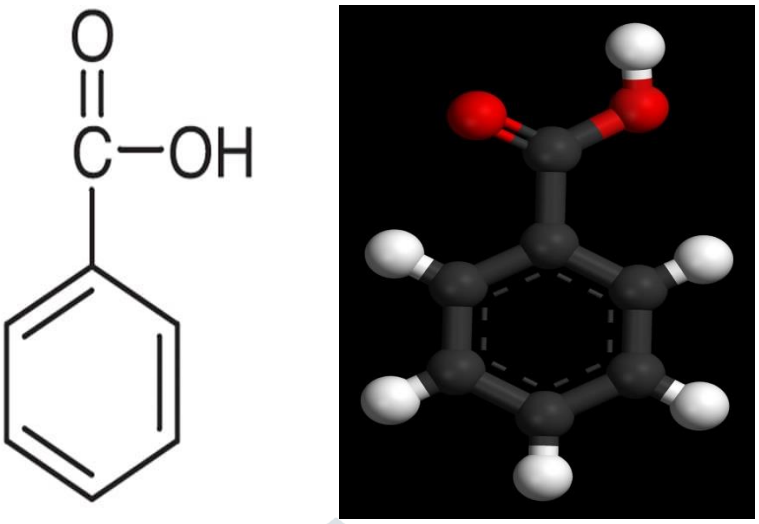

Fig. 3. Chemical structure and 3D structure of Benzoic acid

- **Salicylic acid:**
  Molecular Formula: C6H4(OH)COOH
  Molecular weight: 138.12 g/mol

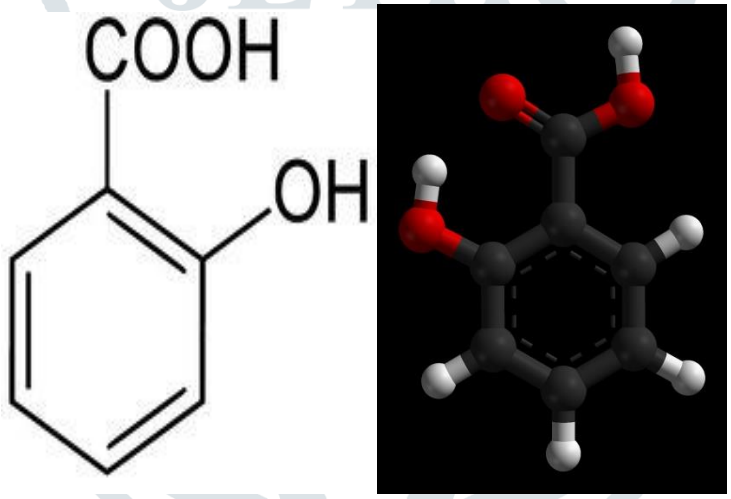

Fig. 4. Chemical structure and 3D Structure of Salicylic acid

❖ Chemical database search:

Absolutely, chemical databases play a pivotal role in medicinal chemistry, providing a wealth of information crucial for drug discovery and development. Here's a brief overview of the types of chemical databases you mentioned:

1. **Markush Databases:** Provide information about chemical structures in a generalized form, often used in patient-related searches.
2. **Chemical Abstracts:** Offer comprehensive information on chemical literature, including abstracts, substance information and references.
3. **Compound Registers:** Internal databases that keep records of compounds synthesized or aquired by a research organization.
4. **Biological Activity Databases:** Contain information on the biological effects of various compounds, aiding researchers in understanding potential drug activities.
5. **MDL Data Report:** A database providing dataon chemical structures, properties and associated information, often used in drug discovery.
6. **Activity Databases:** Focus on the biological activity of compounds, helping researchers identify potential leads for drug development.
7. **Crystallographic Databases:** Store crystallographic data, essential for understanding the 3D structures of molecules.
8. **Graphical Databases:** Include graphical representations of chemical structurs, aiding in visualizing molecular relationships.
9. **NMR Specrta Database:** Contains nuclear magnetic resonance spectra data, valuable for elucidating molecular structures.

10. Reaction Databases: Document chemical reactions and synthetic pathways, aiding in the design and optimization of synthetic routes.

11. Thermo-physical Databases: Provide information on the thermodynamic and physical properties of compounds, essential for drug formulation. The integration of these databases allows medicinal chemists to assess a diverse range of information, facilitating efficient decision- making in the drug discovery process.

After a chemical database search, the representation of chemical structures is typically presented in a format that allows for easy interpretation. The most common way to represent chemical structures is using line notation, often referred to as a structural formula. This formula provides a visual depiction of the arrangement of atoms and bonds in a molecule.

Other common representations include:

1. SMILES (Simplified Molecular Input Line Entry Systems): A concise and human-readable notation for representing chemical structures using ASCII characters.

2. InChl (International Chemical Identifier):

A standerdise and machine readable texual indentifier for chemical compounds.

3. Molecular Diagrams: Visual representations of chemical structures using graphics, showing the arrangement of atoms and bonds.

4. 3D Molecular Models: Interactive three-dimensional representations of molecules, helpful for visualizing spatial arrangements. Choosen representation depends on the context and the specific needs of the user. These representations are crucial for communicating and sharing information about chemical structures among researchers, facilitating further analysis amd experimentation in the field of medicinal chemistry.

E) Pharmacophore modelling:

A pharmacophore is a concept in molecular modeling and drug design that identifies the essential structural and chemical features of a molecule necessary for it to interact with a specific biological target . It serves as simplified representation of the molecular features responsible for a drug's biological activity.

Key components of pharmacophore include:

a. Functional Groups: Sprcific chemical groups or atoms within a molecule that contribute to its biological activity. For example, a certain type of functional group might be crucial for binding to a particular receptor.

b. Spatial Arrangemet: The 3D arrangements of atoms and groups in the molecule that is important for effective interaction with the target. This involves considering the relative positions of key features.

c. Hydrophobic and Hydrophilic Regions: Identification of regions in the molecule that are hydrophobic (water-repellent) or (water-attracting), as these properties influence the molecule's interactions within a biological system.

d. Electrostatic Features: Consideration of charges and potential hydrogen bonding sites in the molecule. Electrostatic interactions can be crucial for binding to a target.

e. Flexibility: Understanding the permissible variations in the molecule's structures while maintaining its biological activity. This accounts for the dynamic nature of molecular interactions.

Pharmacophore models are often used in computer-aided drug design to screen and identify new compounds with potential therapeutic effects. By understanding the key features required for a molecule to ineract with a target, researchers can optimize existing drugs or design new ones more efficiently.

Identifying a pharmacophore typically involves the following steps:

1. Selection of active compounds: In this step, a set of known active compounds with the desired biological activities are collected.
2. Molecular Alignments: The active compounds are aligned in a way that highlights common structural features or spatial arrangements.
3. Feature Extraction: Key molecular features essential for biological activity, such as hydrogen bond donors/acceptors, hydrophobic regions and aromatic centers are identified.
4. Pharmacophore Hypothesis Generation: A hypothesis that represents the spatial arrangement of essential features required for biological activity is developed.
5. Validation: The pharmacophore hypothesis using inactive compounds to ensure specificity is validated.
6. Optimization: Refine the pharmacophore model based on experimental data or additional information, adjusting feature locations and characteristics.
7. Applications: Use the validated pharmacophore to screen databases for potential new compounds with the desired activity.

These steps may vary based on the choosen method, whether ligand-based or structure-based and available data.

F) Docking:

Molecular docking is the computational technique used to determine the binding affinity of a small molecule (ligand) to a target (protein) to form a stable complex. The goal is to identify the compounds that could serve as effective drugs by stimulating their binding to specific biological targets.

Types of molecular docking:

a. Rigid Docking:

In rigid docking, the computational simulation involves a three-dimensional rearrangement of one compound to find the best match with another compound in terms of a scoring systems. This assumes both compounds are rigid structures. It explores how well the ligand can fit into the receptor's binding site, assessing shape complementarity and scoring the interaction, regardless of the ligand's potential binding activity. It does not consider conformational changes in either the ligand or the target during the docking process.

b. Flexible Docking:

Flexible docking is a computational approach that allows for flexibility in either the ligand, the target or both during the docking simulation. Unlike rigid docking, which assumes fixed structures, flexible docking considers conformational changes that may occur in the ligand, the target or both providing a more realistic representation of molecular interactions. This method is particularly useful when studying systems where flexibility is a crucial factor in ligand-receptor binding.

c. Ligand-based docking:

Ligand-based docking focuses on the properties of the ligand (small molecule) without explicitly considering the three-dimensional structure of the target protein. This method relies on information derived from the ligand itself, such as its shape, electrostatic

properties and other molecular descriptors. Ligand-based docking is particularly useful when the three-dimensional structure of the target is not available or when studying ligands with known bioactivity but uncertain binding sites.

d. Protein-ligand docking:

Protein-ligand docking is a computational method used to predict the preferred binding mode and affinity between a protein and a ligand. It involves simulating their interactions to identify the most energetically favorable binding pose. It is the most common type of the docking.

e. Structure-based docking:

Structure-based docking relies on the three-dimensional structures of both the protein and ligand to predict their binding interactions. It involves computational algorithms that explore potential binding orientations and estimate the binding affinity based on factors such as energy calculations and geometric complementarity.

f. Blind docking:

Blind docking refers to docking a ligand to the whole surface of a protein without any prior knowledge of the target pocket. Blind docking involves several trials and several energy calculations before a favorable protein-ligand complex pose is found.

Factors affecting molecular docking:

1. Intermolecular forces:
   - Hydrophobicity
   - Electrostatic forces
   - Dipole forces
   - H- bonding
   - Vander waal forces

2. Intramolecular forces:
   - Bond length
   - Bond angle
   - Dihydral angle

G) Analysis of docking:

Analyzing docking results involve assessing the binding poses and scores to understand the interaction between the ligand and receptor. Here's a basic analysis approach:

- Visual Inspection: Use molecular visualization tools to examine the binding poses. Check if the ligand is located in the expected binding site and observe its orientation and interactions with the receptor.
- Scoring Function Evaluation: Evaluate the docking scores. Lower scores typically indicate better binding affinity. Compare scores between different ligands or poses to prioritize candidates.
- Interaction Analysis Identify the ligand and receptor, such as hydrogen bonds, hydrophobic interaction and electrostatic interactions. Assess the significance of these interactions for binding affinity.
- Binding Site Occupancy: Confirm that the ligand occupies the predicted binding site. Deviations may indicate inaccuracies in the docking procedure or limitations in the model.
- Conformational Changes: Check if the docking predicts conformational changes in the receptors upon ligand binding. This information can be crucial for understanding the binding mechanism.
- Energy Minimization: Perform energy minimization on the docked complexes to refine the structures and potentially improve the accuracy of the predicted binding poses.
- Validation against Experimental Data: If available, compare your docking results with experimental data. Experimental validation provides confidence in the accuracy of the predictions.
- Ranking and Prioritization: Rank the docking poses base on their scores and interaction profiles. Prioritize poses with favourable binding characteristics for further investigation.
- Consensus Scoring: Consider using multiple scoring functions or approaches to obtain a consensus score. This can enhance the reliability of the predictions.
- Statastical Analysis: If conducting virtual screening, analyse the statistical significance of your results. False positive and false negative rates are essential matrics for evaluating the screening performance.

Docking results are predictive and should be interpreted cautiously. Experimental validation is crucial to confirm the actual binding affinity and pose of a ligand in a given complex.

H) ADMET:

ADMET or absorption, distribution, metabolism and excretion plays a crucial role in drug development by assessing how a therapeutic molecule behaves in the body. Understanding these processes helps to ensure a medication reaches its target, produces desired effects and can be safely eliminated, guiding risk assessments as well as optimize pharmacokinetic and safety profile of novel drugs.

Absorption: The process by which a drugs enters the bloodstream from its site of administration (e.g. oral, intravenous, topical)
Importance: Determines how efficiently the drug is taken up into the bloodstream, influencing its bioavailability.

Distribution: The movement of a drug throughout the body, distributing to various tissues and organs.
Factors: Influenced by blood flow, drug properties and tissue characteristics.
Significance: Impacts the concentration of the drug at the target site and potential side effects in other tissues.

Metabolism: The biotransformation of a drug by enzymes, primarily in the liver, into metabolites.

Pupose: Converts drugs into forms more easily excreted, enhances or reduces pharmacological activity and influences drug interactions.
Enzymes: Cytochrome P450 enzymes are crucial in drug metabolism.
Excretion: The removal of drugs and their metabolites from the body, often through urine or feces.
Organs involved: Kidneys (major role in renal excretion), liver, lungs and intestines.
Role: Ensures elimination, preventing drug accumulation and potential toxicity.
Understanding these ADMET processes aids in optimizing drug formulations, dosage regimens and safety profiles during the drug development lifestyle.

Combinatorial chemistry:

Cominatorial chemistry is a method used in drug discovery and material science, involving the systematic creation of diverse chemical compounds in a single step. It accelerates the process of finding valuable substances by synthesizing and testing multiple compounds simultaneously, allowing researchers to explore a wide range of possibilities in as shorter time.

Principle:

The principle of combinatorial chemistry lies in the efficient exploration of chemical space. By generating diverse combinations of chemical building blocks in parallel, researchers can rapidly create and screen a large number of compounds. This approach aims to identify novel and potentially useful molecules more quickly than traditional one-at a-time synthesis methods.

Types:

1. Solid Phase Combinatorial chemistry
2. Solution Phase Combinatorial Chemistry

1. Solid Phase Combinatorial Chemistry:

It is a specific application of combinatorial chemistry that involves the synthesis of diverse compounds on a solid support. This method is widely used in the synthesis of peptides, oligonucleotides and small organic molecules. Here's an overview of the process:

- Solid Support: Begin with a solid support, often a resin or polymer bead, to which the first building block is attached. The solid support simplifies purification and allows for parallel synthesis.
- Protecting Groups: Introduce protecting groups to block specific reactive sites on the solid support and the chemical building blocks (monomers). Protecting groups prevent unwanted reactions and allow controlled synthesis.
- Coupling Reactions: Couple the first building block (monomer) to the solid support. This forms a covalent bond between the solid support and the first building block.
- Repetitive Steps: Repeat the cycle of deprotection and coupling for subsequent building blocks. Introduce a variety of building blocks in parallel, creating a diverse library of compounds.
- Cleavage: Once the desired length or complexicity is achieved, cleave the compounds from the solid support. This results in a mixture of compounds that can be further analyzed.
- Analysis and Screening: Evaluate the compounds for desired properties using techniques like high-throughput screening or other analytical methods. Identify lead compounds with specific activities or characteristics.

Solid-phase combinatorial chemistry is particularly valuable in peptide and oligonucleotide synthesis. The solid support simplifies the purification process and the parallel synthesis approach accelerates the generation of compound libraries, making it a powerful tool in drug discovery and material sciences.

2. Solution Phase Combinatorial Chemistry:

In combinatorial chemistry, the solution phase involves synthesizing chemical compounds in a liquid medium rather than on a solid support. This methods allows for the creation of diverse compound libraries by mixing different reactants in solution, enabling rapid screening for desired properties or biological activities. The majority of synthetic chemistry occurs in the solution phase. The typical solvent used in solution phase synthesis is PEG.

HTS (High Throughput Screening):

High Throughput Screening (HTS) is a drug discovery process that involves the rapid testing of a large number of compounds to identify potential candidates with specific biological activities. It is commonly used in the pharmaceutical industry to assess the effects of various substances on biological targets, such as enzymes or receptors, in a quick and automated manner. The goal is to identify compounds that show promising activity for further development in drug research and development.

Over the past two decades, High Throughput Screening (HTS) has gained widespread popularity in the pharmaceutical sector, becoming a standard practice in drug discovery. This approach is not only used to identify potential drug candidates but also plays a role in assessing toxicological, pharmacokinetic and metabolic information related to novel medications.

HTS employs fully automated robotic technologies, enabling the daily testing of numerous chemicals for various biological and chemical processes. With its simplicity, speed, cost effectiveness and high efficiency. HTS has become a crucial component in the search for new drugs.

Types of HTS assays:

1. Biochemical test
   - Homogenous test
   - Heterogenous test

2. Cell based analysis
   - First messenger assay
   - Reporter gene assay
   - Test for cell proliferation

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1. Biochemical Tests:

- **Homogenous Assay:** Involves measurements based on the physical/chemical characteristics of the analyte or its interactions with the environment. It's simple process with just one phase and can be linked with various HTS detection techniques like radiometric or fluorescence methods.
- **Heterogenous Assay:** Requires additional procedures like filtration and centrifugation to separate components for analysis. It's employed when homogenous assays face challenges or when a high signal-to-background ratio is crucial.

2. Cell-Based Analysis:

- **First Messenger Assay:** Focuses on tracking the initial events triggered by an active cell-surface receptor.
- **Second Messenger Assay:** Tracks transactions initiated by cell-surface receptors, often involving quick, transient fluorescence signals responsive to changes in intracellular factors like calcium ion content and membrane potential.
- **Receptor Gene Assay:** Monitors cellular responses at the translational level, indicating changes in signal transduction pathways.
- **Test for Cell Proliferation:** Examines overall cell growth or lack there of in response to external stimuli.

Sources of Drugs:

Natural therapeutic agents contains active ingredients from various sources like microorganisms, minerals, animals and plants. These medicinal compounds can be extracted from different origins, including plant parts, secretions and exudates forming a diverse range of treatments. Drugs, in general, may originate from natural, synthetic or biosynthetic sources expanding the avenues for therapeutic development.

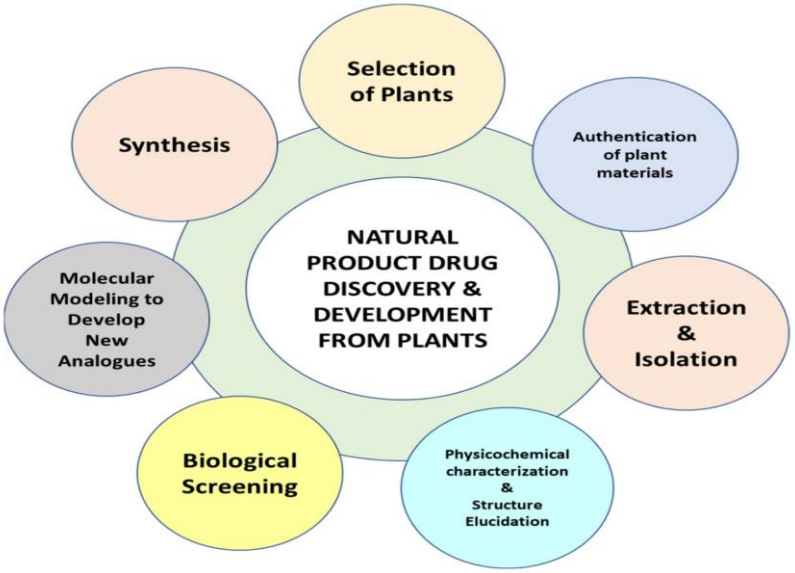

Fig..5 Process involved in the discovery and development of natural products

Medicinal drugs are derived from six primary sources:

1. Plant sources: Historically, plants were the earliest pharmaceutical source. Various plant components like leaves, roots, bark and fruits are utilized.

Example: Digitalis purpurea leaves yield cardiac glycosides, while cinnamon bark contains antimalerial like quinine.

2. Animal sources: Drugs such as thyroxin for hypertension are obtained from sheep thyroid. Cod liver provides vitamin A and D. Anterior pituitary produces gonadotropins for treating infertility. Animal blood is used in vaccine production.

3. Mineral/earth sources: Includes metallic and nonmetallic substances. Iron from metallic sources treats iron deficiency anemia. Mercurial salts, derived from minerals, are also used to treat syphilis.

4. Microbiological organism sources:

5. Semi-synthetic / synthetic sources:

- **Synthetic sources:** Medicines are considered synthetic when both their chemical structure and nucleus are altered from a natural source. An example is Emetine Bismuth Iodide.
- **Semi-synthetic Sources:** Medicines are termed semi-synthetic when the chemical structure changes, but the drug's natural source's nucleus is retained. Examples include apomorphine, amoxicillin and methyl testosterone. Many contemporary medications, like anti-anxiety and anti-convulsant drugs, falls into this category.

6. Recombinant DNA technology: Involves using restriction endonucleases to cleave DNA, linking the desired gene to rapidly replicating DNA, be it viral, bacterial or plasmid.

Advantages: Non-toxic, easily accessible, inert, less negative consequences, cost-effective, quick to degrade, improved stability, clinically relevant.

Disadvantages: Batch-to-batch variation, low manufacturing volume.

Conclusion:

Drug design is the process of coming up with novel treatments based on an understanding of a biological target. This review talks about several forms of drug discovery, lead discovery, lead modification and drug design principles. As compared to computational approaches, the process of discovering new drugs through laboratory experimentation takes a long time and costs a lot of money.

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