CADD ANSWERS

SHORT :

1. **What is Lead Compound in drug discovery?**
    - A lead compound is a chemical structure with biological activity.
    - It serves as a starting point for drug development.
    - It undergoes modifications to improve efficacy and safety.
    - Example: **Sulfanilamide** led to the development of sulfa drugs.
2. **Define Bioisosterism.**
    - Bioisosterism is the replacement of functional groups with similar ones.
    - It retains biological activity while improving properties.
    - Used in drug modification to enhance potency and reduce toxicity.
    - Example: **Replacing –OH with –NH_2 in drug molecules.**
3. **Mention advantages of CADD.**
    - Reduces time and cost in drug discovery.
    - Improves drug-target interactions using simulations.
    - Helps predict ADME (Absorption, Distribution, Metabolism, Excretion).
    - Example: **Molecular docking used in anti-cancer drug design.**
4. **Give the structure of Isoniazid.**
    - **Isoniazid (INH)** is a first-line anti-tuberculosis drug.
    - **Structure:** $C_6H_7N_3O$
    - Contains a pyridine ring and hydrazide (-$NHNH_2$) group.
    - Example: **Used against Mycobacterium tuberculosis.**
5. **What is HTS? Define in short.**
    - **HTS (High-Throughput Screening)** tests thousands of compounds.
    - Uses automated techniques to identify lead molecules.
    - Helps in drug discovery by screening potential drugs.
    - Example: **Fluorescence assays used in antiviral drug discovery.**

6. **Write down the steps of Drug Target Selection.**
    - Identify disease-related biomolecules (target identification).
    - Validate the target for therapeutic use.
    - Study drug-target interactions using computational methods.
    - Example: **Kinase proteins in cancer targeted for inhibition.**
7. **Define in vivo tests.**
    - Experiments conducted inside living organisms.
    - Used to assess drug effects in real biological conditions.
    - Includes animal and human trials.
    - Example: **Testing antibiotics in mice models for infection studies.**
8. **What is potency?**
    - Potency is the drug's ability to produce a desired effect.
    - Measured by EC_{50} or IC_{50} values.
    - Higher potency requires a lower dose for the same effect.
    - Example: **Morphine is more potent than aspirin.**
9. **What is ADME process?**
    - **Absorption:** Drug enters the bloodstream.
    - **Distribution:** Drug spreads to tissues.
    - **Metabolism:** Drug is processed in the liver.
    - **Excretion:** Drug is eliminated (urine, bile).
    - Example: **Paracetamol undergoes hepatic metabolism before excretion.**
10. **What is nonrandom screening?**

- A targeted approach in drug discovery.
- Uses knowledge of biological pathways.
- Focuses on compounds with known potential.
- Example: **Screening kinase inhibitors for cancer therapy.**

LONG :

1. Explain Screening and Its Different Methods.

Definition:

Screening in drug discovery is the process of identifying biologically active compounds from a large chemical library.

Methods of Screening:

1. **Random Screening** – Tests a large number of compounds without prior knowledge of activity.
2. **Non-random (Targeted) Screening** – Focuses on compounds known to interact with biological targets.
3. **High-Throughput Screening (HTS)** – Uses robotics and automated assays to test thousands of compounds quickly.
4. **Virtual Screening** – Uses computational methods (docking, AI) to predict active compounds.
5. **Fragment-Based Screening** – Screens small molecular fragments and combines them to form potent drugs.
6. **Structure-Based Screening** – Uses 3D structures of targets to identify lead molecules.
7. **Ligand-Based Screening** – Uses known active molecules to find similar compounds.
8. **Phenotypic Screening** – Observes cellular responses rather than targeting specific molecules.
9. **Functional Screening** – Assesses compounds based on their biological effects (e.g., enzyme inhibition).

Example & Working:

- **Example: HTS in COVID-19 drug discovery**, where thousands of molecules were screened to find inhibitors of the SARS-CoV-2 main protease.
- **Working:** Compounds are tested using **fluorescence-based HTS assays**, identifying those that bind to and inhibit the viral enzyme.

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2. Explain Bioisosterism and Its Classification in Drug Design.

Definition:

Bioisosterism is the replacement of functional groups in a drug molecule with similar ones to **retain activity while improving pharmacokinetics**.

Classification:

1. **Classical Bioisosteres:**
    - Have similar valency and electronic structure.
    - Example: **-OH → -NH_2 replacement in sulfa drugs.**
2. **Non-Classical Bioisosteres:**
    - Do not follow classical rules but mimic biological effects.
    - Example: **Replacing benzene with thiophene in drugs.**
3. **Ring System Bioisosteres:**
    - Substituting aromatic rings with heterocyclic rings.
    - Example: **Replacing benzene with pyridine in drug structures.**
4. **Functional Group Bioisosteres:**
    - Exchange of functional groups to improve activity.
    - Example: **-COOH replaced by -SO_2NH_2 in NSAIDs.**
5. **Spatial Bioisosteres:**
    - Similar molecular shape and volume.
    - Example: **Replacing Cl with F in corticosteroids for better bioavailability.**

Example & Working:

- **Example: F in fluoroquinolones enhances bacterial inhibition**.
- **Working:** Fluorine replacement increases **lipophilicity**, allowing **better bacterial cell penetration**.

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3. What is Biological Assessment? Explain in Detail Any One Technique Involved in Bioassay.

Definition:

Biological assessment (bioassay) measures the biological effects of a substance on living organisms.

Bioassay Techniques:

1. **In Vivo Bioassay** – Testing in live animals (e.g., mouse toxicity studies).
2. **In Vitro Bioassay** – Testing in isolated cells or tissues (e.g., enzyme inhibition assay).
3. **Binding Assays** – Measures drug-receptor interaction (e.g., radioligand binding).
4. **Microbial Assays** – Testing drug effects on bacteria (e.g., penicillin activity on Staphylococcus).
5. **Toxicity Assays** – Measures adverse effects (e.g., LD_{50} determination in animals).
6. **Immunoassays** – Uses antibodies to detect molecules (e.g., ELISA test for drugs).
7. **Cell-Based Assays** – Observes effects on live cells (e.g., cancer cell apoptosis).
8. **Enzyme Assays** – Measures enzyme inhibition or activation (e.g., cholinesterase inhibitors).
9. **Functional Assays** – Observes physiological changes (e.g., blood pressure changes in rats).

Example & Working:

- **Example: ELISA for insulin quantification.**
- **Working:** Antibody-coated wells bind to insulin, a secondary antibody with an enzyme generates a color signal, and insulin concentration is determined spectrophotometrically.

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4. Explain the Discovery of Penicillins.

Discovery Timeline:

1. **1928:** Alexander Fleming discovered penicillin from *Penicillium notatum*.
2. **1939-1941:** Florey and Chain purified and tested it.
3. **1945:** Large-scale production for WWII soldiers.

Mechanism of Action:

1. Inhibits **bacterial cell wall synthesis**.

2. Binds to **penicillin-binding proteins (PBPs)**.
3. Prevents **peptidoglycan cross-linking**.
4. Causes bacterial **lysis and death**.

Types of Penicillins:

1. **Natural Penicillins** – Penicillin G and V.
2. **Semi-Synthetic Penicillins** – Ampicillin, Amoxicillin.
3. **Beta-Lactamase Resistant** – Methicillin, Oxacillin.
4. **Extended Spectrum** – Piperacillin, Ticarcillin.

Example & Working:

- **Example: Amoxicillin for bacterial infections.**
- **Working:** Amoxicillin inhibits **PBPs in Streptococcus**, preventing cell wall formation and causing bacterial death.

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5. Explain Discovery of Drugs Through Metabolism Studies.

Definition:

Metabolism studies help identify active metabolites with potential drug effects.

Process:

1. **Drug metabolism occurs in the liver** (Phase I & II reactions).
2. **Active metabolites are identified using chromatography & mass spectrometry.**
3. **Metabolites may be more potent than the parent drug.**
4. **Identified metabolites undergo further optimization.**

Examples of Drugs Discovered from Metabolism Studies:

1. **Acetaminophen (Paracetamol) from phenacetin.**
2. **Losartan (active metabolite of EXP3174).**
3. **N-Desmethyl imipramine from imipramine.**
4. **Codeine metabolism leads to morphine.**

5. **Minoxidil from antihypertensive use to hair growth treatment.**

Example & Working:

- **Example: Paracetamol from phenacetin.**
- **Working:** Phenacetin undergoes **O-dealkylation in the liver**, forming paracetamol, which has better safety and analgesic properties.

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6. Explain Clinical Development or Human Clinical Trials.

Definition:

Clinical trials are systematic studies in humans to evaluate drug safety and efficacy.

Phases of Clinical Trials:

1. **Preclinical Studies** – Animal and lab testing.
2. **Phase 1:** Tests safety in **healthy volunteers (20-100 participants).**
3. **Phase 2:** Tests efficacy in **small patient groups (100-300).**
4. **Phase 3:** Large-scale trials in **thousands of patients (3000+).**
5. **Phase 4:** Post-marketing surveillance for long-term safety.

Regulatory Approvals:

- **FDA, EMA, and ICH guidelines regulate trials.**
- Drugs must pass all phases before marketing approval.

Example & Working:

- **Example: COVID-19 vaccine clinical trials (Pfizer, Moderna).**
- **Working:**
    - **Phase 1:** Tested in healthy individuals for immune response.
    - **Phase 2 & 3:** Assessed in thousands for protection rates.
    - **Phase 4:** Ongoing monitoring for long-term effects.