CADD

ASSIGNMENT – 2025

Q1. Explain Screening and its different methods.

1. Screening is a process of identifying potential drug candidates from a large collection of compounds.
2. It is done to select compounds having desired biological activity.
3. Screening helps in finding lead compounds for further development.
4. Primary screening is done to identify whether the compound has any biological activity.
5. Secondary screening is done to confirm and analyze the exact pharmacological activity.
6. High-throughput screening is an automated technique to test thousands of compounds quickly.
7. Virtual screening uses computational techniques like docking to predict active compounds.
8. In vitro screening involves testing compounds on isolated tissues, cells, or enzymes.
9. In vivo screening tests compounds on live animals to check therapeutic and toxic effects.
10. Biochemical screening identifies the interaction of a compound with specific enzymes or receptors.
11. Microbial screening tests compounds against different bacteria or fungi.
12. Clinical screening evaluates safety and efficacy in human subjects.
13. Screening is essential in drug discovery to reduce time and cost by selecting only promising candidates.

Q2. Explain Bioisosterism and its classification in drug design.

1. Bioisosterism involves replacing an atom or group in a drug molecule with another having similar physicochemical properties.
2. It is used to improve drug properties like potency, solubility, and stability.
3. It also helps to reduce toxicity and side effects.
4. Classical bioisosteres are groups that have similar size and electronic features.
5. Examples of classical bioisosteres include replacement of -OH with -NH_2 or H with F.
6. Non-classical bioisosteres have different structures but produce similar biological effects.
7. An example is replacing a carboxylic acid group with a tetrazole ring as seen in Losartan.
8. Bioisosterism can increase receptor binding affinity.
9. It helps overcome metabolic degradation of drugs.
10. It is useful in overcoming drug resistance issues.

11. Prodrugs are sometimes designed using bioisosterism.
12. It is an important technique in medicinal chemistry for modifying lead molecules.
13. Bioisosteric replacements can be used to improve pharmacokinetics and pharmacodynamics.

Q3. What is biological assessment? Explain in detail any 1 technique involved in Bioassay.

1. Biological assessment or bioassay measures the potency or effect of a substance on living systems.
2. It determines the biological activity of drugs.
3. Bioassay is essential when chemical analysis isn't sufficient.
4. It can measure both therapeutic and toxic effects.
5. Qualitative bioassays check for the presence or absence of biological activity.
6. Quantitative bioassays measure the degree of activity.
7. Matching method is one bioassay where the effect of a test drug is compared with a standard drug.
8. It involves adjusting doses of both until they produce equal effects.
9. The potency is calculated based on dose comparison.
10. Example: Measuring muscle contraction force in response to acetylcholine and a test drug.
11. Graded response assay uses different doses to produce a range of responses.
12. Quantal assay measures all-or-none responses like death or sleep.
13. Bioassay is important for evaluating drugs like insulin, digitalis, and hormones.

Q4. Explain the discovery of Penicillin.

1. Penicillin was discovered by Alexander Fleming in 1928.
2. He observed that colonies of Staphylococcus bacteria were killed by a mold contamination.
3. The mold was identified as Penicillium notatum.
4. Fleming extracted the active substance and named it penicillin.
5. It showed strong antibacterial activity, especially against gram-positive bacteria.
6. Florey and Chain later purified penicillin for clinical use.
7. It was mass-produced during World War II to treat wound infections.
8. Penicillin works by inhibiting bacterial cell wall synthesis.
9. It was the first widely used antibiotic in medicine.

10. It significantly reduced death rates from bacterial infections.
11. Deep fermentation techniques increased its yield for commercial production.
12. It laid the foundation for discovering other antibiotics.
13. Penicillin's discovery revolutionized the treatment of infectious diseases.

Q5. Explain discovery of drugs through metabolism studies.

1. Metabolism studies analyze how a drug is absorbed, distributed, metabolized, and excreted.
2. These studies help identify active metabolites.
3. Some metabolites may be more active than the parent drug.
4. Prodrugs are inactive compounds activated by metabolic enzymes.
5. Example: Codeine converts to morphine in the liver.
6. Metabolism can reveal toxic metabolites for safety improvement.
7. Example: Acetaminophen produces toxic NAPQI at high doses.
8. Active metabolites can sometimes become new drugs.
9. Example: Terfenadine's metabolite Fexofenadine is safer and effective.
10. Metabolism studies use liver microsomes, animal models, and human plasma.
11. Modern software like MetaSite predicts metabolism pathways.
12. It helps optimize drug structure for better pharmacokinetics.
13. Metabolism-based discoveries can improve drug safety, efficacy, and half-life.

Q6. Explain clinical development or human clinical trials.

1. Clinical development involves testing new drugs in human volunteers.
2. It ensures the drug's safety, efficacy, and therapeutic use.
3. Phase I involves 20-100 healthy volunteers.
4. It assesses safety, dosage, and pharmacokinetics.
5. Phase II involves 100-300 patients with the disease.
6. It evaluates drug efficacy and side effects.
7. Phase III involves 1000-3000 patients in multiple centers.
8. It confirms efficacy, monitors adverse effects, and compares with standard treatments.

9. Phase IV is post-marketing surveillance.
10. It detects rare or long-term side effects after public use.
11. Clinical trials require ethical approval and informed consent.
12. They follow guidelines of regulatory authorities like FDA and DCGI.
13. Clinical trials protect public health and ensure safe medicines.

Q7. Explain Hammett substituent constant.

1. Hammett substituent constant measures the electronic effect of substituents on a molecule.
2. It indicates whether a group is electron-donating or electron-withdrawing.
3. Represented by the symbol σ (sigma).
4. Developed by Louis Hammett in 1937.
5. Based on the effect of substituents on benzoic acid dissociation.
6. A positive σ value indicates an electron-withdrawing group.
7. A negative σ value indicates an electron-donating group.
8. The Hammett equation relates reaction rates to substituent effects.
9. Equation: $\log(k/k_o) = \rho\sigma$.
10. k is the reaction rate with a substituent, k_o without it.
11. ρ is the reaction constant for a specific type of reaction.
12. Used in QSAR studies to predict biological activity.
13. Helps medicinal chemists design better drugs by modifying substituents.

Q8. Describe about COMSIA.

1. COMSIA stands for Comparative Molecular Similarity Indices Analysis.
2. It is a 3D-QSAR technique used to relate chemical structure with biological activity.
3. COMSIA evaluates five molecular fields: steric, electrostatic, hydrophobic, hydrogen bond donor, and acceptor.
4. It compares the similarity of these fields in a set of molecules.
5. Molecular alignment is essential before COMSIA analysis.
6. Uses Partial Least Squares (PLS) statistical method.
7. It provides 3D contour maps showing favorable and unfavorable regions.

8. COMSIA is more flexible and sensitive than CoMFA.
9. It does not require the use of cut-off values for interaction energies.
10. Widely used in antiviral, anticancer, and CNS drug design.
11. Example: Applied in designing HIV-1 protease inhibitors.
12. It helps identify regions for structural modification.
13. COMSIA improves lead optimization by visualizing activity-determining regions.

Q9. Explain History and development of QSAR.

1. QSAR stands for Quantitative Structure-Activity Relationship.
2. It mathematically relates chemical structure to biological activity.
3. The idea began with Crum-Brown and Fraser in 1868.
4. They proposed that biological activity is related to chemical structure.
5. In 1935, Hansch introduced physicochemical parameters like hydrophobicity and electronic effects.
6. Hammett (1937) introduced the substituent constant (σ) concept.
7. Free-Wilson analysis (1964) used indicator variables for different substituents.
8. Hansch analysis (1964) used regression analysis to correlate activity with logP and σ.
9. Introduction of 3D-QSAR techniques like CoMFA (Comparative Molecular Field Analysis) in 1988.
10. Further advancement led to COMSIA, which considers more molecular fields.
11. Modern QSAR uses machine learning and AI for better predictions.
12. QSAR is now essential in lead optimization and drug design.
13. It reduces experimental efforts by predicting biological activity computationally.

Q10. What is 3D-QSAR and explain the steps involved in it.

1. 3D-QSAR is an advanced form of QSAR that uses three-dimensional properties of molecules.
2. It correlates 3D structural features with biological activity.
3. It considers steric, electrostatic, and other field effects.
4. Common methods include CoMFA and COMSIA.
5. Step 1: **Data Collection** — gather structures and biological activities of compounds.
6. Step 2: **Molecular Modeling** — draw and energy-minimize the structures.

7. Step 3: **Molecular Alignment** — superimpose molecules on a common framework.
8. Step 4: **Grid Generation** — place a 3D grid around molecules.
9. Step 5: **Field Calculation** — measure steric and electrostatic fields at each grid point.
10. Step 6: **Statistical Analysis** — use Partial Least Squares (PLS) regression to relate fields to activity.
11. Step 7: **Validation** — test the model's predictive power using test compounds.
12. Step 8: **Contour Map Generation** — visualize favorable and unfavorable regions.
13. 3D-QSAR improves understanding of structure-activity relationships and guides drug design.

11. Explain Hammett substituent constant.

1. Introduced by Louis Hammett in 1937.
2. It measures the electronic effect of substituents on a benzene ring.
3. Represented by σ (sigma) values.
4. Electron-withdrawing groups have positive σ values (e.g., NO_2 = +0.78).
5. Electron-donating groups have negative σ values (e.g., OH = –0.37).
6. Calculated by comparing reaction rates or equilibrium constants.
7. $\sigma = \log(K / K_o)$, where K is substituted and K_o is unsubstituted compound's rate.
8. Used in QSAR to predict biological activity.
9. Indicates how substituents influence electron density in molecules.
10. Helps understand metabolic stability, binding affinity, and reactivity.
11. Example: Nitrobenzene reacts faster in electrophilic substitution than phenol.
12. Important for selecting substituents in drug optimization.
13. Still widely applied in modern drug design.

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12. Explain Free-Wilson approach. Give its advantages and disadvantages.

1. Developed by Free and Wilson in 1964.
2. Relates biological activity to presence/absence of substituents at molecular positions.
3. Uses indicator (dummy) variables (1 = present, 0 = absent).
4. Applies linear regression for activity prediction.
5. No need for physicochemical parameters like logP or σ.
6. Advantage: Simple, easy to apply, especially with diverse substituents.

7. Advantage: Can directly compare effects of different groups at the same site.
8. Advantage: No requirement of measuring substituent properties.
9. Disadvantage: Requires large and well-planned dataset.
10. Disadvantage: Cannot predict activity for new untested substituents.
11. Disadvantage: Doesn't consider 3D structure or interaction effects.
12. Used for initial SAR studies.
13. Forms foundation for advanced QSAR methods.

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13. Explain scoring function for docking.

1. A mathematical formula to predict the binding strength of a ligand to a target.
2. Used in molecular docking studies.
3. Estimates binding affinity (binding energy or docking score).
4. Types: Force-field based, Empirical, and Knowledge-based.
5. Force-field based use physical interaction energies (e.g., electrostatic, van der Waals).
6. Empirical scoring uses weighted contributions of factors like H-bonds, hydrophobicity.
7. Knowledge-based uses statistical data from known complexes.
8. Example: Autodock uses empirical scoring.
9. Good scoring functions differentiate active from inactive compounds.
10. Must be fast, reliable, and able to rank ligands correctly.
11. Important for virtual screening and lead optimization.
12. Helps predict binding pose stability.
13. Guides medicinal chemists for better drug candidates.

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14. What is rigid docking?

1. A type of molecular docking where both ligand and receptor remain rigid.
2. No flexibility is allowed in bond angles or torsions.
3. Simplifies calculations and reduces computational time.
4. Suitable for small ligands and rigid binding sites.
5. Fast and requires fewer resources.

6. Less accurate than flexible docking.
7. Cannot accommodate conformational changes in protein or ligand.
8. Used for large-scale virtual screening.
9. Example software: DOCK.
10. Good for initial hit identification.
11. Poor at modeling induced-fit effects.
12. Produces multiple docking poses for ranking.
13. Followed by flexible docking for refinement.

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15. Explain different methods for handling ligand flexibility.

1. Important as ligands adopt multiple conformations.
2. **Systematic Search**: Rotates bonds incrementally to generate conformers.
3. **Random Search**: Randomly selects torsion angles and checks energy.
4. **Genetic Algorithm**: Uses evolutionary principles to optimize conformations.
5. **Monte Carlo Simulation**: Random conformer generation with energy minimization.
6. **Simulated Annealing**: Gradually cools the system to find low-energy conformers.
7. **Fragment-based Approach**: Builds ligand from flexible fragments.
8. Helps predict biologically relevant binding poses.
9. Reduces false-negative results.
10. Used in flexible docking protocols.
11. Important for large, rotatable ligands.
12. Example software: AutoDock Vina, GOLD.
13. Essential for accurate binding energy calculation.

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16. Explain manual docking.

1. Oldest form of molecular docking.
2. Done by visual inspection and manual placement of ligand into binding site.
3. Uses computer graphic software (e.g., PyMOL).
4. Relies on human expertise and chemical intuition.

5. Quick for simple systems or known interactions.
6. No scoring function involved.
7. Cannot model induced-fit or flexibility.
8. Useful for educational and hypothesis generation.
9. Can guide automatic docking set-up.
10. Risk of human bias.
11. Often inaccurate for complex systems.
12. Now replaced by automated docking.
13. Still used for pre-docking analysis and refinement.

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17. What is flexible docking?

1. Docking method where ligand and/or protein is flexible.
2. Allows bond rotations, angle changes, and conformational shifts.
3. Simulates real biological binding more accurately.
4. More computationally intensive than rigid docking.
5. Can handle induced-fit effects.
6. Increases accuracy of docking results.
7. Uses algorithms like genetic, Monte Carlo, or simulated annealing.
8. Example software: GOLD, AutoDock Vina.
9. Important for large, flexible ligands.
10. Helps predict multiple binding poses.
11. Provides better binding affinity estimations.
12. Essential for lead optimization phase.
13. Reduces false positives in virtual screening.

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18. How do we do biological screening based on docking?

1. Predict binding of compounds to biological targets using docking.
2. Use virtual libraries of drug-like molecules.
3. Dock each ligand into target's active site.

4. Score and rank ligands based on binding energy.
5. Select top-ranked compounds for biological testing.
6. Confirm activity through in vitro assays.
7. Filter out inactive compounds early.
8. Saves time and resources in drug discovery.
9. Validates computational predictions experimentally.
10. Identifies potential lead compounds.
11. Can prioritize ligands with desired properties.
12. Example: Screening antivirals for COVID-19 main protease.
13. Helps in hit-to-lead and lead optimization phases.

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19. Explain the objectives of Bioinformatics.

1. Manage and analyze large biological data.
2. Develop databases for biological information storage.
3. Predict structures and functions of biomolecules.
4. Study evolutionary relationships (phylogenetics).
5. Design new drugs and vaccine candidates.
6. Integrate genomics, proteomics, and metabolomics data.
7. Interpret experimental results computationally.
8. Develop algorithms for sequence alignment and modeling.
9. Identify genetic mutations causing diseases.
10. Simulate biological processes and interactions.
11. Enable personalized medicine approaches.
12. Enhance understanding of complex biological systems.
13. Support systems biology and big data biology projects.

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20. What are the applications of Bioinformatics?

1. DNA, RNA, and protein sequence analysis.
2. Genome annotation and gene prediction.

3. Molecular modeling and structure prediction.
4. Drug discovery and vaccine development.
5. Comparative genomics and evolutionary studies.
6. Analysis of gene expression (microarray, RNA-seq).
7. Protein-protein and protein-ligand interaction studies.
8. Personalized medicine and pharmacogenomics.
9. Biological database development (e.g., GenBank, PDB).
10. Disease gene identification and mutation analysis.
11. Functional annotation of genes and proteins.
12. Systems biology and metabolic pathway analysis.
13. Biodiversity and ecological data analysis.

21. What is cheminformatics and also elaborate its steps for chemical data curation in detail.

1. Cheminformatics is the application of computer and informational techniques to chemical problems.
2. Involves storage, retrieval, analysis, and visualization of chemical data.
3. Supports drug discovery, materials science, and chemical property prediction.
4. Uses chemical databases like PubChem, ChEMBL.
5. Helps predict properties like solubility, toxicity, and bioactivity.
6. Data curation ensures chemical data is accurate, consistent, and useful.
7. **Steps for Chemical Data Curation:**
    - **Data Collection:** Gather chemical structures from reliable databases.
    - **Structure Standardization:** Convert structures to consistent formats (SMILES, InChI).
    - **Duplicate Removal:** Identify and eliminate identical structures.
    - **Error Checking:** Fix incorrect valencies, atom types, or charges.
    - **Canonicalization:** Standardize tautomers, stereochemistry, and ionization states.
    - **Property Calculation:** Compute molecular weights, logP, H-bond donors/acceptors.
    - **Annotation:** Add biological activity, ADMET data, and references.
8. Ensures high-quality datasets for QSAR and docking.
9. Reduces false predictions due to poor-quality data.
10. Example: Cleaning a dataset before QSAR modeling.

11. Helps detect and correct data inconsistencies.
12. Critical in virtual screening and chemical library management.
13. Maintains reproducibility in computational studies.

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22. What are the computational models for ADME?

1. ADME = Absorption, Distribution, Metabolism, Excretion properties of drugs.
2. Computational ADME models predict these properties before lab testing.
3. Saves time, reduces costs in drug development.
4. **Types of Models:**
    - **Rule-based Models:** Use guidelines like Lipinski's Rule of Five.
    - **QSAR Models:** Correlate chemical structure with ADME properties.
    - **Physiologically Based Pharmacokinetic (PBPK) Models:** Simulate drug movement in body compartments.
    - **Machine Learning Models:** Use AI/ML to predict ADME from large datasets.
5. Predict properties like solubility, oral bioavailability, blood-brain barrier penetration.
6. Example: Predicting logP for lipophilicity estimation.
7. Reduces failure rate in clinical trials.
8. Can identify toxicity risks early.
9. Supports lead optimization.
10. Incorporates descriptors like molecular weight, H-bond donors/acceptors.
11. Widely used in pharma industries.
12. Example tools: pkCSM, admetSAR, SwissADME.
13. Improves drug safety and efficacy profiles.

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23. Explain target databases.

1. Databases storing information about biological macromolecular targets.
2. Include proteins, DNA, RNA involved in disease processes.
3. Contain sequence, structure, function, and ligand-binding data.
4. Important for identifying druggable targets.
5. Help in target-based drug discovery (TBDD).

6. Provide details like binding sites, cofactors, and active site residues.
7. Example: Protein Data Bank (PDB) for 3D structures.
8. UniProt for protein sequences and annotations.
9. DrugBank links drugs with their targets.
10. ChEMBL provides bioactivity data against targets.
11. Used in virtual screening, docking, QSAR.
12. Help understand target functions and drug resistance.
13. Essential for selecting suitable targets in new drug development.

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24. Explain the characteristics of biological data and related data management problems.

1. Biological data is complex, heterogeneous, and voluminous.
2. Includes DNA, RNA, protein sequences, structures, pathways, expression profiles.
3. Generated from diverse sources (genomics, proteomics, imaging).
4. Highly interconnected and dynamic.
5. Often incomplete, noisy, and redundant.
6. Requires integration from multiple platforms.
7. Data management problems:
    - **Data Heterogeneity:** Different formats and types (FASTA, PDB, XML).
    - **Data Volume:** Massive size (genome projects).
    - **Redundancy:** Multiple entries for same biological entity.
    - **Data Quality:** Errors in sequencing or annotation.
    - **Interoperability:** Compatibility issues between databases.
    - **Security & Privacy:** Protecting sensitive genetic data.
8. Requires specialized software and database systems.
9. Example: Managing patient genomic data for personalized medicine.
10. Involves data curation, validation, and storage strategies.
11. Needs high-performance computing resources.
12. Bioinformatics tools manage, analyze, and interpret this data.
13. Vital for drug discovery, clinical trials, and disease studies.

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25. Explain non-covalent interactions.

1. Weak, reversible interactions between molecules without bond formation.
2. Important in drug-receptor, enzyme-substrate interactions.
3. Types of non-covalent interactions:
    - **Hydrogen Bonding:** Attraction between H and electronegative atoms (O, N, F).
    - **Ionic Interactions:** Between oppositely charged groups.
    - **Hydrophobic Interactions:** Non-polar groups cluster to avoid water.
    - **Van der Waals Forces:** Weak attractions due to temporary dipoles.
    - **π–π Stacking:** Between aromatic rings.
4. Stabilize 3D structures of proteins, DNA, and drug-receptor complexes.
5. Essential for biological recognition processes.
6. Example: H-bonds between DNA base pairs (A-T, G-C).
7. Determine drug binding affinity and specificity.
8. Measured in molecular docking and QSAR studies.
9. Cumulative effect provides significant binding energy.
10. Critical in molecular dynamics and energy minimization.
11. Disrupted easily by temperature or solvents.
12. Used to optimize drug design for better binding.
13. Often preferred in reversible, safe drug actions.

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26. Explain energy minimization.

1. Process to find the most stable (low-energy) conformation of a molecule.
2. Removes steric clashes and unrealistic bond angles/torsions.
3. Uses computational algorithms to optimize molecular geometry.
4. Minimizes the total potential energy of a molecule.
5. Important before molecular docking, dynamics simulations.
6. Force fields (AMBER, CHARMM) calculate energies from bond lengths, angles.
7. Algorithms used: Steepest Descent, Conjugate Gradient, Newton-Raphson.

8. Ensures accurate docking results by refining structures.
9. Reduces computational artifacts in 3D models.
10. Example: Minimizing a protein-ligand complex before interaction studies.
11. Provides realistic biologically-relevant conformations.
12. Can be done for isolated molecules or complexes.
13. Essential step in virtual drug screening workflows.

1. A **Lead Compound** is a chemical compound that shows desired biological or pharmacological activity and can be modified to improve its properties for drug development.

2. Bioisosterism is the replacement of an atom or group in a drug molecule with another that has similar physical or chemical properties to improve drug activity or reduce toxicity.

3. Advantages of CADD:

- Saves time and cost in drug discovery.
- Identifies potential drug candidates quickly.
- Reduces the need for extensive lab testing.

4. Structure of Isoniazid:
$C_6H_7N_3O$
Chemical Structure:
NC(=O)c1cccnc1

5. HTS (High-Throughput Screening) is an automated technique used to quickly test thousands of compounds for biological activity against a target.

6. Steps of Drug Target Selection:

- Disease selection
- Target identification
- Target validation
- Assay development

7. In vivo tests are experiments performed on living organisms like animals or humans to study drug effects under natural conditions.

8. Potency is the amount of drug required to produce a given biological effect. Higher potency means a lower dose is needed for the effect.

9. ADME stands for **Absorption, Distribution, Metabolism, and Excretion** — processes that determine the drug's fate inside the body.

10. Nonrandom Screening involves testing compounds selected based on known biological or chemical properties, unlike random or blind screening.

11. QSAR (Quantitative Structure-Activity Relationship) is a mathematical model that correlates the chemical structure of compounds with their biological activities.

12. Difference between SAR and QSAR:

- **SAR** is qualitative, relating structure to activity.
- **QSAR** is quantitative, using statistical models to predict activity.

13. Hydrophobicity is the tendency of a molecule or group to repel water or prefer non-polar environments.

14. Partition Coefficient (P) is the ratio of a compound's concentration in a lipophilic (oil) phase to a hydrophilic (water) phase at equilibrium.

15. Limitations of Hammett σ Constant:

- Limited to aromatic compounds.
- Fails for non-linear, non-electronic effects.
- Not applicable for complex or biological systems.

16. Steric effects refer to the influence of the spatial arrangement of atoms in a molecule on its reactivity and interaction with other molecules.

17. Molar Refractivity is a measure of the total polarizability of a molecule related to its volume and refractive index.

18. Physicochemical properties in QSAR include molecular weight, logP, solubility, polarity, and electronic or steric factors that influence drug activity.

19. Partition Coefficient is the same as Q14:
The ratio of a substance's concentration in two immiscible phases like octanol and water.

20. Substituent Hydrophobicity Constant (π) represents the hydrophobic or lipophilic nature of a substituent relative to hydrogen in a standard system.

21. Molecular Docking is a computational method that predicts the preferred orientation of a small molecule (ligand) when bound to a target protein (receptor), allowing for the analysis of binding affinity and interaction.

22. Uses of Docking:

- Predict ligand-receptor binding interactions.
- Identify potential drug candidates.
- Guide the design of new drugs.
- Understand the mechanism of drug action.

23. Types of Docking:

- **Rigid docking**: Ligand and receptor are considered rigid during the docking process.
- **Flexible docking**: Ligand and/or receptor flexibility is taken into account during the docking process.

24. Degrees of Freedom in Flexible Docking refer to the number of independent motions that the ligand or receptor can undergo, such as translation, rotation, and bond flexibility.

25. Components of Docking Software:

- **Scoring function**: Calculates the binding affinity of ligand-receptor interactions.
- **Search algorithm**: Explores possible binding modes.
- **Energy minimization**: Refines the predicted complex.

26. Different Types of Molecular Docking:

- **Rigid docking**
- **Flexible docking**
- **Induced-fit docking** (adjusts protein structure upon ligand binding).

27. Application of Hit Identification in Molecular Docking:
It helps to identify initial lead compounds (hits) from a large library of molecules by predicting their binding affinity to a target protein.

28. Application of Molecular Docking in Lead Optimization:
Docking helps to refine and optimize lead compounds by enhancing their binding affinity and reducing undesirable properties.

29. De Novo Drug Design involves designing novel drug-like compounds from scratch based on the 3D structure of the target protein, without using known molecules as templates.

30. LUDI Program is a computational tool used in **de novo drug design** to generate new ligand molecules by inserting functional groups into the binding site of a receptor.

31. Bioinformatics is the application of computational tools and techniques to analyze and interpret biological data, such as DNA sequences, protein structures, and gene expressions.

32. Objectives of Bioinformatics:

- To develop algorithms and databases for biological data.
- To understand molecular biology through computational models.
- To facilitate drug discovery and personalized medicine.

33. Mass Spectra Analysis is a technique that measures the mass-to-charge ratio of ions to identify the composition of a substance, providing information about molecular structure, composition, and fragmentation patterns.

34. Steps for Chemical Data Curation:

- Data collection from various sources.
- Standardization of chemical data (naming conventions, formatting).
- Data validation and quality control.

- Integration into a central database for analysis.

41. Molecular Modeling is the computational technique used to predict the 3D structure of molecules and their interactions. It includes techniques like molecular mechanics, quantum mechanics, and molecular dynamics to simulate molecular behavior.

42. Partial Charges refer to the distribution of charge within a molecule, where atoms have fractional charges based on their electronegativity. **Dipole Moment** is a measure of the polarity of a molecule, indicating the separation of positive and negative charges.

43. Molecular Mechanics is a computational method used to model the physical behavior of molecules by treating atoms as balls and bonds as springs, using classical mechanics to calculate the potential energy and optimize structures.

44. Energy Term Parameters of Molecular Mechanics:

- Bond stretching
- Angle bending
- Torsional rotation
- Nonbonded interactions (van der Waals and electrostatic)

45. Difference between Molecular Mechanics and Quantum Mechanics:

- **Molecular mechanics** uses classical physics to model molecular systems, focusing on bond stretching, angle bending, and nonbonded interactions.
- **Quantum mechanics** considers the electronic structure of molecules, solving wavefunctions to understand molecular properties at a fundamental level.

46. Monte Carlo Methods are stochastic techniques used to sample possible molecular configurations by random sampling. It differs from **molecular dynamics**, which uses deterministic simulations based on Newtonian mechanics to study molecular behavior over time.

47. Methods of Quantum Mechanical Calculations:

- **Hartree-Fock (HF)**
- **Density Functional Theory (DFT)**
- **Post-Hartree-Fock methods** like MP2, CI

48. Operations or Calculations Useful for Molecular Mechanics:

- Energy minimization
- Force field calculations
- Optimization of molecular geometry
- Calculation of vibrational frequencies

49. Programs Used in Ab Initio Methods:

- **Gaussian**
- **Q-Chem**
- **Molpro**
- **VASP** (for electronic structure calculations)

50. Molecular Mechanics Does Not Express the Potential Energy Mainly in Terms of:

- **Electron-electron interactions**, which are described by quantum mechanical methods. Molecular mechanics primarily focuses on bond, angle, and nonbonded interactions.