SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES

AFFILIATED TO THE DR.MGR MEDICAL UNIVERSITY,CHENNAI APPROVED BY PHARMACY COUNCIL OF INDIA,NEW DELHI. COIMBATORE -641035

COURSE NAME : COMPUTER AIDED DRUG DESIGN(BP 807 ET)

VIII SEM / IV YEAR

TOPIC :VIRTUAL SCREENING;DRUG LIKELINESS SCREENING

Introduction to Virtual Screening

In-silico Technique for Drug Discovery

Evaluates Large Chemical Libraries

Identifies Potential Drug-like Compounds

Key Role in CADD (Computer Aided Drug Design)

Reduces Time, Cost, & Labor

Bridge to Laboratory Experiments

Early-Stage Lead Identification & Optimization.
Predicts Biological Activity

Need for Virtual Screening

Challenges of Traditional Screening

- Millions of Compounds in Databases
- Time-Consuming & Expensive
- High Requirements: Chemicals, Instruments, Manywar

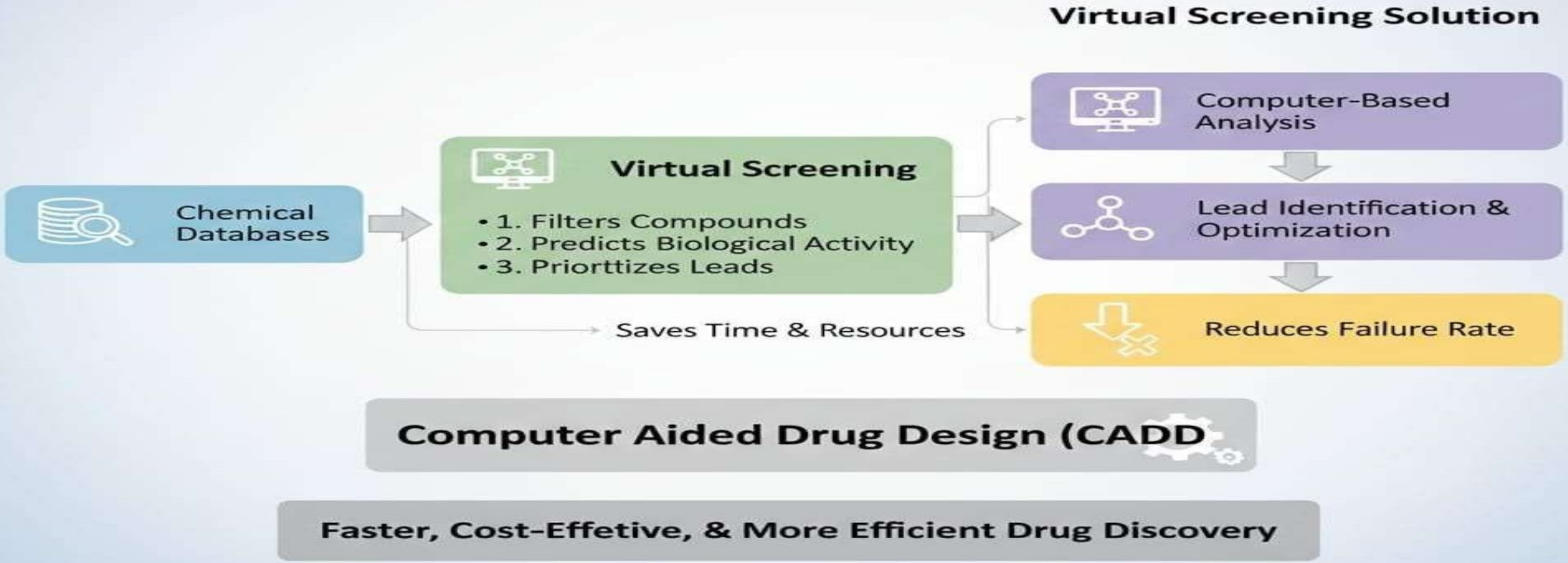
Efficiency & Speed Improvement

Virtual Screening Solution

- Computer-Based Analysis
- Saves Time & Resources, Selects Promising Molecules
- Reduces Experiments & Material Waste

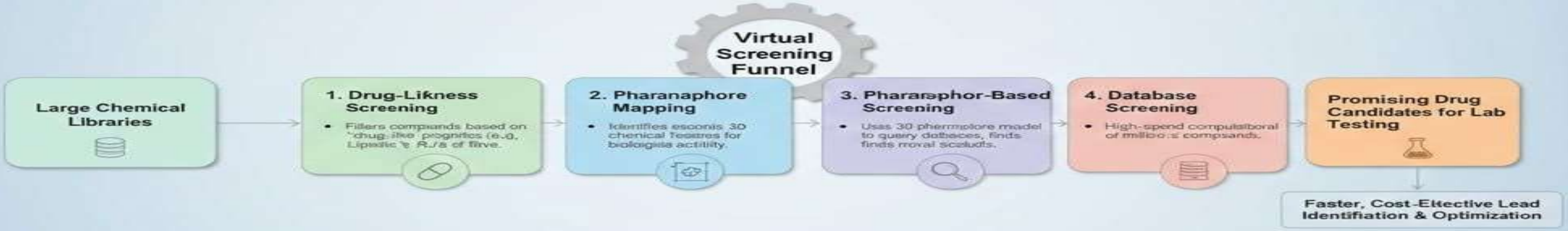
Increases Chance of Early Lead Compound Identiifation

Role of Virtual Screening in Drug Discovery



Virtual Screening Techniques (Overview)

Compuatonal methods to identify promising drug candidates



Advantages of Virtual Screening

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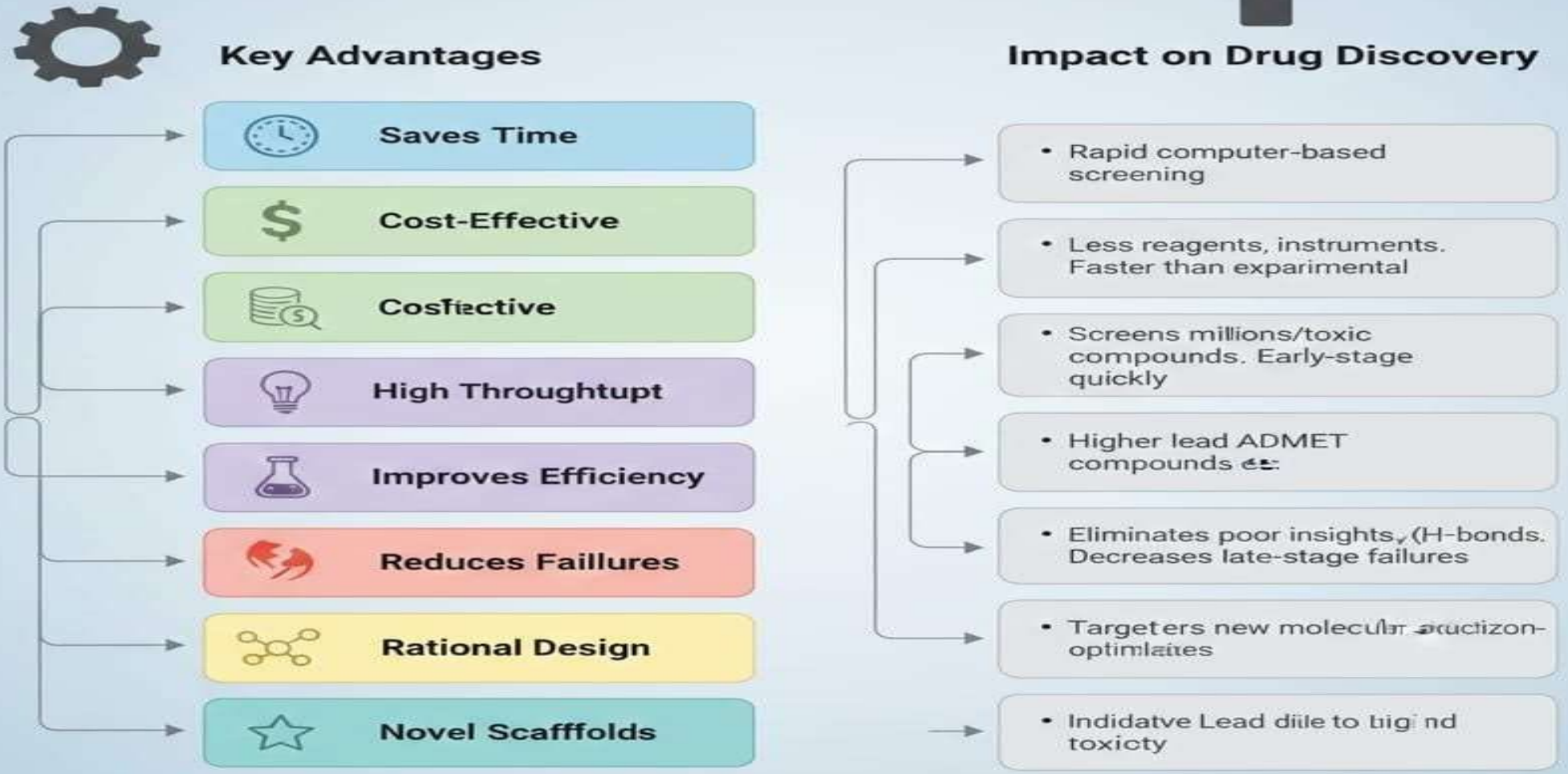
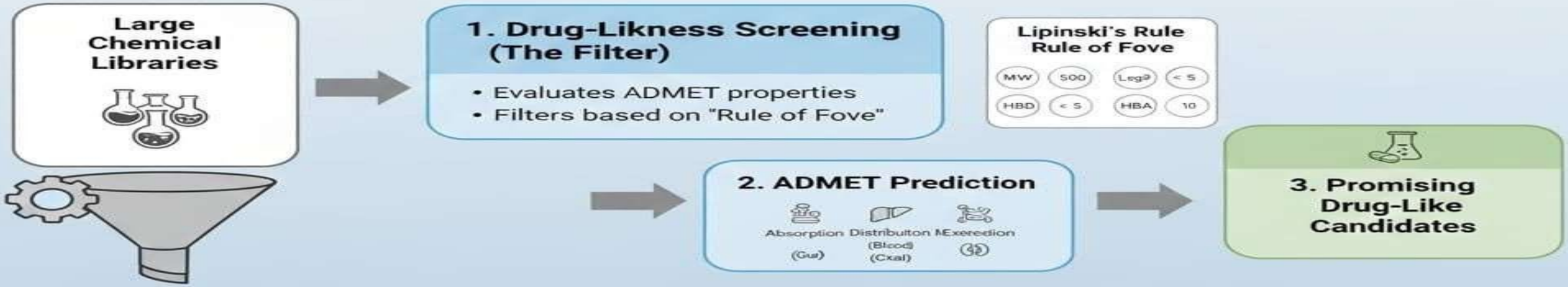


Introduction of Drug-Liktness Screening

Ensuring molecules have "drug potential" early on

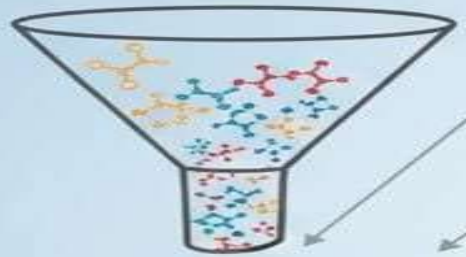


Reduces Time, Cost, & Late-Stage Failures. Increases Success Rate.

An Essential Pre-Filtering Step in Virtual Screening

Importance of Drug-Likness Screening

Large Chemical Libraries



Drug-Likness Screening (The Filter)

Early Candidate ID
- Identifies suitable

Procentenies
- Identifies suitable molecules

Reduces Failures
- Filters poor ADMET properties

Saves Time & Cost
- Prevents abor ADMET

Saves Time & Cost
- Prevents uneussary experiments

Enhances VS
- **Efficiences** large libraries

Improves Oral Bioavaiability
- Ensurs absorption/ permiiabllity

Supports Rational
- Guides structural modification

Enhances VS Efficiency
- Manages large libraries

Minimizs Toxicity Risk
- Screens harmful compounds

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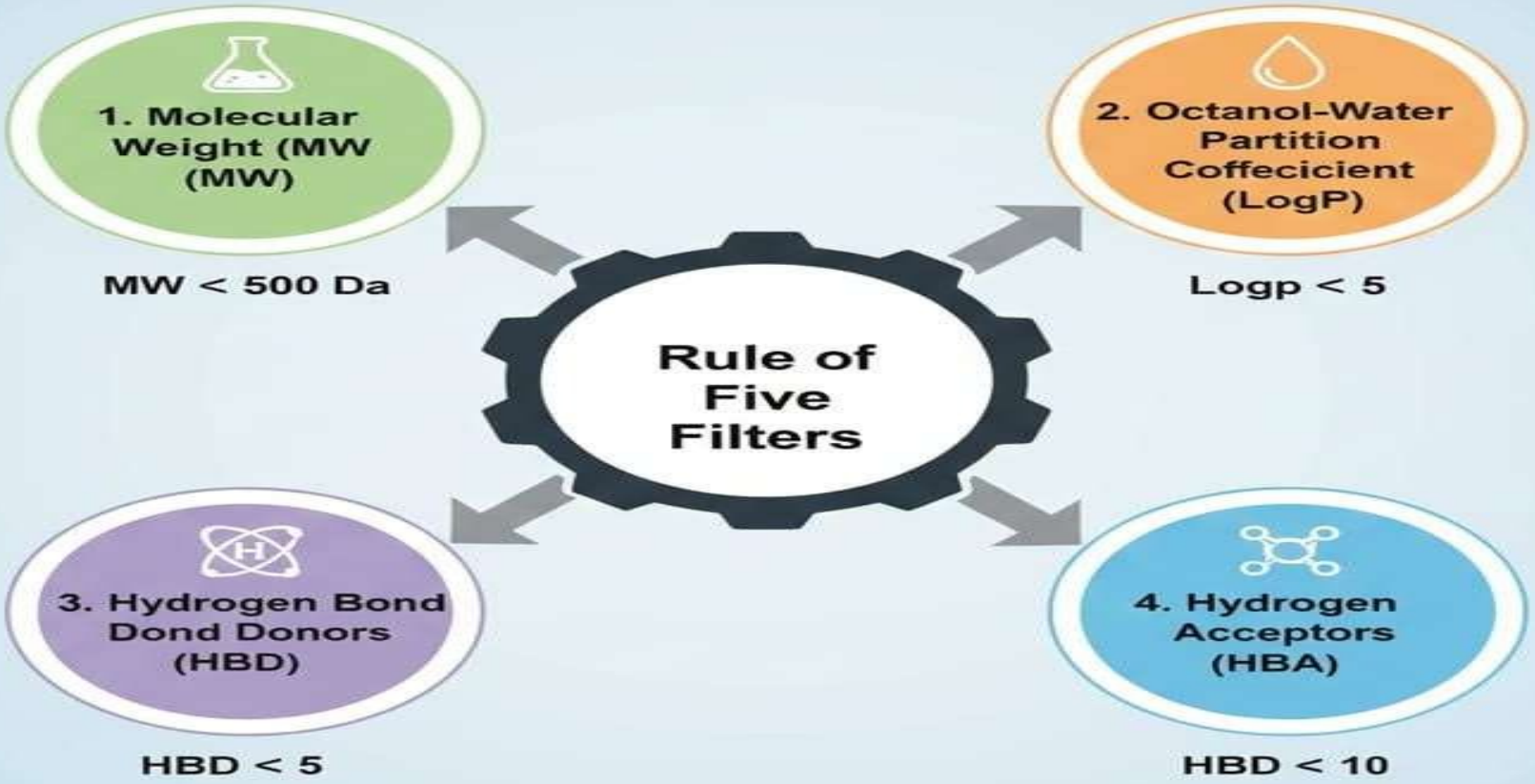
- Screens harmful compounds

Increass Clinical Success
- Higher approval probablity

Faster, Smarter, & Safer Drug Discovery

Crucial for virtual screening success

Lipinki's Rule of Five



If a compound violates >2 rules, it is likely to have poor oral biaalavibility.

Used for Drug-Lilkess Prediction & Early-Stage Filtering

Significance of Lipinski's Rule of Five

Smarter, Faster, More Effective Drug Discovery

A Corsıntone of Virtual Screening Success

Other Drug-Likiness Rules

Drug-Likness Screening (Beyond Lipinski)

1. Veber's Rule
- Rotatable bonds ≤ 10
- TPSA ≤ 140 Å²

2. Ghose Filter
- LogP: −0.4 to 5
- TPSA ≤ 140 Å²

3. Egan's Rule
LogP ≤ 5
LogP ≤ 5
TPSA ≤ 131 Å²

2. Noer's Rule
MW: 160–480
LogP: −0.4 to 5
MR: 40–100
Atoms: 20–70

4. Muegge's Rule
(Bayer Filter)
LogP: −2–5
TPSA ≤ 150
RBD ≤ 5
HBA ≤ 10

3. Egan's Rule
LogP: −2 to 5
LogP: −≥ 150
Rings ≤ 7

Improved Prediction: Absorption, Permebilty, & Safety

5. Rule of Three
(Fragment-Based Discovery)
MW ≤ 300
LogP ≤ 3
HBA ≤ 3

6. Pffzer's 3/75 Rule
LogP > 3
MBD ≤ 3
TPSA < 75 Å²

Multiple rules complement Lipinski's to enhance drug discovery success.

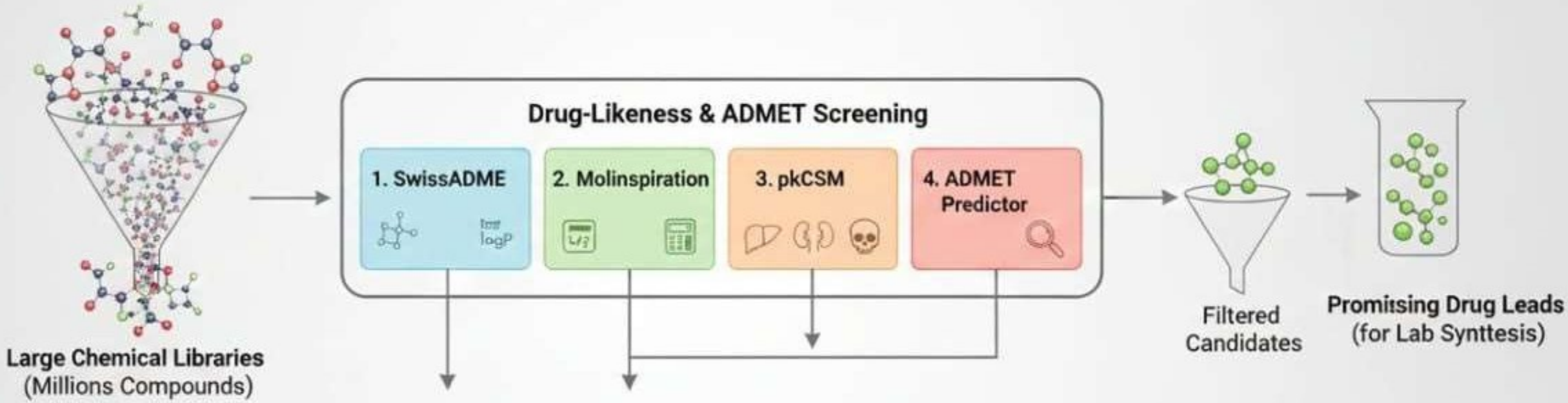
ADMET Screening: The Pharmaokostic & Safety Filter

Predicting a Drug's Journey & Fate in the Body

Ensuring Clinical Success: Reduces Failures, Saves Time & Cost

DRUG COMPOUNDS ARE INVOLVED IN CLINICAL TRAIL PHASES

TOOLS FOR DRUG LIKELINESS AND ADMET SCREENING



Virtual Screening Pipeline: Reducing Failure, Saving Time

Advantages of Drug-Likiness Screening

Larg-
Drug-Likening
(The Smart Filter)

Drug-Likness
Screening
(The Smart Filter)

1. Early Elimination
- Filters poor properties
- Rresvents synstesis/testing
- Minimizes resources

2. Saves Time & Cost
- Favorable absorption
- Crucial for oral drugs

4. Reduces Drug Failure
- Narrows down libraries
- Boost latektage attrition

6. Supports Rational Design
- Guides structural mods
- Balances potency/PK

7. Minimizes Toxicity Risk
- Higher approval chance
- Better pre-to-clinical transition

Drug-lilkness screening makes drug discovery Faster, Safer, & More Cost-Cost-Effeective, Increasing Success

A Corontoine of Virtual Screening Success

Disavantages of Drug-Likiness Screening

1 Limited to Known Rules
- Based on Lipinski, Veber, etc.
- Excludes novel compounds

2. Cannot Predict Biological Activity
- Evaluates properties, NOT efficacy
- No guarntee target binding

3 False Positives & Negatives
- Passs filter, Fails lab (false positive)
- Fails filter, Is active nesgtive)

? Limitations

5.Not Suitable for All Drug Types
- Errors in algorthms/datbases
- Misleading results

4. Overlooks Complex ADMET
- Early rules are too simple
- Requires later experimental validation

6. Not Suitable for All Drug Types
- Peptides, biologics, prodrug
- May be wrognly excluded

Drug-likiness screening is valuable for early filtering but cannot replace experimental valiation and may miss unvevcational drug candiates.

Summary: Virtual Screning & Drug-Likiness Screening

1. Virtual Screening (VS)

Definition:
- Compuational search to find liikely binders.

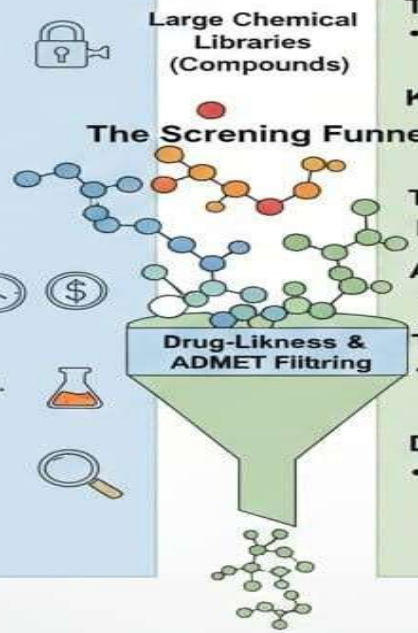
Definition:
- Compuational search ⇒

Techniques:
- Drug-likness, Pharamaphore, Docking.

Workflow
- Target Prep ⇒ Fiitering ⇒ Docking ⇒ ⇒ Validation.
- Needs accurate structures

Advantages:
- Needs accurate structures, False ++).

Limitations
- Saves Time/Cost, Reduces Failure, Novel ScaNovel Scaffods



2. Drug-Likeness Screening (DLS)

Definition:
Evaluates drug-like properties (e.g., Lipinski's).

Tefinition:
- Lipinski (MW<500, etc.), ADMET.

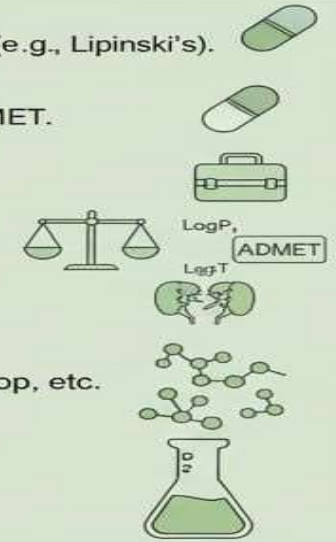
Key Parameters/Rules:
Lipinki (MW<500, etc,), ADMET

Tools
pkCSM, QikProp, etc.

Advantages
- SwissADME, pkCSM, QikProp, etc.

Tools
- Early elimination, Improves Safety.

Disavartages
- Limited rules, No Saves Cost, No efficacy, False ++).



Promising Drug Candidates (for Lab Validation)

Summary: Faster, Safer, & Smarter Drug Discovery

ASSESSMENTS

Q1: Virtual screening is primarily used to: A) Synthesize new chemical compounds B) Identify promising drug candidates from large compound libraries C) Measure drug toxicity in humans D) Conduct clinical trials

Q2: Lipinski's Rule of Five does not include which parameter?
A) Molecular weight ≤ 500 Da B) LogP ≤ 5 C) Hydrogen bond donors ≤ 5 D) Topological polar surface area ≤ 140 Å²

Q3: Veber's rule emphasizes:
A) Molecular weight and lipophilicity

B) Molecular flexibility and polar surface area
C) Toxicity prediction

D) Oral solubility only

Q4: pkCSM is mainly used to: A) Perform molecular docking B) Predict ADMET properties C) Synthesize compounds D) Visualize 3D protein structures

Q5: Which combination represents both screening and pharmacokinetic evaluation? A) Molecular docking + ELISA B) Drug-likeness screening + ADMET screening C) Flow cytometry + Western blot D) QikProp + PCR

REFERENCES

Lipinski, C. A., Lombardo, F., Dominy, B. W., & Feeney, P. J. (1997). Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Advanced Drug Delivery Reviews, 23(1-3), 3–25.

Schrödinger. QikProp: ADME predictions for drug discovery. https://www.schrodinger.com/qikprop

Sliwoski, G., Kothiwale, S., Meiler, J., & Lowe, E. W. (2014). Computational methods in drug discovery. Pharmacological Reviews, 66(1), 334–395.

Daina, A., Michielin, O., & Zoete, V. (2017). SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Scientific Reports, 7, 42717.


Thank You!