Drug likeness & drug properties Part -1

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DRUG DISCOVERY

1

TARGET TO HIT

Evaluation of physicochemical & *in vitro* ADME properties

2

HIT TO LEAD

Optimization of physicochemical & drug-like properties

3

LEAD TO CANDIDATE IDENTIFICATION

Optimization of drug-like properties, IVIVC, PK/PD Correlation

4

CANDIDATE SELECTION

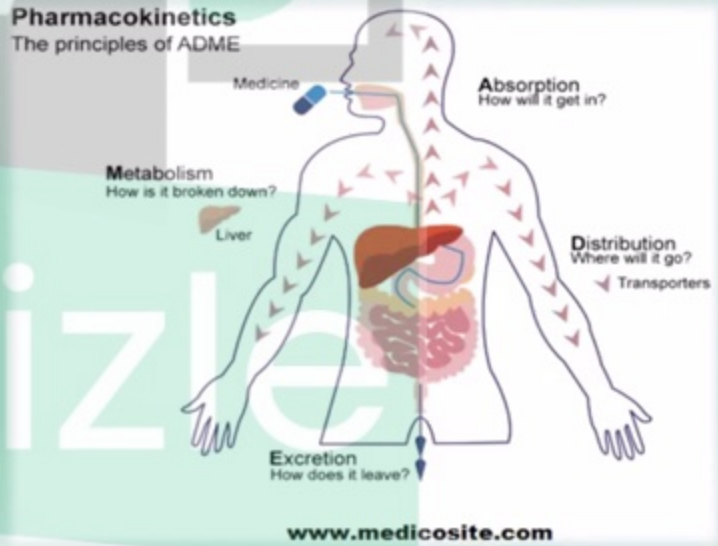
Dose range finding, safety/tox evaluation, interspecies scaling

Clinical Candidate

INTRODUCTION

Drug-like is defined as those compounds that have sufficiently acceptable ADME properties and sufficiently acceptable toxicity properties to survive through the completion of human clinical trial

A – Absorption
D – Distribution
M – Metabolism
E – Excretion



Drug-like properties confer good ADME/Toxicity characteristics to a compound.

- Medicinal chemists control properties through structure modification.
- Biologists use properties to optimize bioassays and interpret biological experiments

Drug-like Properties Are an Integral Part of Drug Discovery The structure determines the compound's properties.

Drug properties

Structural properties

- Hydrogen bonding
- Polar surface area
- Lipophilicity
- Shape
- Molecular weight
- Reactivity
- pKa

Physicochemical properties

- Solubility
- Permeability
- Chemical stability

Biochemical properties

- Metabolism
- Protein and tissue binding Transport (uptake, efflux)

Pharmacokinetics (PK) and toxicity Clearance

- Half-life
- Bioavailability
- Drug–drug interaction
- LD50

- When the structural properties interact with the physical environment, they cause physicochemical properties (e.g., solubility).
- When the structural properties interact with proteins, they cause biochemical properties (e.g., metabolism).
- At the highest level, when the physicochemical and biochemical properties interact with living systems they cause PK and toxicity.
- Medicinal chemists control the PK and toxicity properties of the compound by modifying the structure

What is Drug likeliness ?

Druglikeness is a qualitative concept used in drug design for how "druglike" a substance is with respect to factors like bioavailability.

It is estimated from the molecular structure before the substance is even synthesized and tested.

Solubility

- The aqueous solubility of a compound significantly affects its absorption and distribution characteristics.
- A low solubility goes along with a bad absorption
- The general aim is to avoid poorly soluble compounds

Log S Calculation

Our estimated logS value is a unit stripped logarithm (base 10) of the solubility measured in mol/liter

In the following diagram you can see that more than 80% of the drugs on the market have a (estimated)

logS value greater than -4.