Quantitative Structure Activity Relationship (QSAR)

Quantitative Structure-Activity Relationship (QSAR)

What is QSAR?

- **QSAR** stands for **Quantitative Structure-Activity Relationship**.
- It is a method used in drug design to predict how well a chemical compound (like a drug) will work in the body, based on its chemical structure.
- **In simple terms:**
  - We look at the structure of a molecule (what atoms are connected and how).
  - We measure or calculate different properties of that molecule (like its size, shape, how greasy it is, etc.).
  - We then try to relate those properties to the biological activity (how well it kills bacteria, blocks a receptor, reduces inflammation, etc.).
- If we understand these relationships, we can predict how new, untested molecules might behave — even before we make them in a lab.

Why is QSAR important?

- It helps in **saving time and money** in drug discovery.
- It reduces the need for animal or human testing in the early stages.
- It guides chemists in **designing better drugs** by knowing what molecular features are important.

How does it work?

1. **Collect Data**: We take a set of known drugs or compounds.
2. **Calculate Descriptors**: These are the numerical values representing molecular properties (like weight, volume, polarity, etc.).
3. **Create a Model**: Using math or statistics, we find equations that link descriptors to activity.
4. **Validate the Model**: We test if our model can predict the activity of new compounds correctly.

An example:

- Suppose we know that:
  - Adding a methyl group ($-CH_3$) increases antibacterial activity.
  - Making the molecule more polar reduces its activity.
- We can then use this rule to **predict** which molecules will work better as antibiotics.

SAR versus QSAR, and History and Development of QSAR

What is SAR?

- SAR stands for **Structure-Activity Relationship**.
- It is the **basic version of QSAR**.
    - In SAR, we look at how changes in the chemical structure affect the activity, but **we do it qualitatively** (without using numbers).
    - SAR is **based on observations** and trial-and-error.

Example:

- If adding a chlorine group to a molecule increases its activity, we note that in SAR.

SAR vs QSAR:

Feature	SAR	QSAR
Type of approach	Qualitative	Quantitative
Use of math	No	Yes
Output	General idea of which groups increase/decrease activity	Mathematical model to predict activity
Accuracy	Less accurate	More accurate and predictive
Application	Early drug discovery	Advanced drug modeling and prediction

- So, **QSAR is an advanced form of SAR**, where we use mathematical tools to make predictions.

History and Development of QSAR:

Early Days (1860s - 1900s):

- The idea that **structure relates to activity** began in the 19th century.
- Early chemists noticed that similar molecules produced similar biological effects.

1930s:

- **Hammett equation**: First attempt to relate chemical properties (like electron distribution) to reaction rates.

1960s:

- **Hansch and Fujita** developed the **first formal QSAR model**.
- Introduced the Hansch analysis, which related biological activity to hydrophobicity, electronic, and steric factors.

1970s–1990s:

- More types of descriptors were introduced.
- Use of computers began for statistical modeling.

2000s–present:

- 3D-QSAR models like **CoMFA** and **CoMSIA** were developed.
- Machine learning and AI methods started being used.
- QSAR became a standard tool in **Computer-Aided Drug Design (CADD)**.

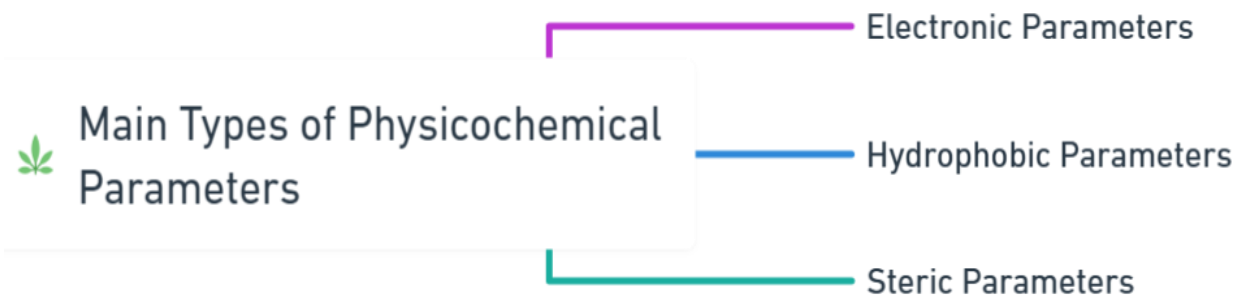
Types of Physicochemical Parameters

- In QSAR studies, we need to describe molecules using numerical values called **physicochemical parameters** (also known as molecular descriptors).
- These parameters represent different physical and chemical properties of the molecule.

Why are these important?

- These parameters help us understand:
  - How a drug moves in the body (absorption, distribution)
  - How it binds to its target (like an enzyme or receptor)
  - How it behaves in water or fat environments

Main Types of Physicochemical Parameters



A. Electronic Parameters

- These describe the electron distribution in the molecule – how electrons are arranged or pulled in different parts of the compound.
- This affects how the drug interacts with the target (like an enzyme or receptor).

Examples:

- Hammett's substituent constant (σ) – tells how electron-donating or withdrawing a group is.
- Dipole moment – how uneven the electron distribution is across the molecule.

Why important?

- Some drug targets are sensitive to the charge or polarity of the molecule, so these values help predict activity.

B. Hydrophobic Parameters

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