Pharmacophores And Bioisosteres

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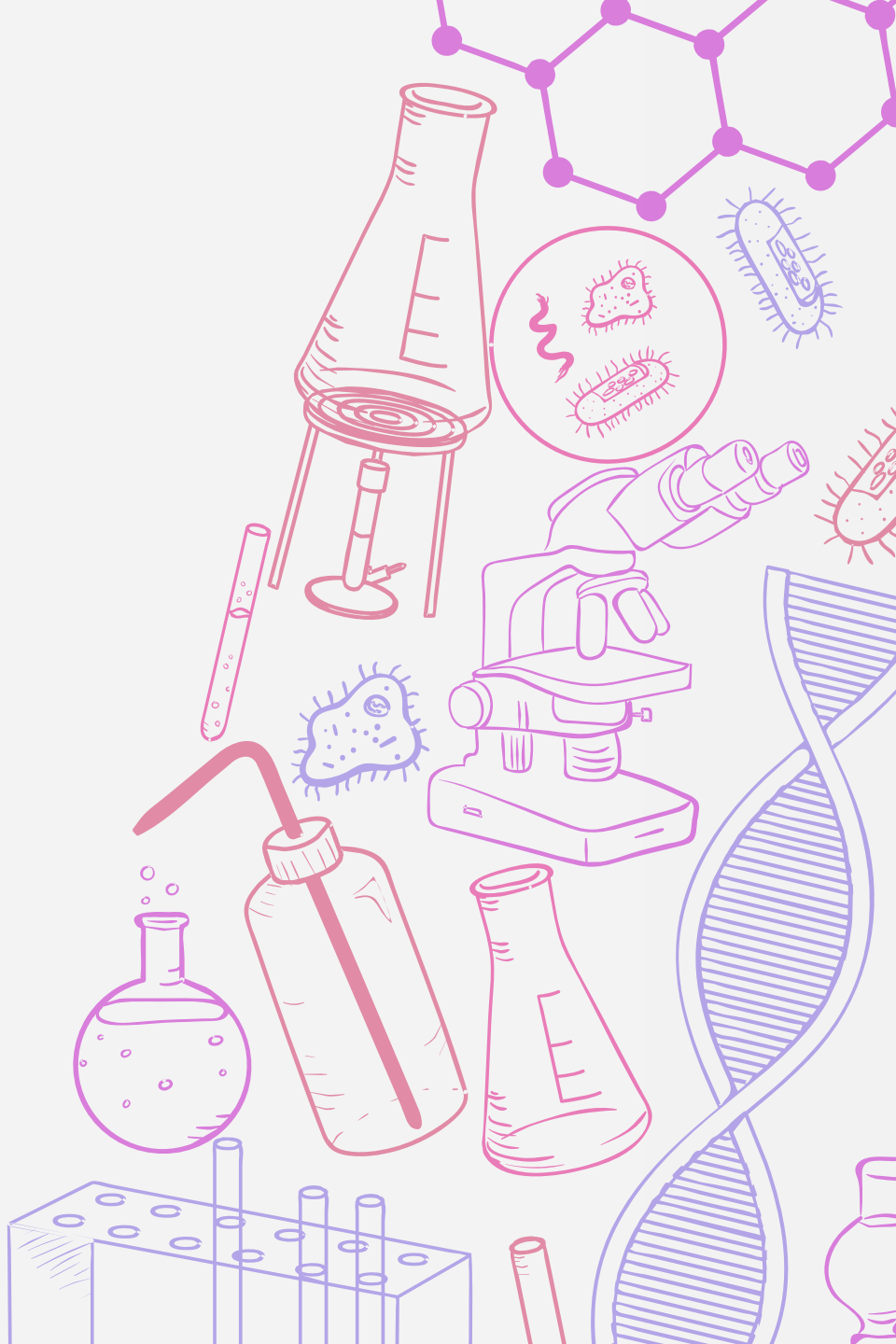
Intended Learning Outcomes

- Define pharmacophores
- ClassifyPharmacophores
- Mention applications of pharmacophores
- Define Bioisosteres
- Classify Bioisosteres
- Mention applications of Bioisosteres

Pharmacophore

A **pharmacophore** is the ensemble of steric and electronic features that is necessary to ensure the optimal supramolecular interactions with a specific biological target structure and to trigger (or to block) its biological response.



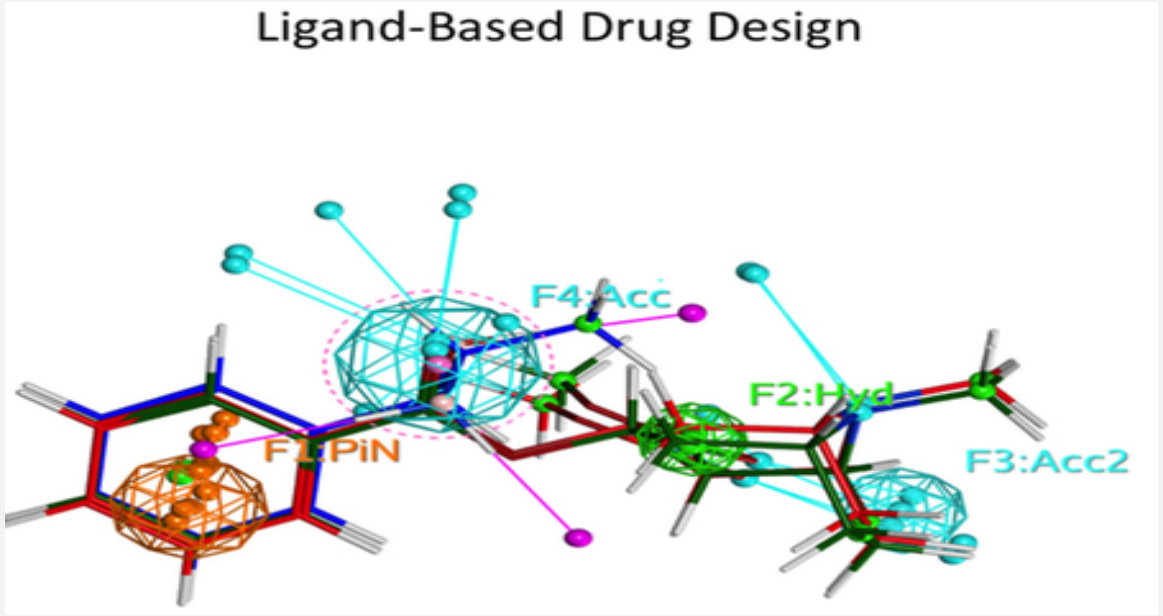
Pharmacophore Classification

Ligand based

Structure based

Ligand based

In the absence of the macromolecular target structure, ligand–based pharmacophore modeling is an essential strategy for drug discovery. In this method, the common chemical characteristics from 3D structures of multiple known ligands are extracted through ligand alignment, which would represent the essential interactions between ligand and potential macromolecular target.



Structure based

The structure - based pharmacophore modeling generates chemical features of the active site and the sterical relationships from 3D structure of macromolecular target of macromolecule - ligand complex. It probes the possible interaction sites between the macromolecular target and the ligands.

Pharmacophore Applications

Ligand based

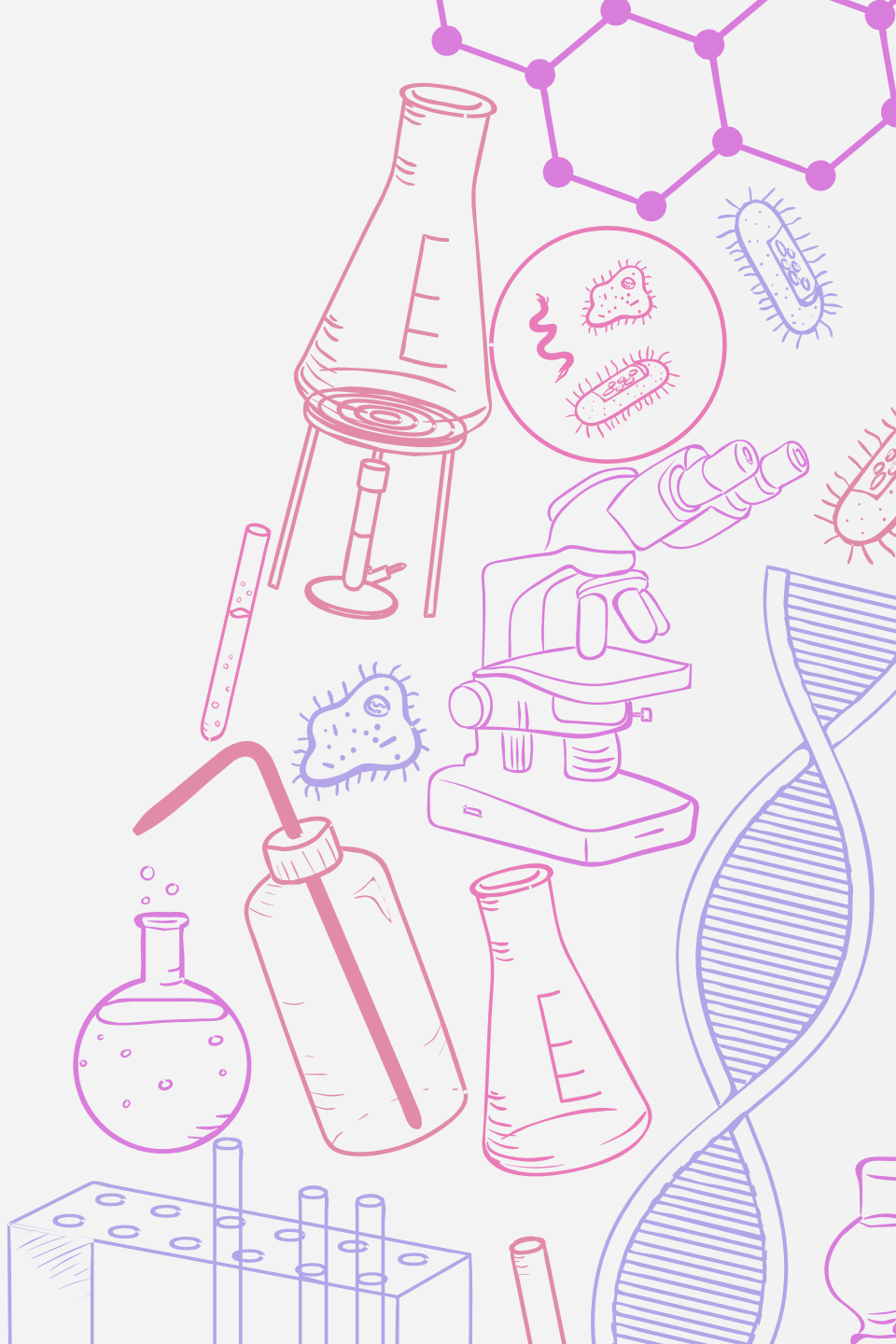
- Virtual Screening
- Lead Optimization

Structure based

- De Novo Drug Design
- Target Identification

Bioisostere

Bioisosteres are chemical substituents or groups with similar physical or chemical properties which produce broadly similar biological properties to another chemical compound.



Bioisostere Classification

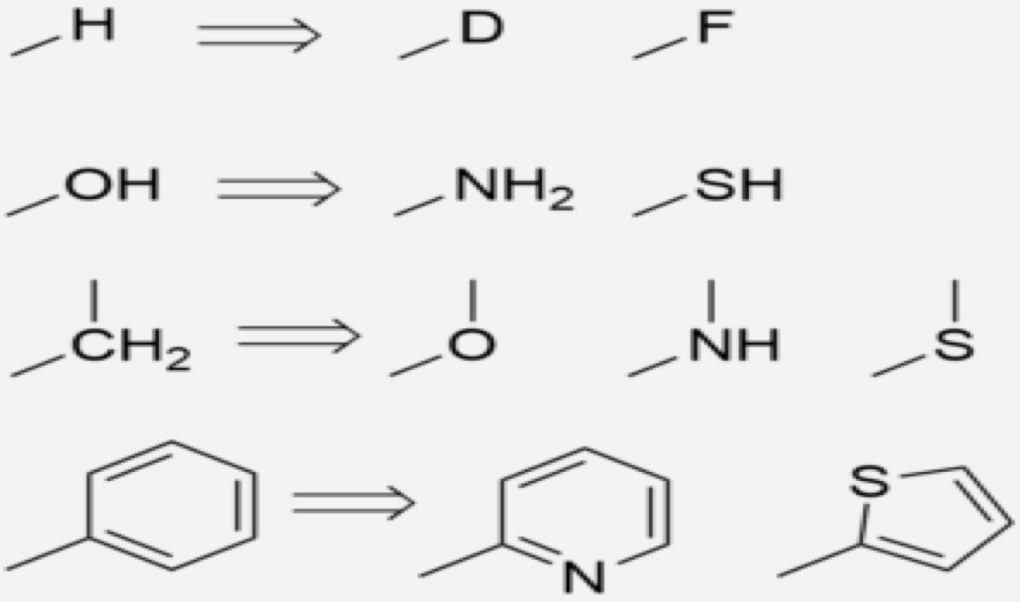
Classical bioisosteres

Non-Classical bioisosteres

Classical **bioisosteres**

Have same stearic and electronic properties

1. Monovalent
2. Divalent
3. Trivalent
4. Tetravalent
5. Ring Equivalent

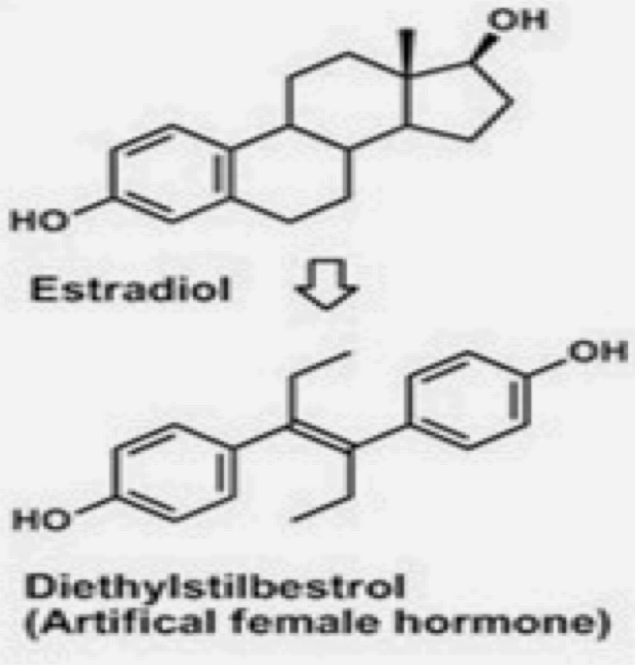


Non-Classical bioisosteres

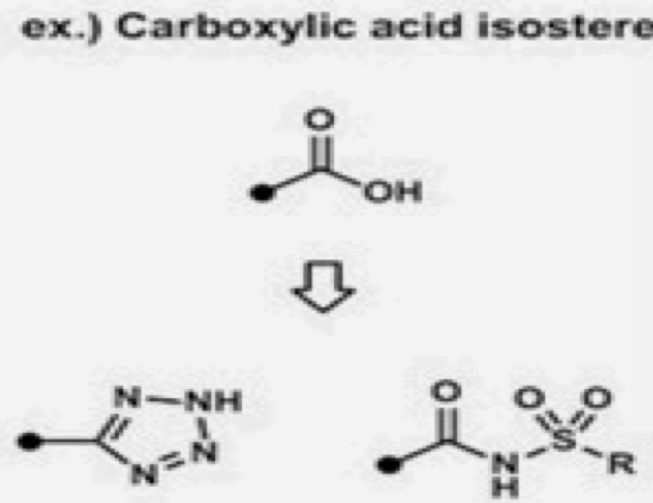
Do not have stearic and electronic properties

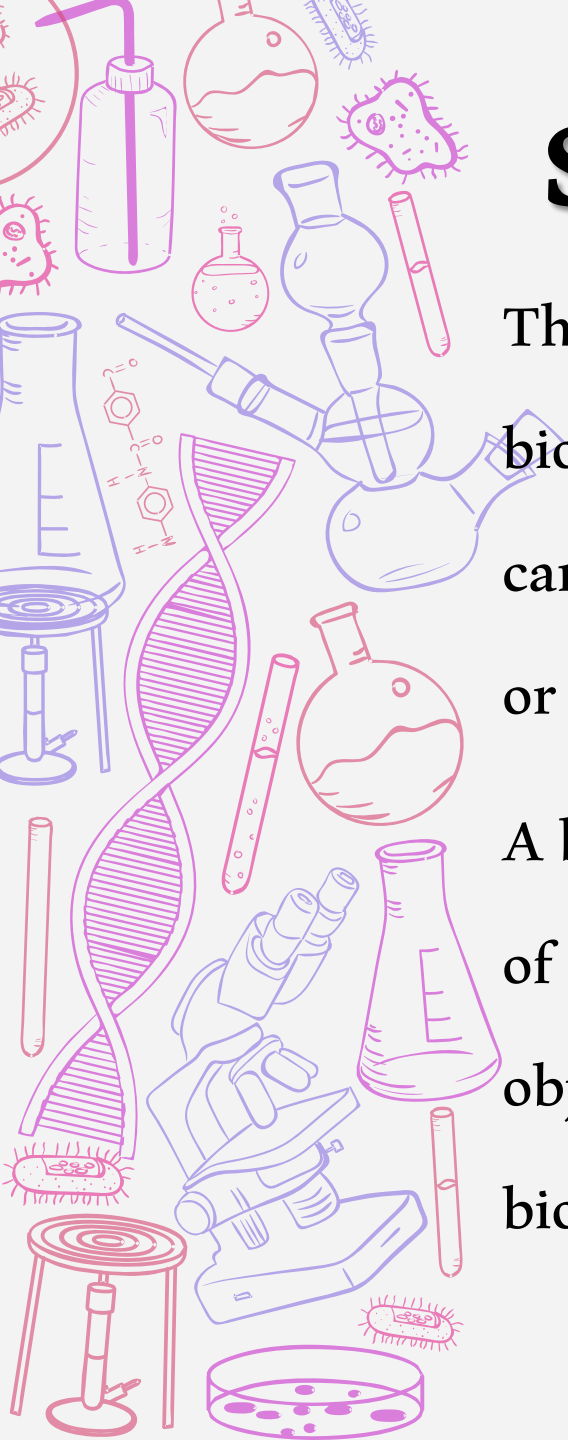
Non-classical bioisosteres divide to two subgroups,

- Cyclic and non-cyclic isosteres



- Exchangeable group





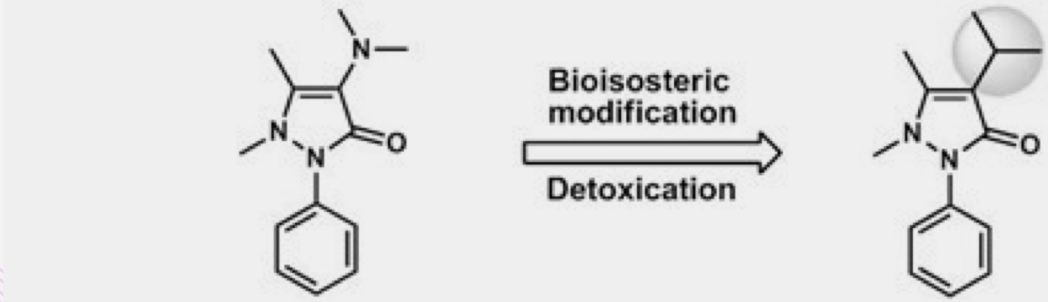
Summary:

The knowledge of a pharmacophore, or the 3D arrangement of features in the biologically active molecule that is responsible for its pharmacological activity, can help in the search and design of a new or better drug acting upon the same or related target.

A bioisostere is a molecule resulting from the exchange of an atom or of a group of atoms with an alternative, broadly similar, atom or group of atoms. The objective of a bioisosteric replacement is to create a new molecule with similar biological properties to the parent compound.

Bioisostere Application

In drug design, the purpose of exchanging one bioisostere for another is to enhance the desired biological or physical properties of a lead compound without making significant changes in chemical structure of lead



Aminopyrine Propylphenazone

Aminopyrine Marketed as an analgesic and anti-inflammatory drug in 1896. In 1922, It was revealed that Aminopyrine was a carcinogen !

Propylphenazone Developed by Roche in 1951. Bioisosteric modification of dimethylamino group removed its carcinogenic action.


Thanks for
listening!

References:

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