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Topic: Pharmacophore

Synonyms:

Related Topics:

Definition:

A Pharmacophore is an ensemble of steric, electrostatic and hydrophobic properties which is essential for optimal supramolecular interactions with a biolocial receptor, to modulate or inhibit a biological effect.
A Pharmacophore does not represent a concrete molecule, but an abstract concept which describes the common molecular properties of interaction with the receptor.
The Pharmacophore anchors the agent with the receptor.
With pharmacophoric models one can define special properties (pharmacophoric points) based on the structure of the receptor or based on the structure of a known agent. This pharmacophoric points can be checked against a database of pharmacophores.

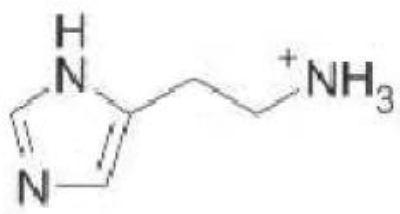
Characterization:

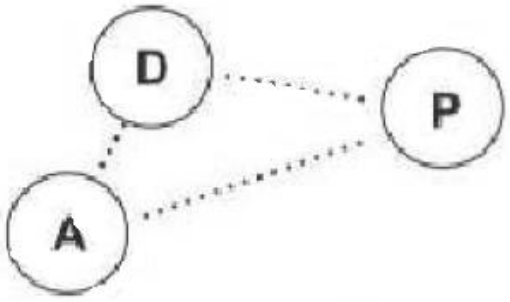
(1) Location of the functional groups (e.g. proton donor/acceptor, hydrophobic parts)
(2) Stabilization of the most effective conformation
(3) Lipinski's rule of five:
    The following properties are essential for good permeation
    - The molecule has less than five proton-donators
    - The molecular weight is smaller than 500 Dalton
    - log P smaller than 5
    - the molecule has less acceptors than 10
    - the molecule should use biological transporters

    otherwise the ligand is attached too strong or it can not be transported.
(4) Minimum of pharmacophoric points: 3

Structures:

An example of a histamine-pharmacophore: (proton donor (D) and acceptor (A), charge (P))





Publications:

[1] Wirkstoffdesign, H.-J. Böhm, G. Klebe, H. Kubinyi; Spektrum-Verlag 1996

Web-Links:

http://www-ra.informatik.uni-tuebingen.de/lehre/ss03/pro_wirkstoffdesign_ausarbeitung/ThorstenTiede.pdf

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