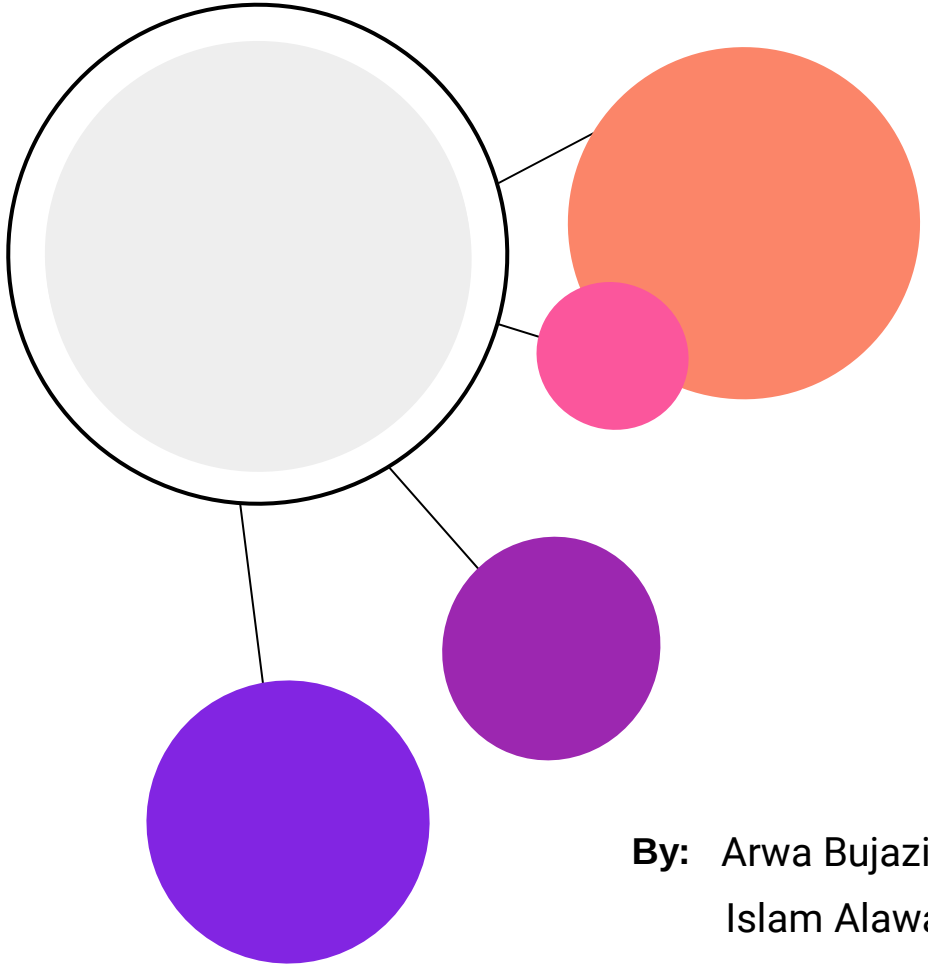
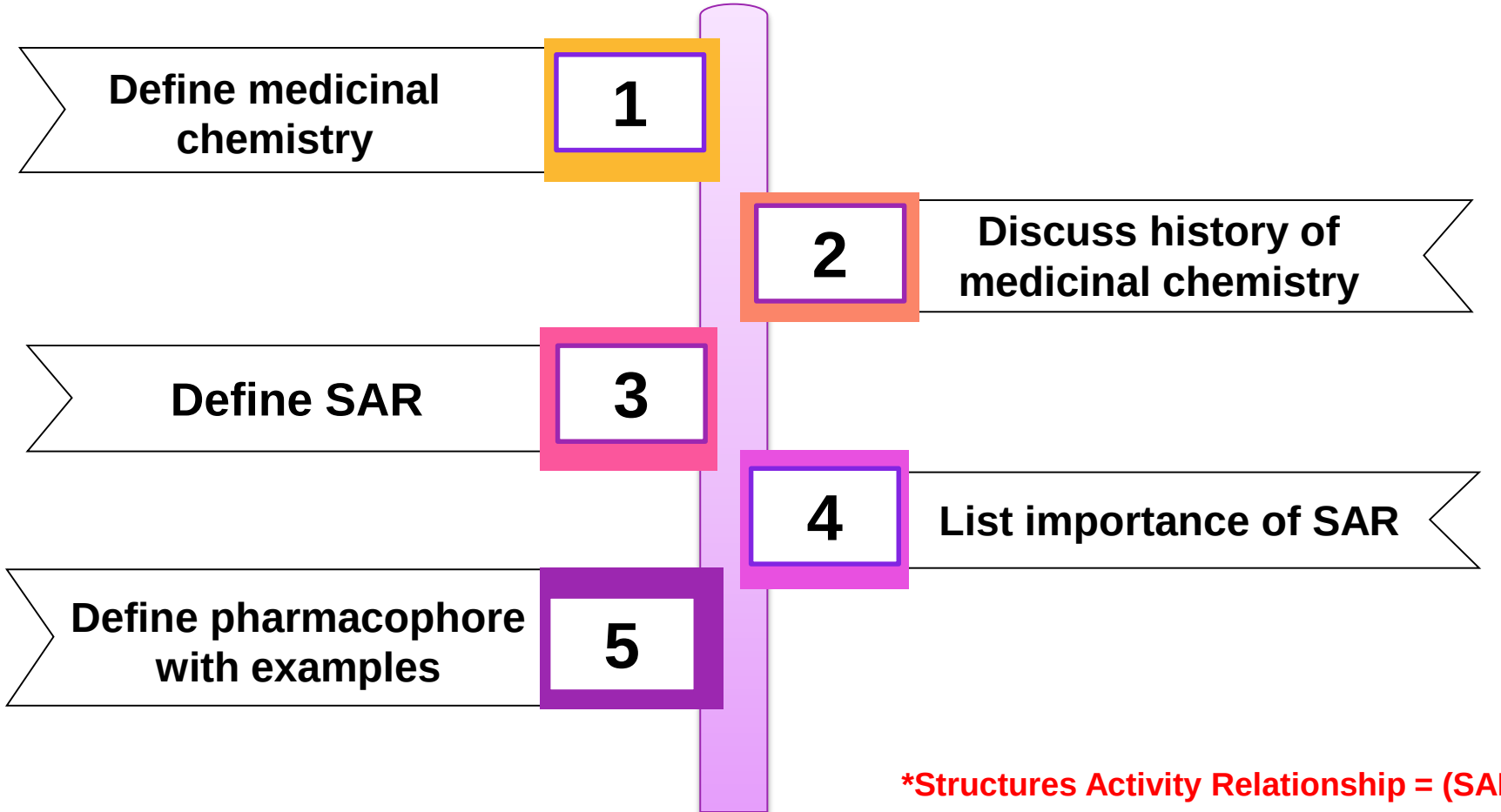


# Structures Activity Relationship (SAR)

**By:** Arwa Bujazia (2797)
Islam Alawami (2929)
Yousef Alsubaihi (3039)

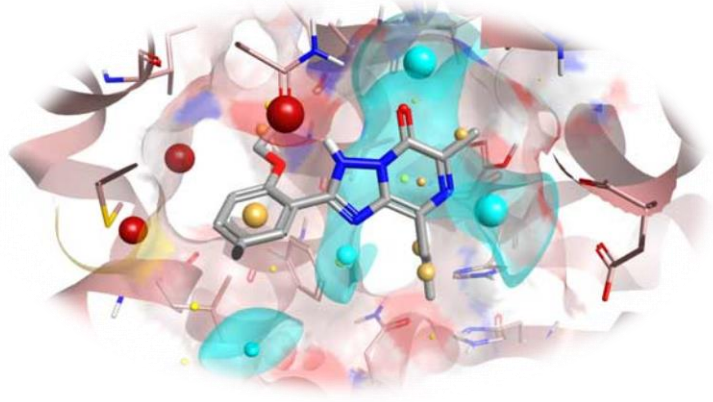
# ILOS:




*Structures Activity Relationship = (SAR)

# What is medicinal chemistry:

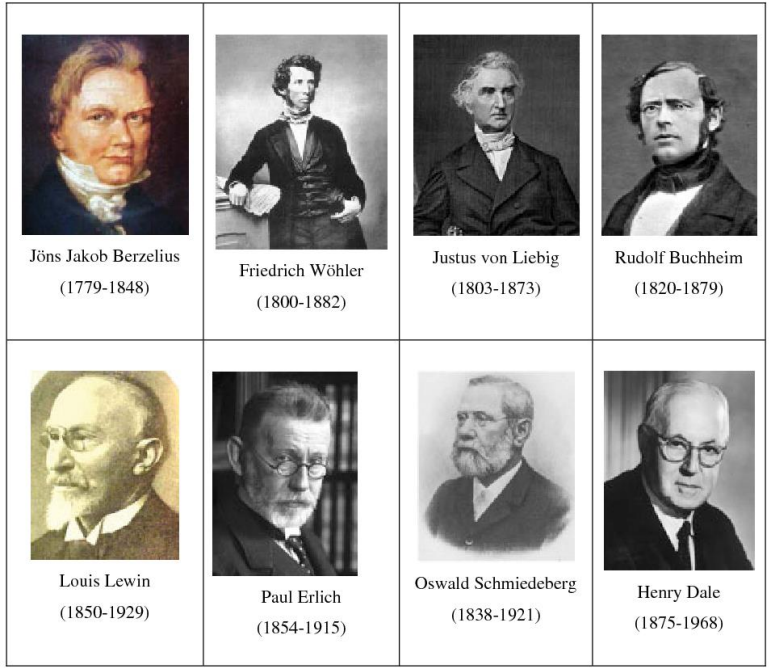
Medicinal chemistry is a chemistry-based discipline, involving aspects of biological, medical and pharmaceutical sciences. It is concerned with the invention, discovery, design, identification and preparation of biologically active compounds, the study of their metabolism, the interpretation of their mode of action at the molecular level and the construction of structure-activity relationships (**SARs**).



# History of medicinal chemistry

In the nineteenth century The isolation of a number of alkaloids including morphine (1805), quinine (1823) and atropine (1834) from crude medicinal plant were extracted.

In the late eighteenth and early nineteenth centuries, chemical experimentation led ultimately to its use in the discovery of new drugs.




Early drug discovery and the rise of pharmaceutical chemistry.

# History of medicinal chemistry

In 1853, Henry How conceived the idea that functional groups in natural products might be modified by chemical reagents. He heated morphine with methyl iodide, hoping to convert the alkaloid to codeine. He obtained, however, a new substance of the quaternary salt of morphine.

In 1898, the first commercially available semisynthetic morphine derivative (ethyl ether) was introduced as a cough sedative in preference to codeine or other opiates.

**Henry Mayo Newhall**
**1825 - 1882**

- Meanwhile, diacetylmorphine was introduced as a safer pain reliever than morphine. It quickly became popular throughout the world.

- During the 1840s, the first use of synthetic organic chemicals were introduced for anesthesia during a tooth removal, such as nitrous oxide, ether, and chloroform.

- In 1864, barbituric acid had been synthesized as a useful hypnotic.

In 1875, salicylic acid was introduced as a possible cure for typhoid fever. It was found to be an effective antipyretic

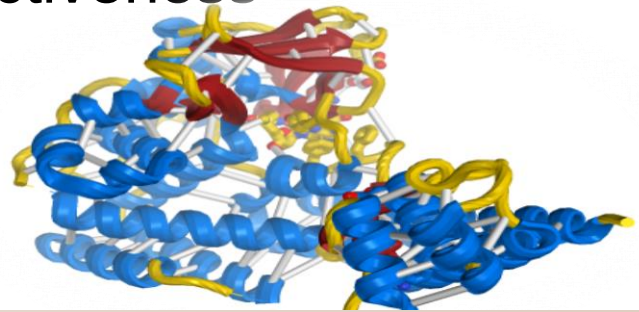
In 1899, Aspirin (Acetyl salicylic acid) was marketed as an antipyretic without the unpleasant side effects. This indicated that the chemical structures from natural products were changed into better drugs.

Finally Medicinal Chemistry began.

# What is Structure activity relationship SAR:

Is the relationship between the chemical structure, molecular arrangement and it’s biological activity.

Hence SAR is a very important concept to understand, in order to optimize drug biological effectiveness



# Important of structures activity relationship

1-Structure Activity Relationships (SAR) can be used to predict biological activity from molecular structure.

2-This powerful technology is used in drug discovery .

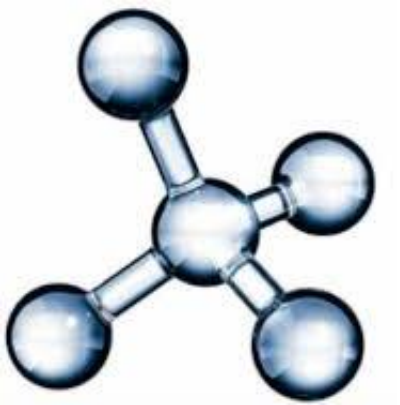
3. It is used to determine pharmacophore.

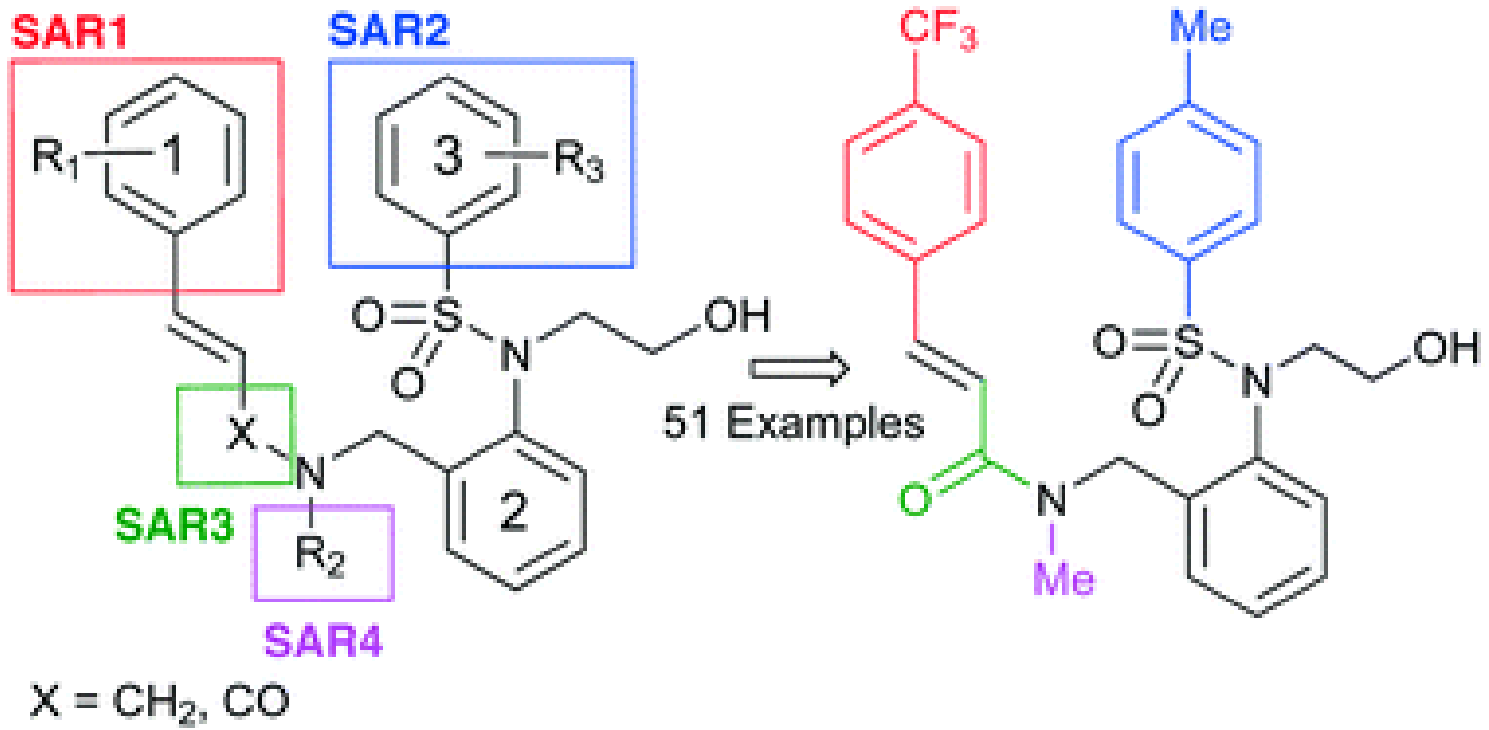
4.To determine some different activity from an existing drug.

5.To fewer unwanted side effects to know the changes in pharmacological properties by performing minor changes in the

6.SAR improve certain properties, including:

- solubility
- potency
- selectivity
- metabolic stability
- permeability
- pharmacokinetics
- tissue distribution
- in vivo efficacy




SAR1
SAR2
SAR3
SAR4
R1
1
3
R3
2
X
N
R2
O=S
O
N
OH
51 Examples
CF3
Me
O=S
O
N
OH
O
N
Me
X = CH2, CO

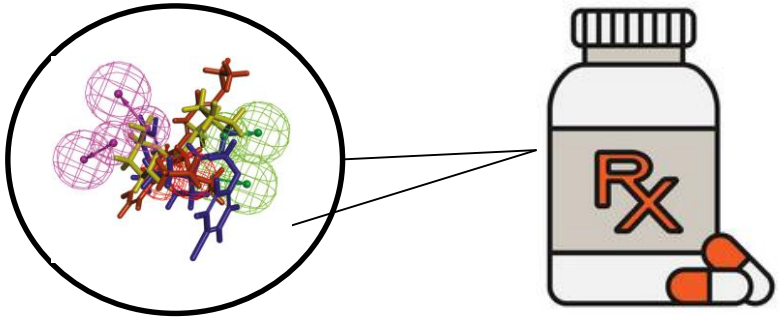
# Define QSAR:

Quantitative structure–activity relationships are related branches of computational modeling that attempt to predict the biological activity of unknown or understudied chemicals/pharmaceutical agents on the basis of chemical structural similarities with other.

The overall concept is that one can learn or predict like effects from such computer models in a timely and cost-effective manner without engaging in animal or wet laboratory experimental studies.

# Define Pharmacophore:

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



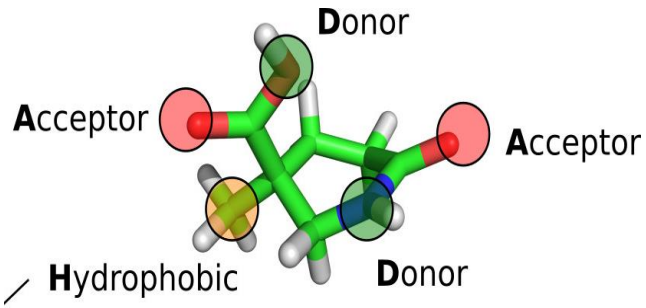
# Characterization:

(1) Location of the functional groups (e.g. proton donor/acceptor)

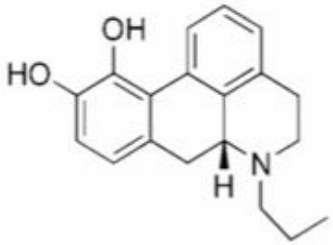
(2) Stabilization of the most **effec**tive **con**formation

(3) Lipin**ski's** rule of five:

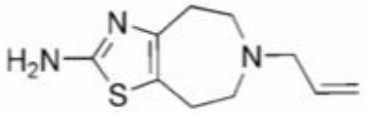
- The molecule has less than five proton-donor
- The molecular weight is smaller than **500 Dalton**
- log P smaller than **5**
- the molecule has less acceptors than **10**
- the molecule should use biological transporters.



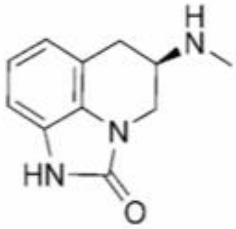
# Examples: **Dopamine receptor targeting drugs**



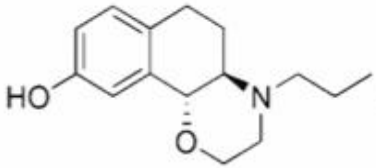

(*R*)-NPA (**1**)



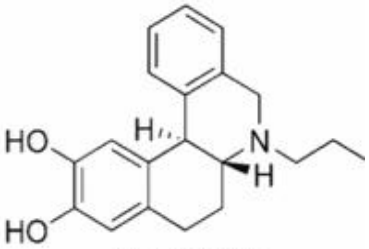

talipexole (**2**)



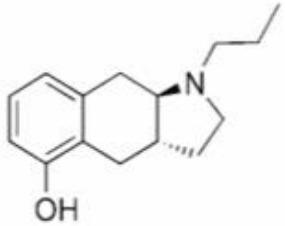

sumanirole (**3a**)



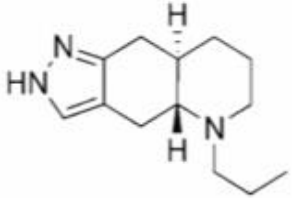

(*R*,*R*)-PHNO (**4a**)



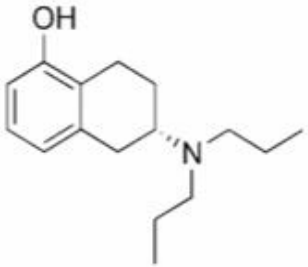

*n*Pr-DHX (**5**)



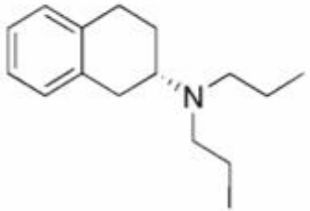

(–)-(3*S*,9*R*)-**6a**



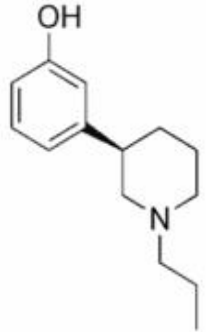

quinpirole (**7**)




(*S*)-5-OH-DPAT (**8a**)



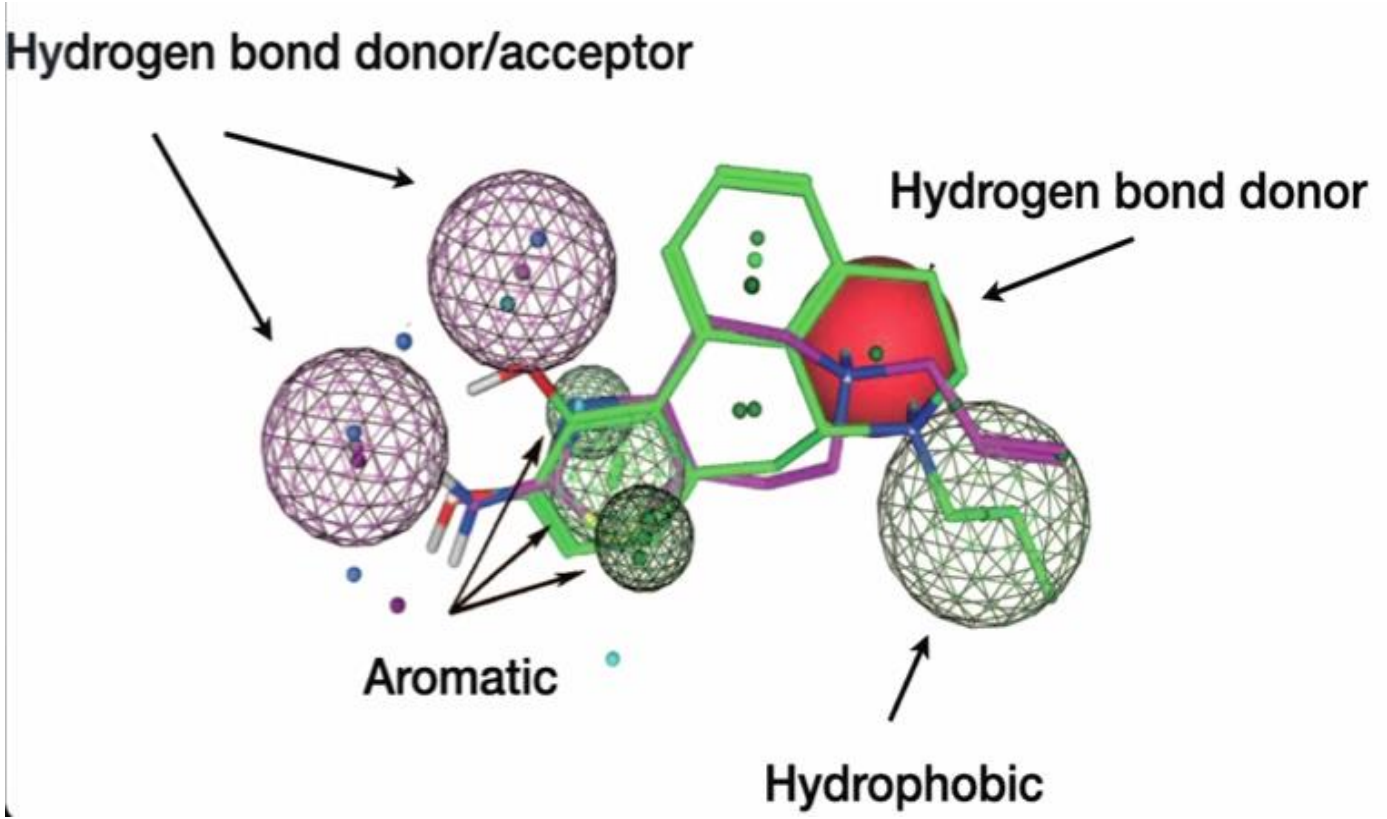

(*S*)-DPAT (**9**)




(*R*)-3-PPP (**10a**)

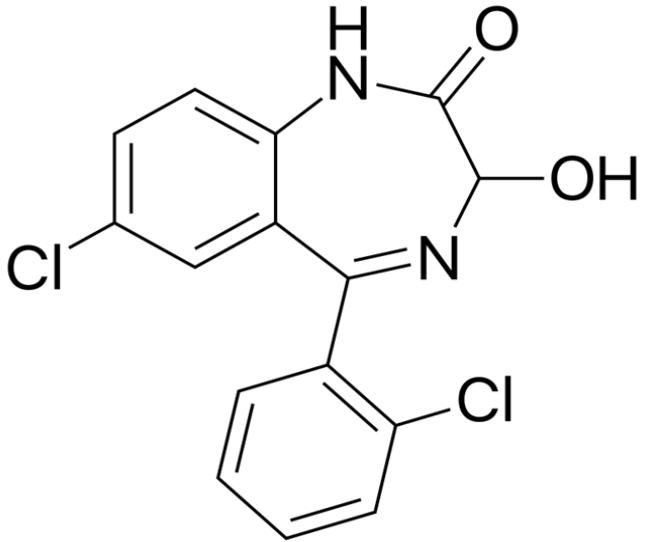
**Agonists**

# Pharmacophore of Agonists



**It is used by people who are suffering from:**

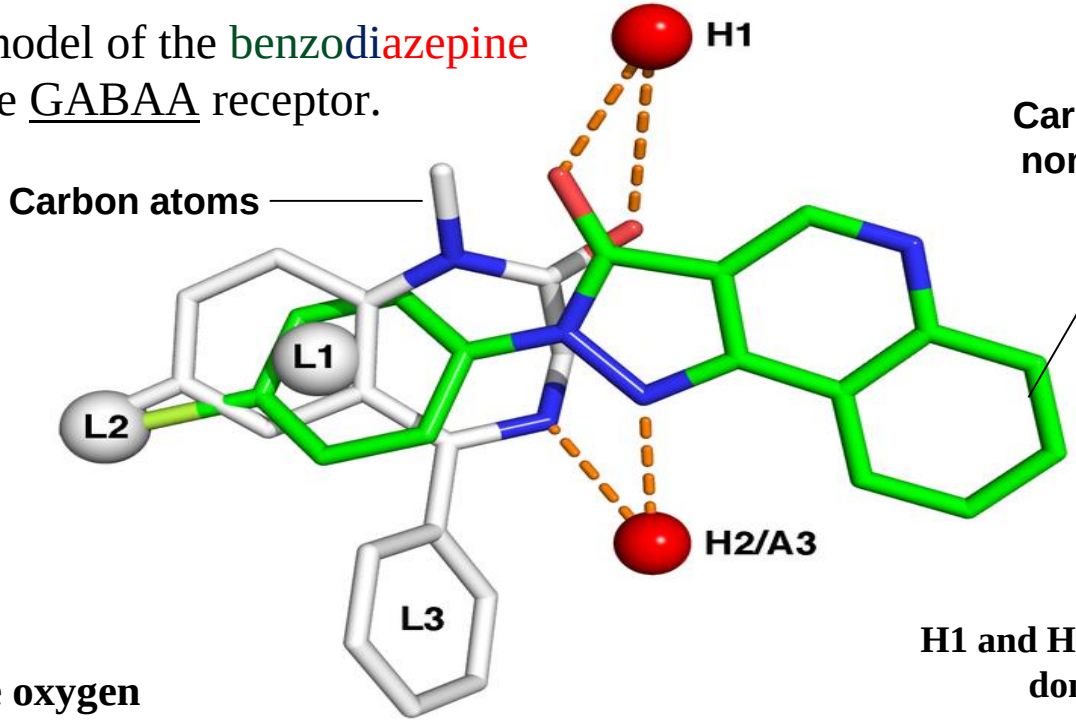
- ❑ Anxiety disorder
- ❑ Sleep problems




**Lorazepam**

# Pharmacophore of Lorazepam

- Pharmacophore model of the benzodiazepine binding site on the GABAA receptor.




**L1, L2, and L3 lipophilic binding sites.**

**Red and blue they are oxygen and nitrogen atoms.**

**H1 and H2/A3 are hydrogen bond donor and accepting**

# Summary:

**Medicinal chemistry** is a chemistry of biological, medical and pharmaceutical sciences.

**SAR** is association between a chemical substructure and the potential of a chemical containing substructure.

**Pharmacophore** is the ensemble of steric and electronic features.

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