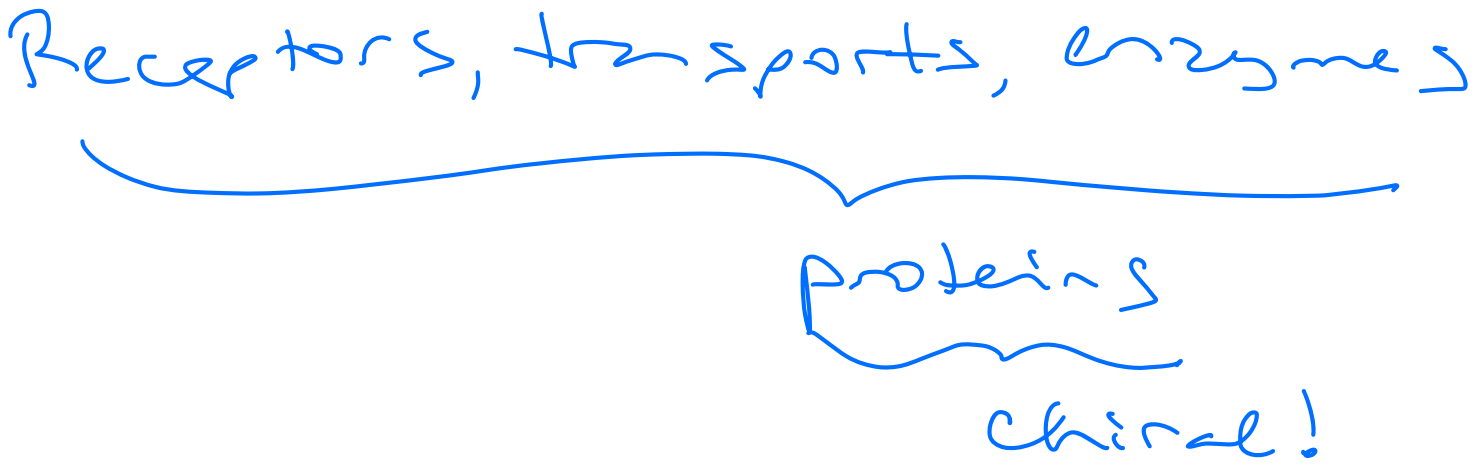


Receptors

Stereochemistry

Stereochemistry

Enantiomers

non superimposable mirror images

R + S

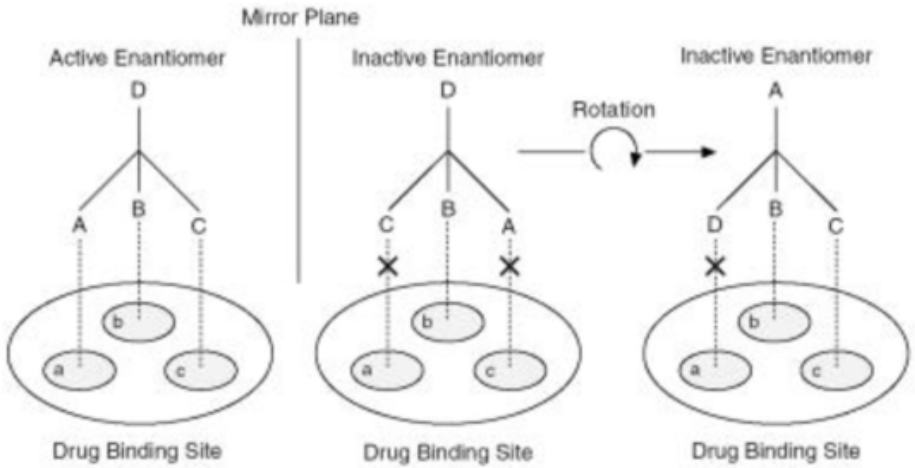
D + L

only physical property that is different is light rotation

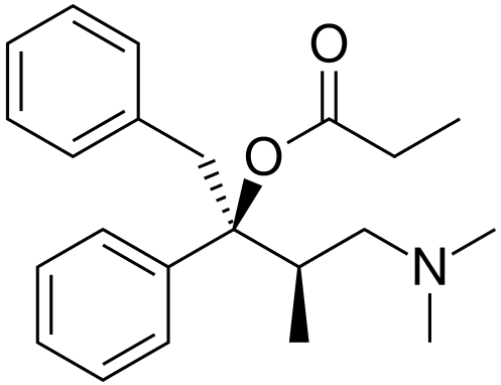
Diastereomers

stereoisomers that are not mirror images

* have different physical properties + can be separated more easily



[a]The active enantiomer has a 3-dimensional structure that allows drug domain A to interact with binding site domain a, B to interact with b, and C to interact with c. In contrast, the inactive enantiomer cannot be aligned to bind the same 3 sites simultaneously. The difference in 3-dimensional structure allows the active enantiomer to bind and have a biological effect, whereas the inactive enantiomer cannot.

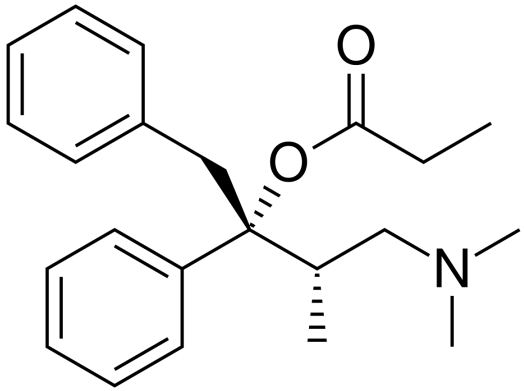


Dextropropoxyphene

2R, 3S

Darvon

analgesic



Levropropoxyphene

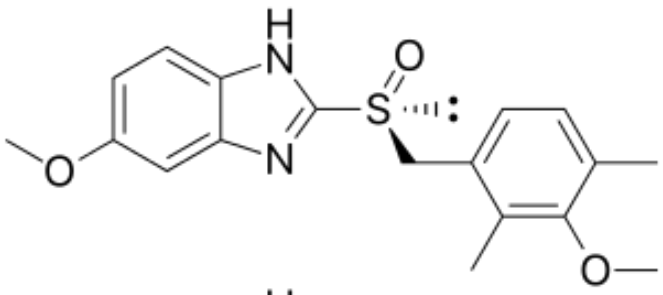
2S, 3R

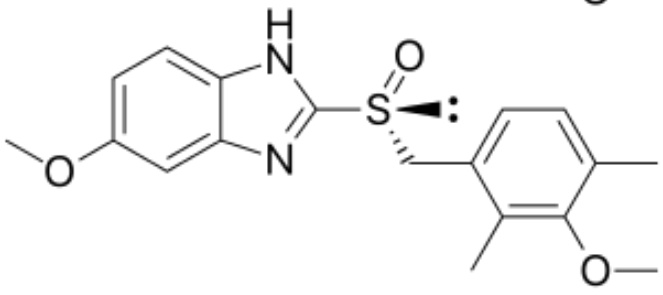
Novrad

antitussive

Drug synthesis often produces a racemic mixture

(S)-(−)-omeprazole (esomeprazole)



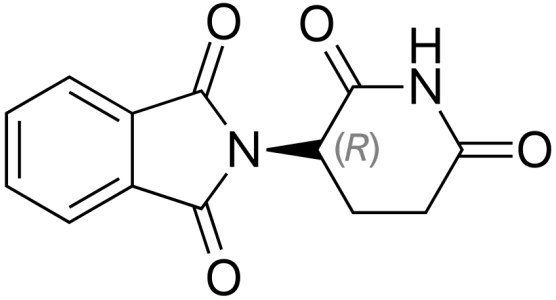


(R)-(+)-omeprazole

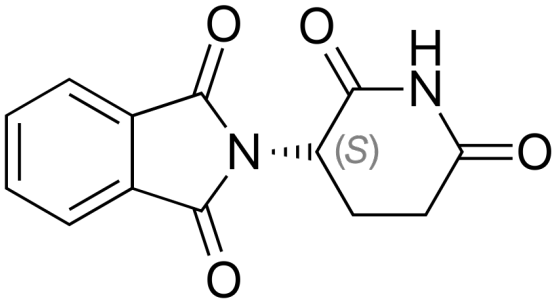
Omeprazole (prilosec) = mixture of both

the S version is sold as nexium

Thalidomide – racemizes in solution

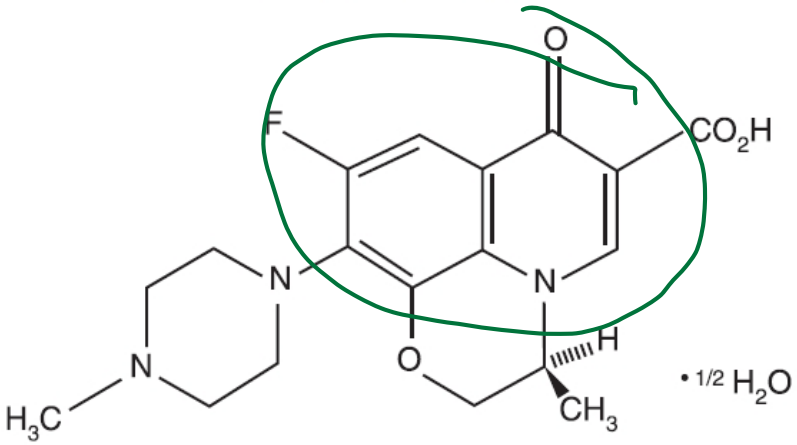


R- is good for nausea



S- teratogen → causes malformation of embryos

Structural formula



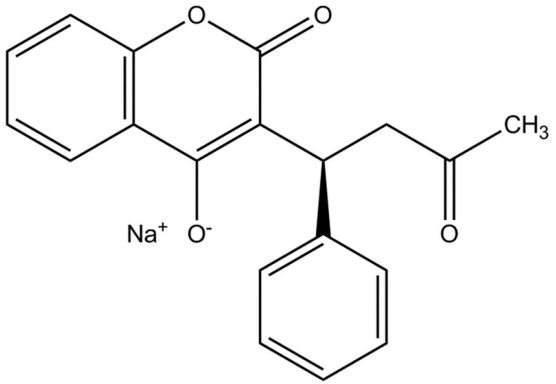
levofloxacin hemihydrate

$C_{18}H_{20}FN_3O_4 \cdot 1/2\ H_2O$ Mol Wt 370.38

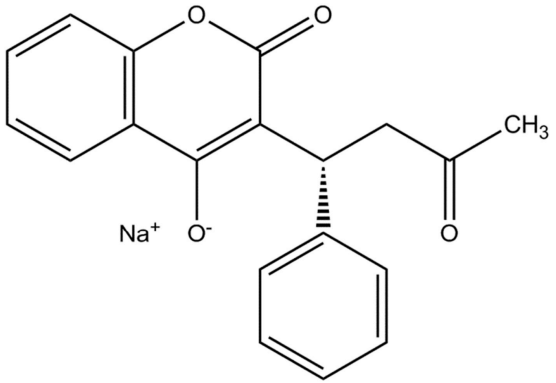
ofloxacin
– racemic mixture

S(-) levofloxacin

more active
enantiomer



R-warfarin sodium



S-warfarin sodium

S is 3-4x more active than R

different activities

different metabolisms

Endismic ratio = 3 to 4

how much more active one is than the other

Eutomer – has higher affinity or activity

Distomer – has lower

Eudismic Index = $\log\left(\frac{K_D \text{ Dist}}{K_D \text{ Eut}}\right)$

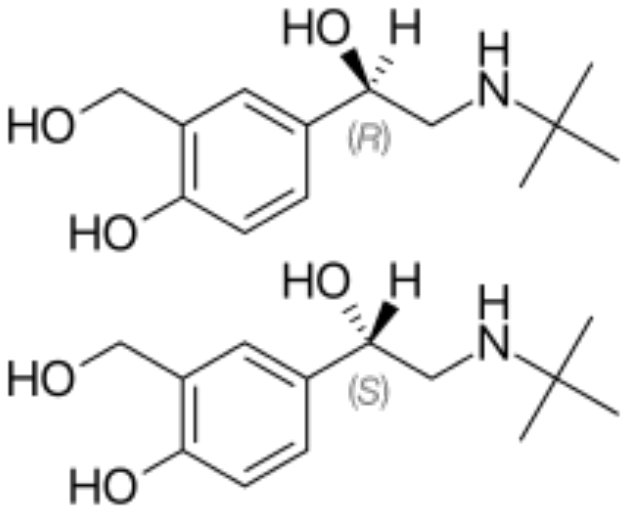
Eudismic Ratio

$= \frac{\text{Act Eut}}{\text{Act Dist}}$

$A \propto \frac{1}{C}$

$= \frac{ED_{50} \text{ Dist}}{ED_{50} \text{ Eut}}$

Sometimes 1 is an agonist & 1 an antagonist



← R-albuterol bronchodilator

← S is antagonist

Comments on binding of ligands and drugs to receptors: