



# Naravne spojine morskega izvora kot vir in navdih za razvoj novih zdravil

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Fakulteta za farmacijo









- kemijski spodad za preživetje









- zelo kompleksne kemijske spojine









- le redko lastnosti učinkovin

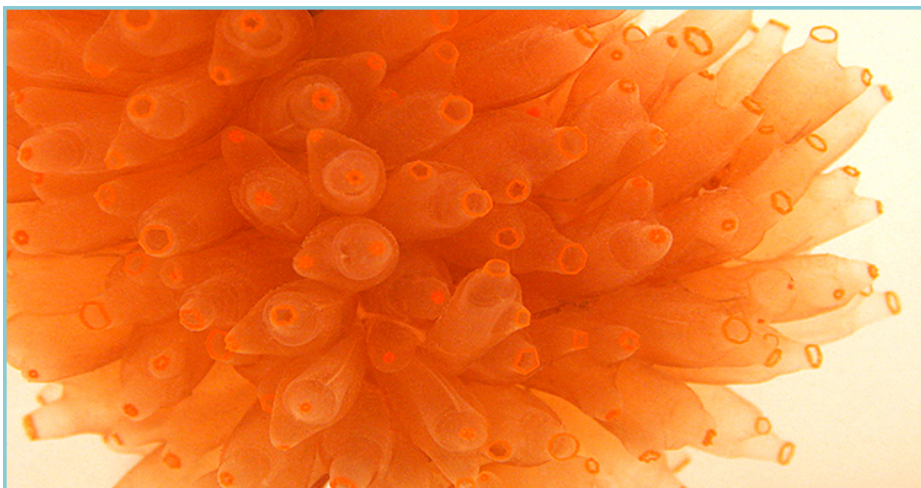




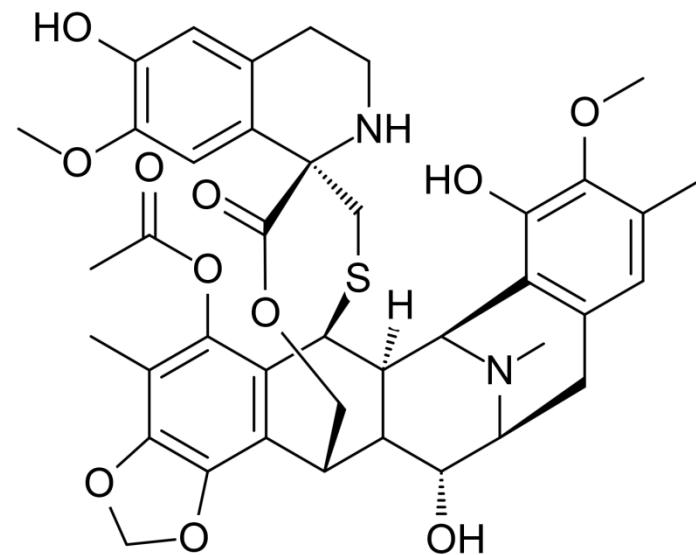




# Trabektedin (Yondelis®)



*Ecteinascidia turbinata*



- rak jajčnikov
- rak mehkih tkiv

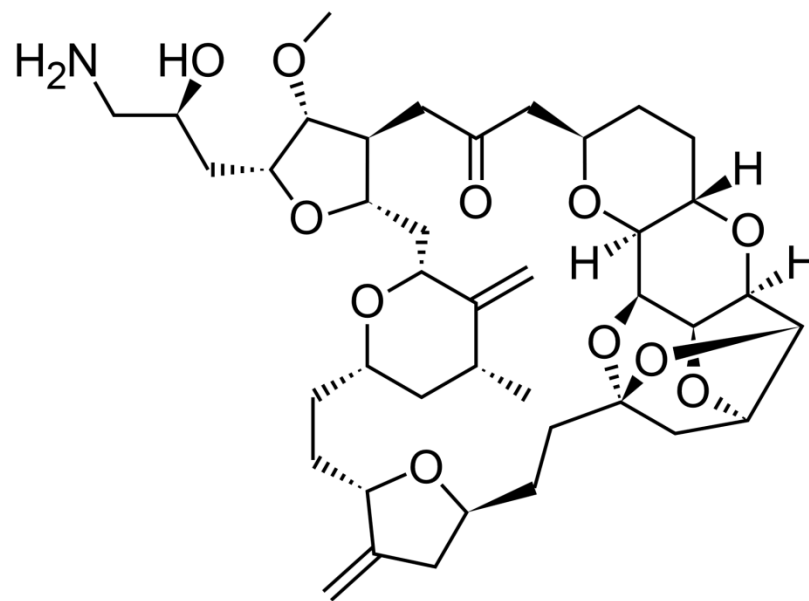




# Eribulin (Halaven®)



*Halichondria okadai*



- metastazirajoči rak dojke

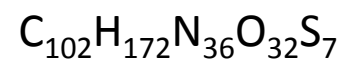
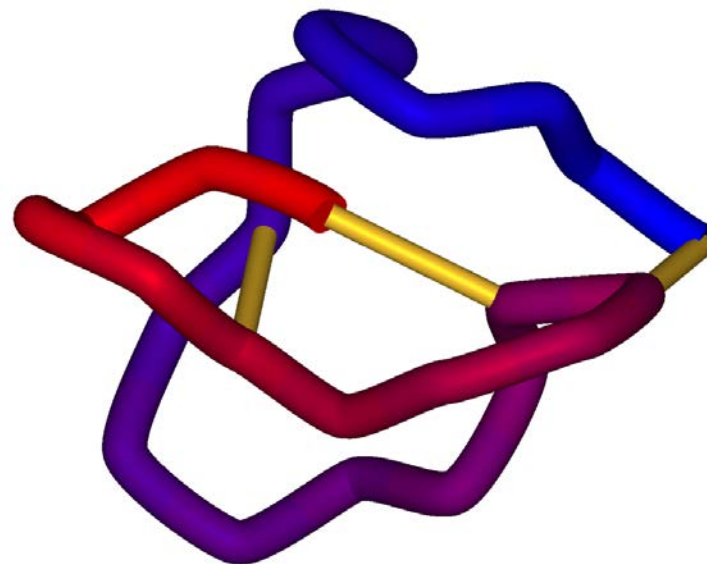




# Zikonotid (Prialt®)



*Conus magus*



- huda kronična bolečina



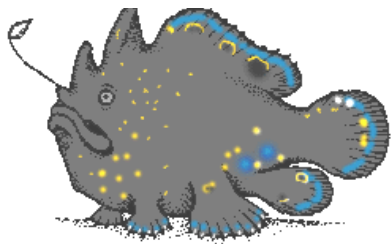
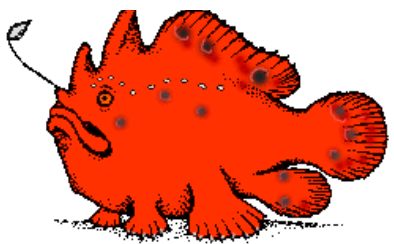


# Mimikrija v naravi





# ... tudi v morju



*Antennarius nummifer*





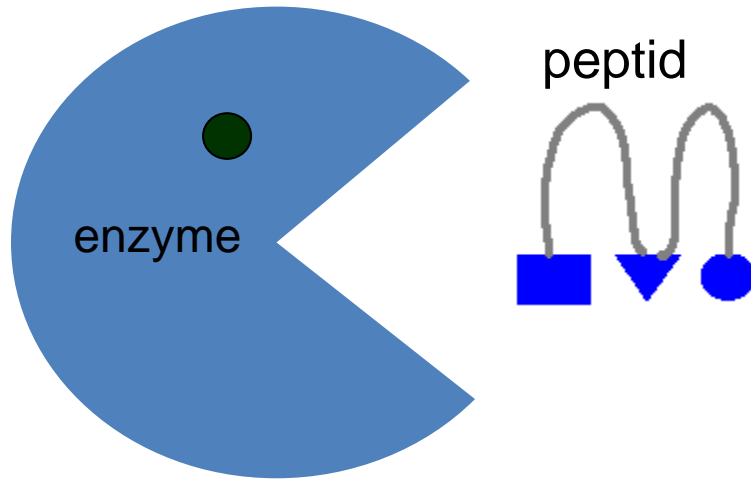
# Peptidi in peptidomimetiki

peptid

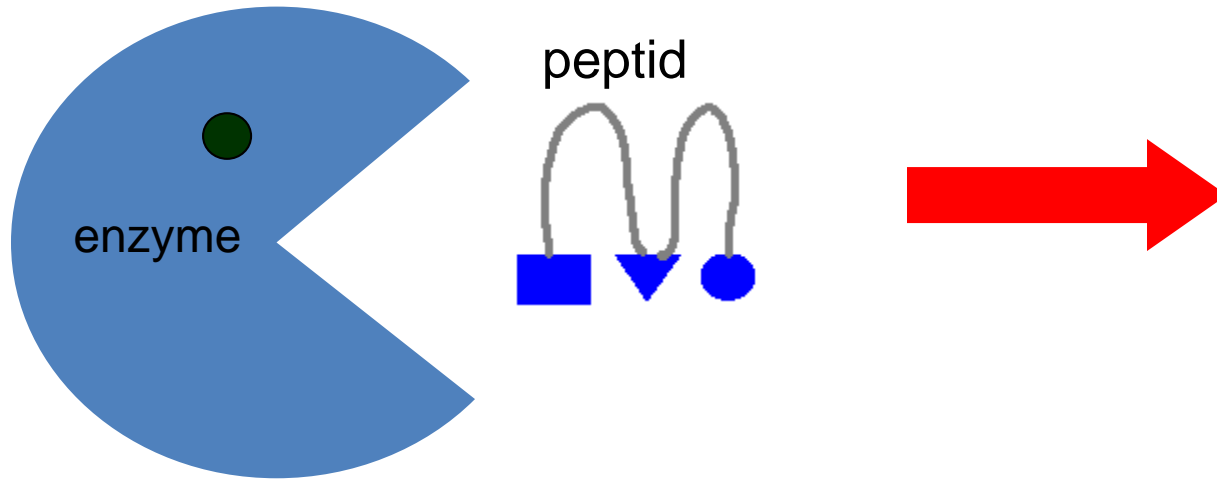




# Peptidi in peptidomimetiki

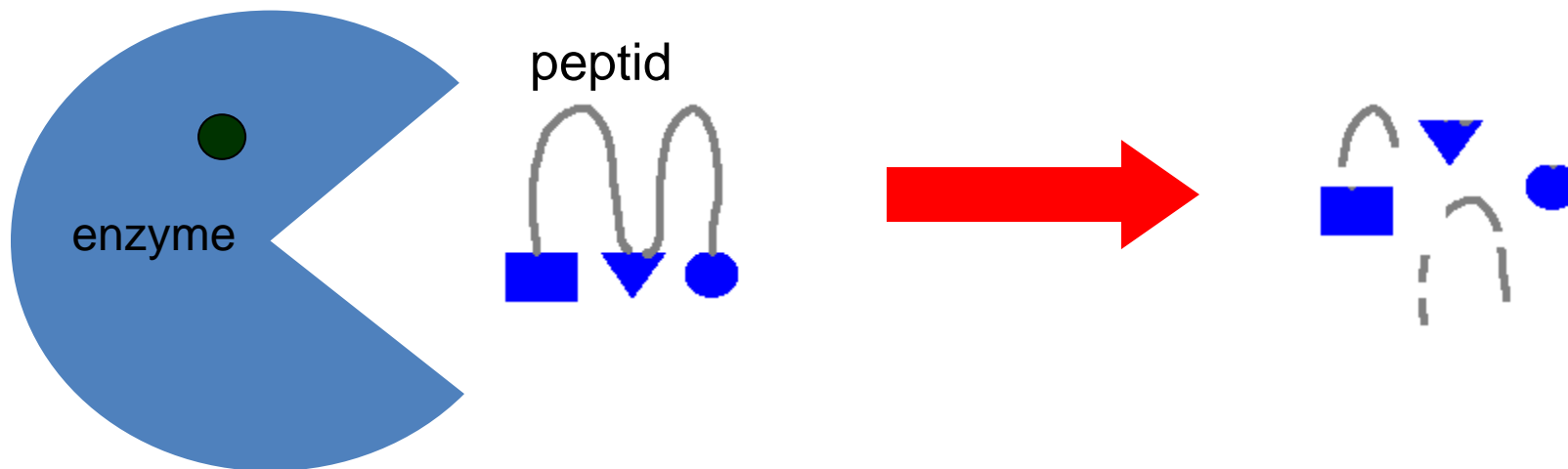


# Peptidi in peptidomimetiki

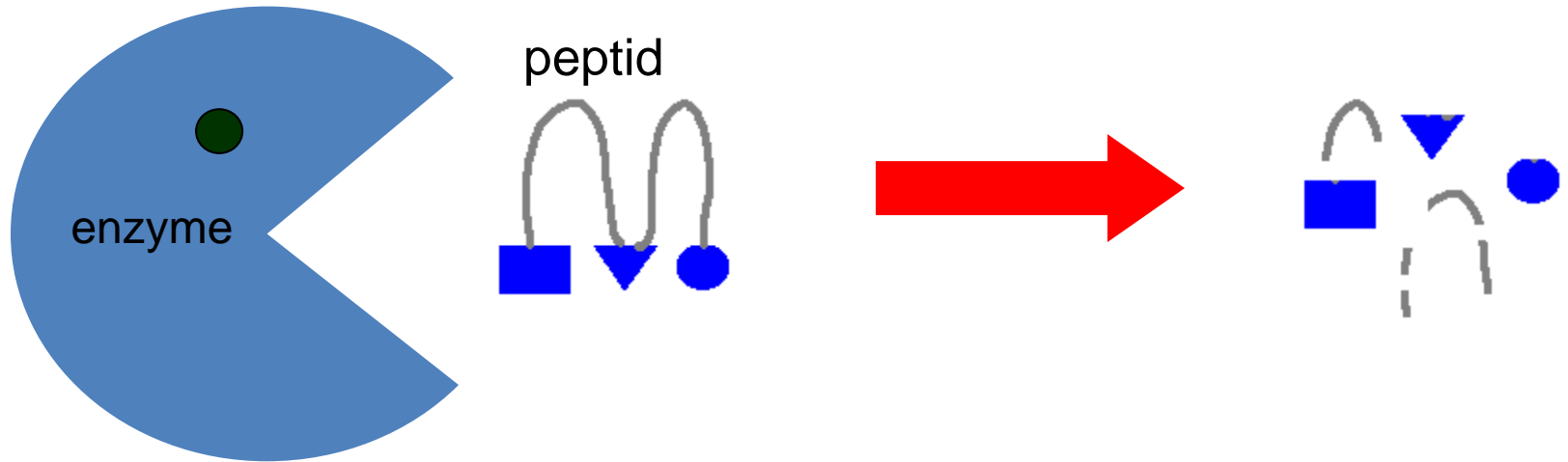




# Peptidi in peptidomimetiki

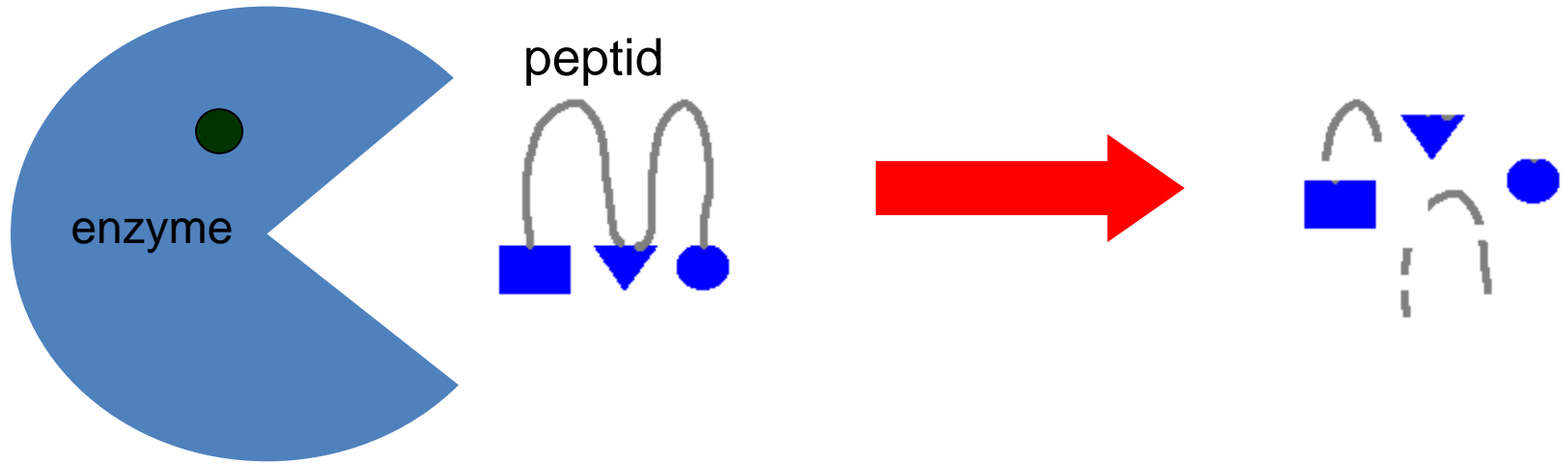


# Peptidi in peptidomimetiki





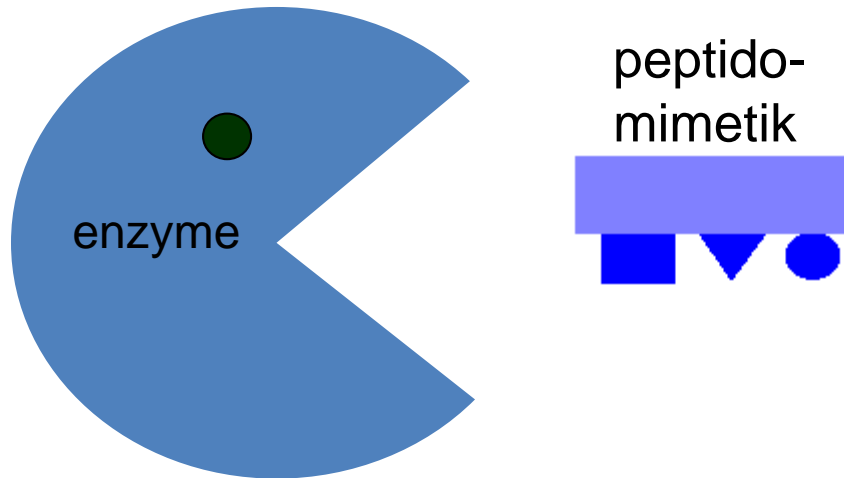
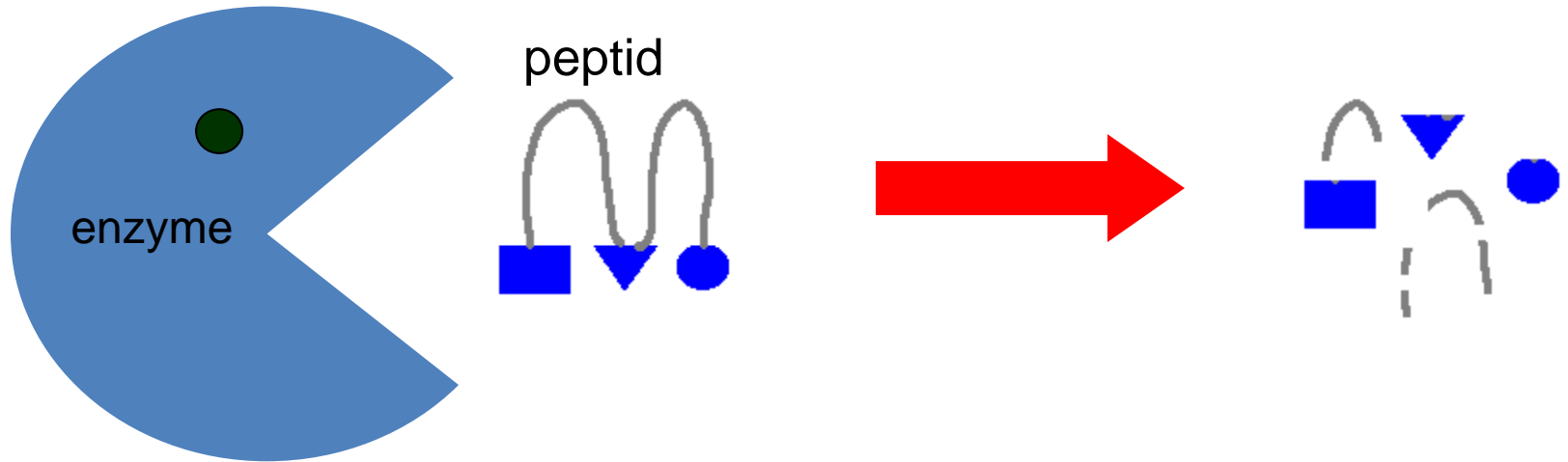
# Peptidi in peptidomimetiki



peptido-  
mimetik

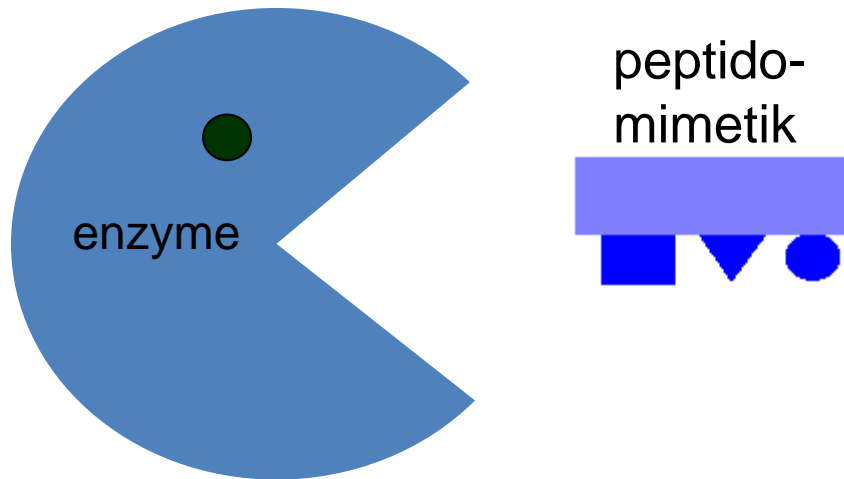
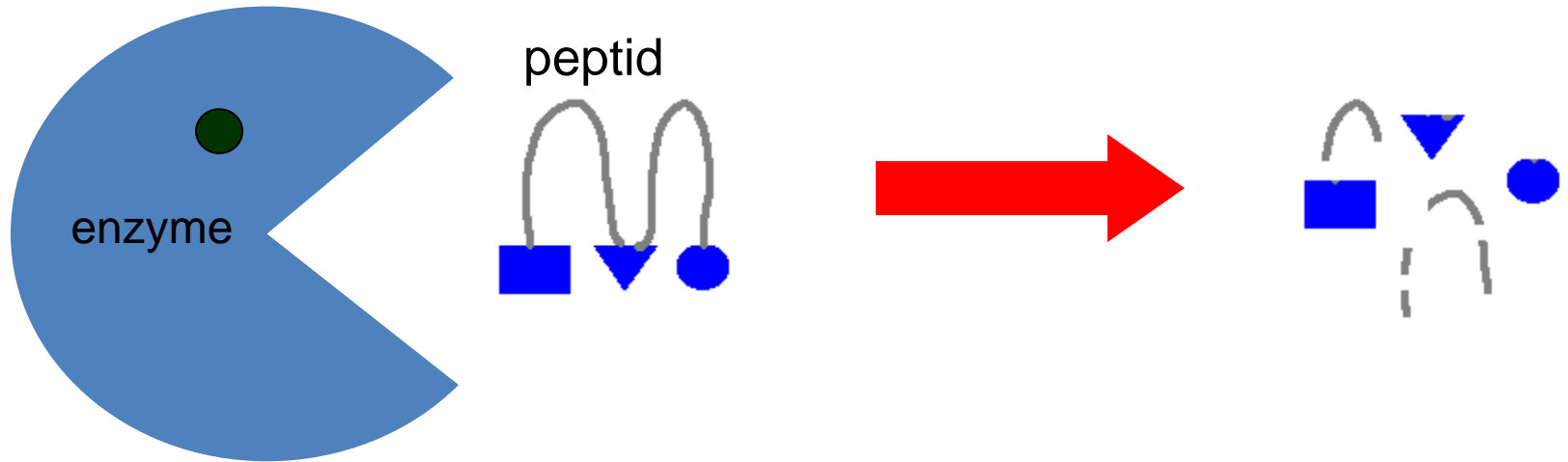


# Peptidi in peptidomimetiki





# Peptidi in peptidomimetiki



V želodcu se ne razgradi !!!

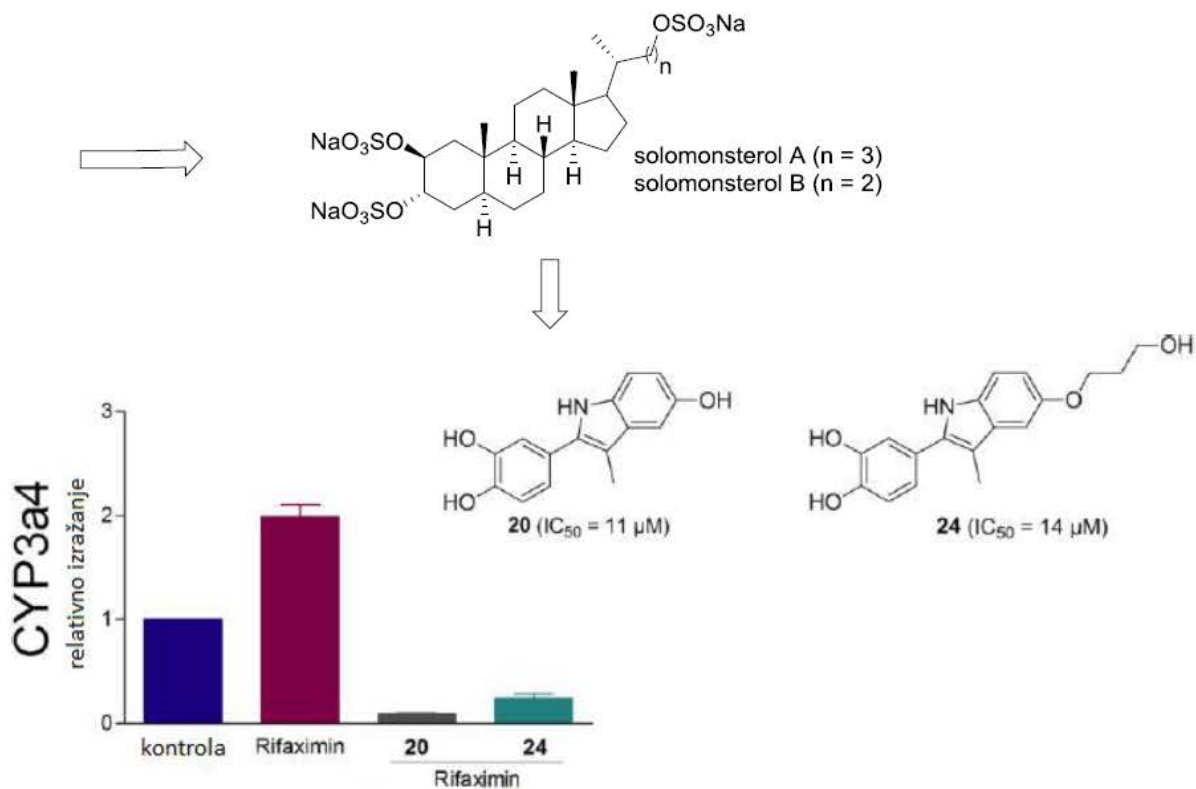
Zdravilo lahko vzamemo skozi usta



# Antagonisti pregnanskega X receptorja (PXR)

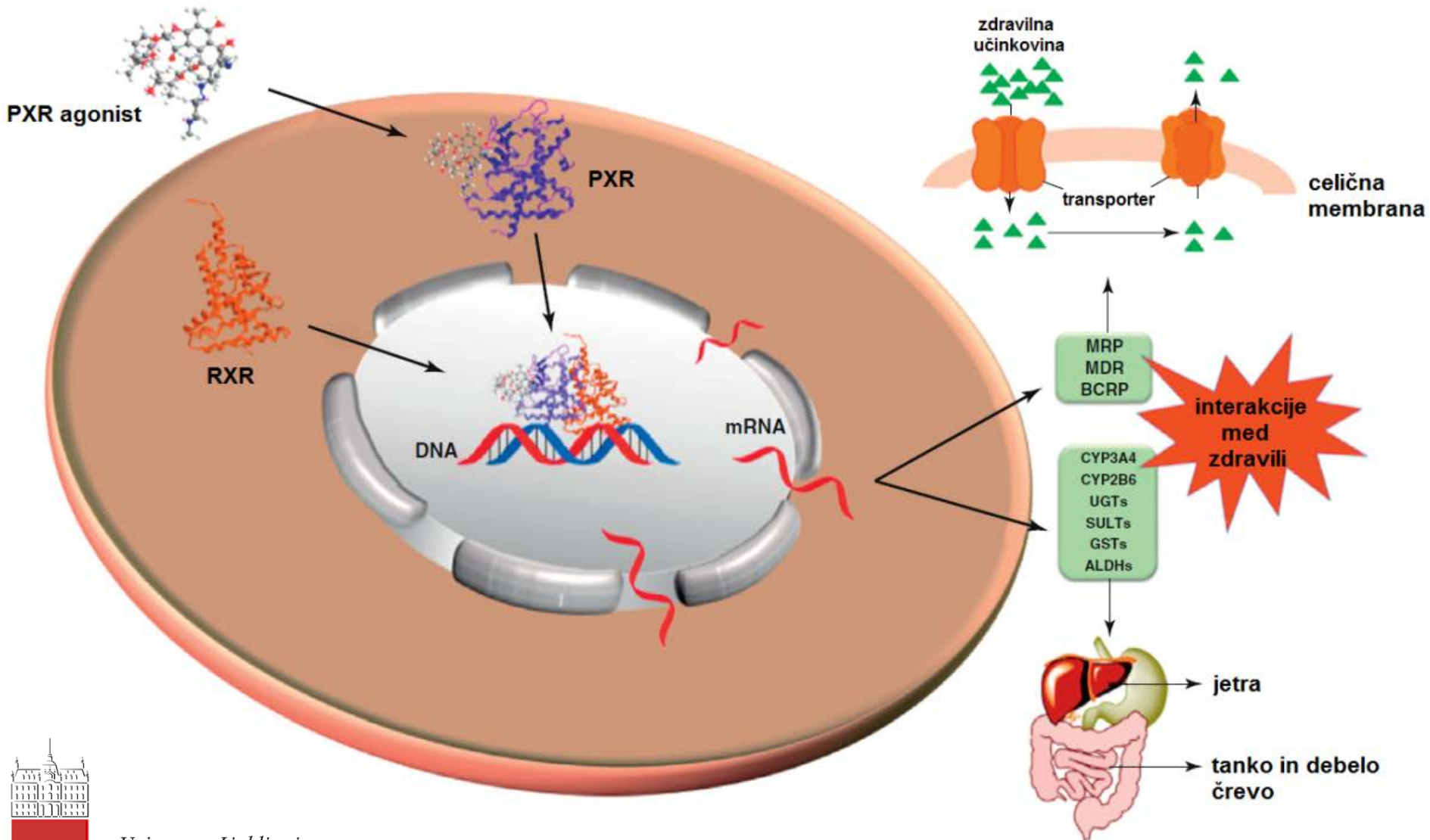


*Theonella swinhoei*





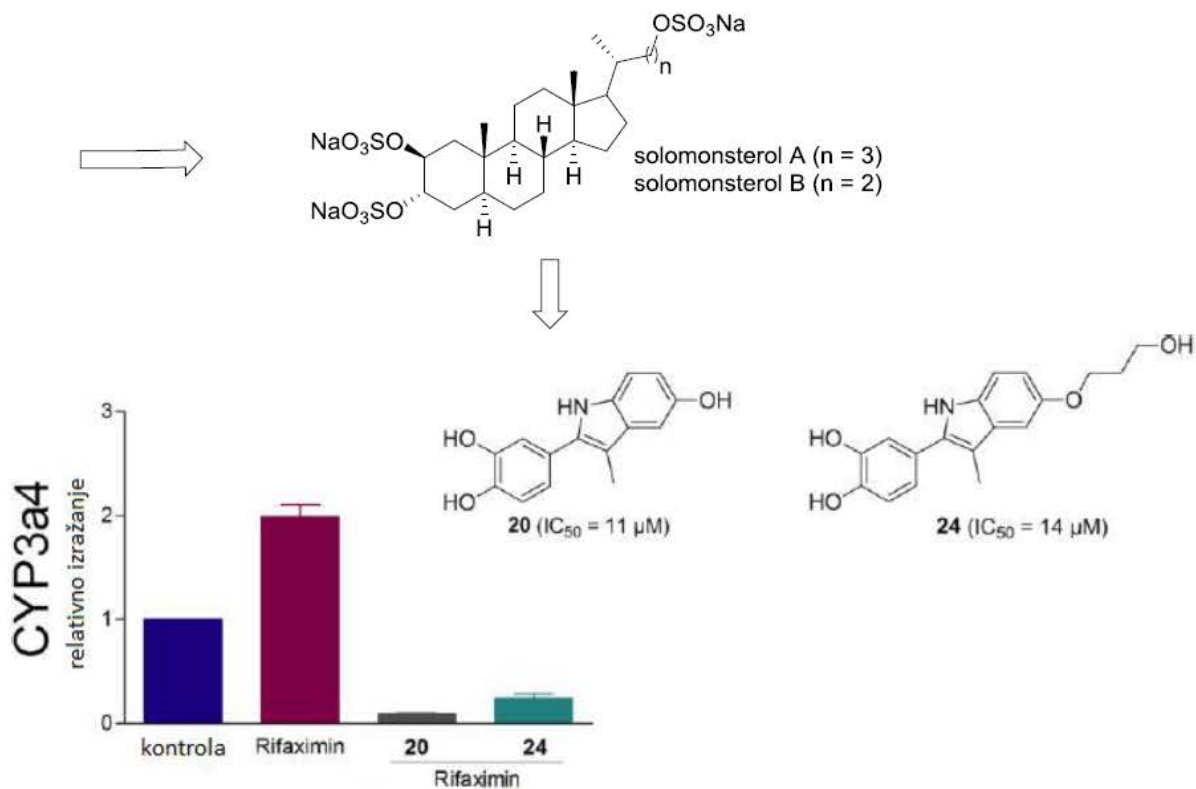
# Pregnanski X receptor (PXR)



# Antagonisti pregnanskega X receptorja (PXR)

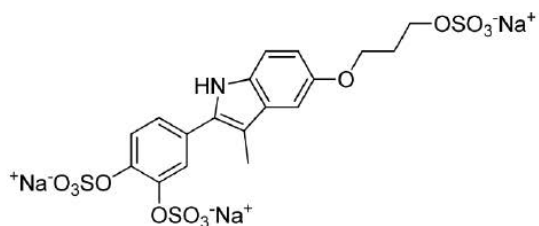


*Theonella swinhoei*

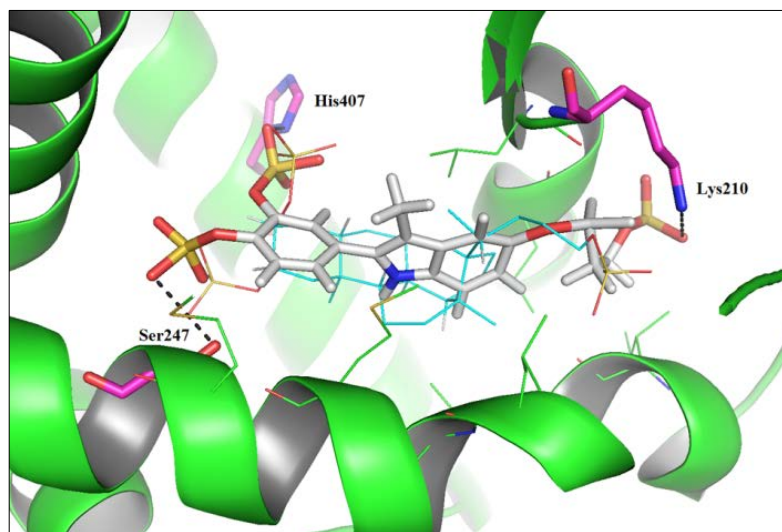
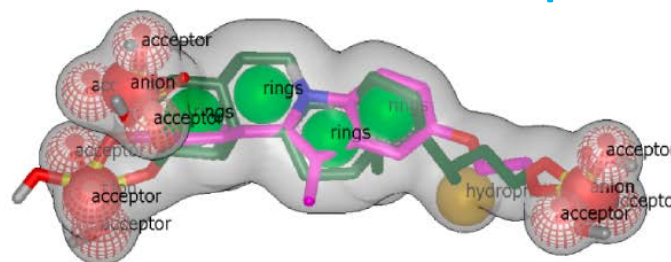
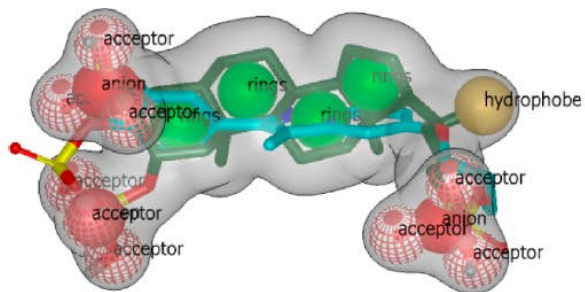




# ...ob pomoči različnih orodij za načrtovanje



podobnost

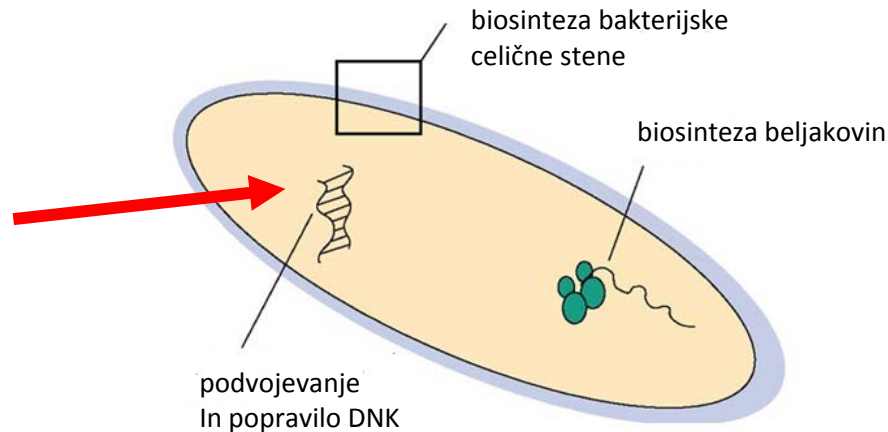


umeščanje  
(sidranje)



# Novi zaviralci bakterijske giraze B

Zaviralci  
DNA giraze B

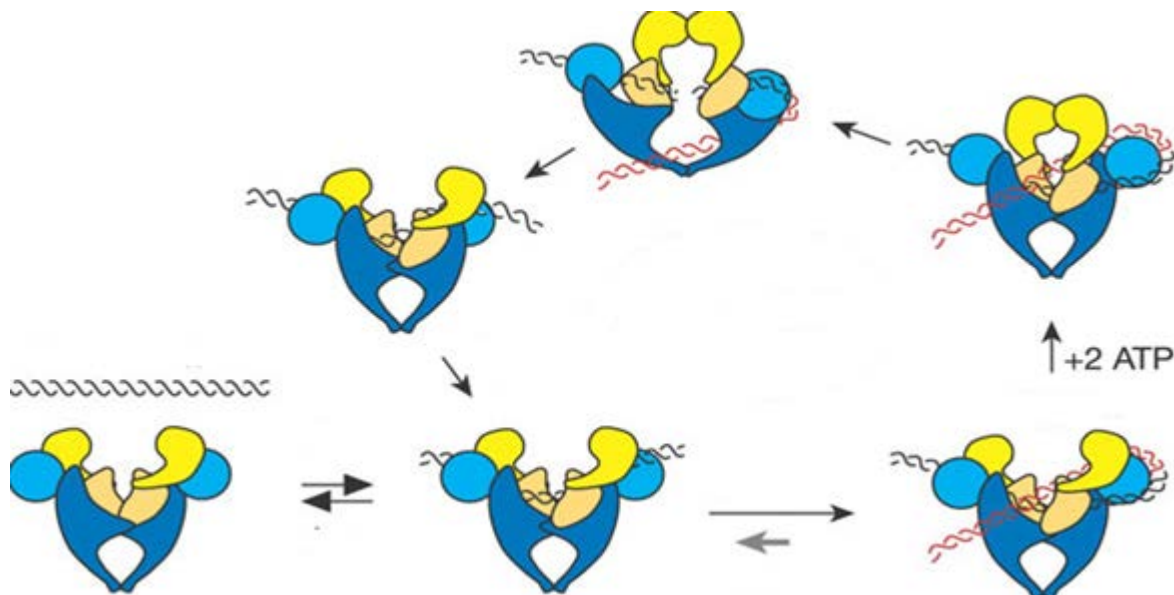


**Giraza A**

Cepi DNK

**Giraza B**

veže ATP (energija)

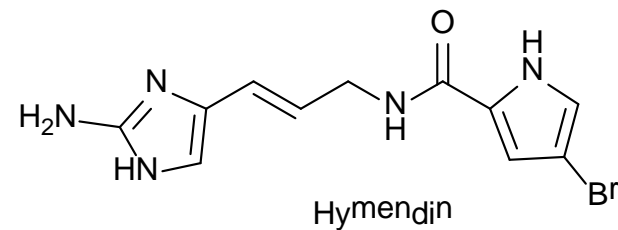
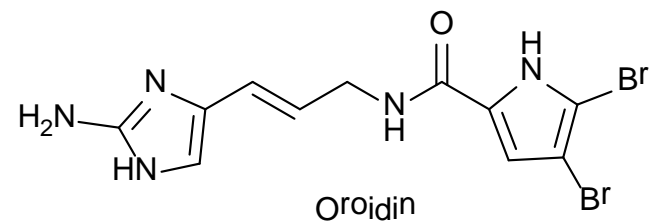
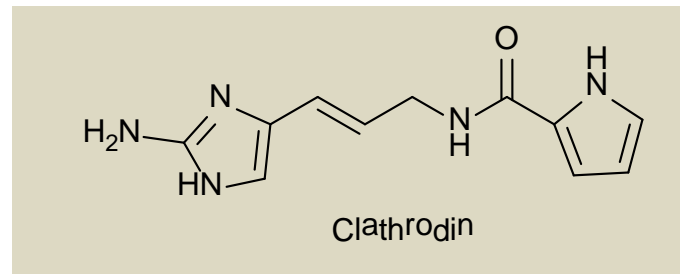




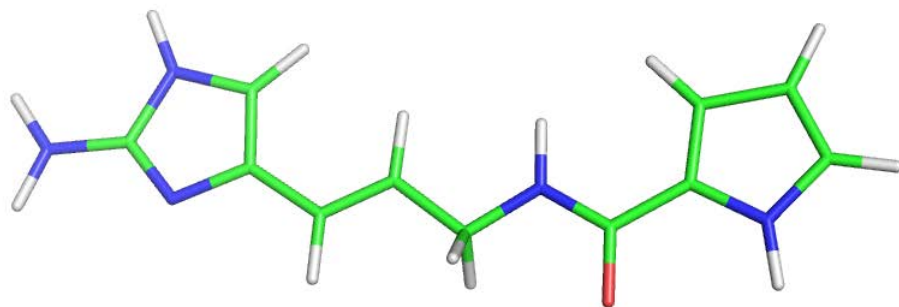
# Izvor ideje - molekula oroidina



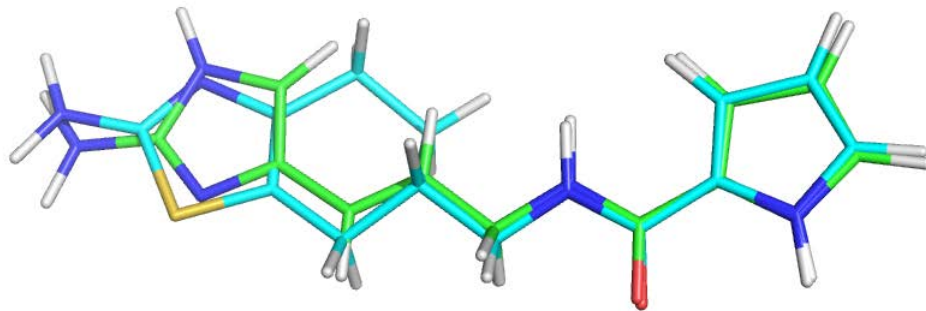
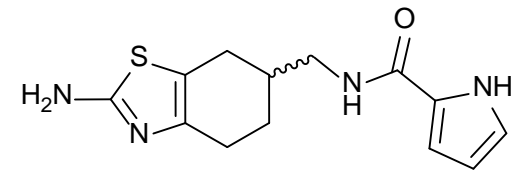
*Agelas clathrodes*



# Izvor ideje - molekula oroidina

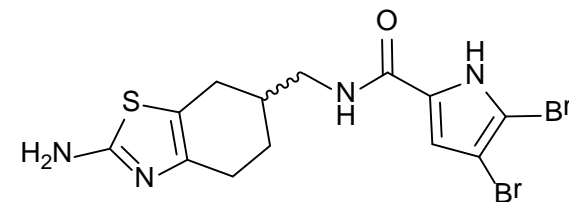
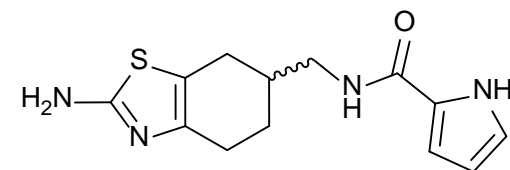
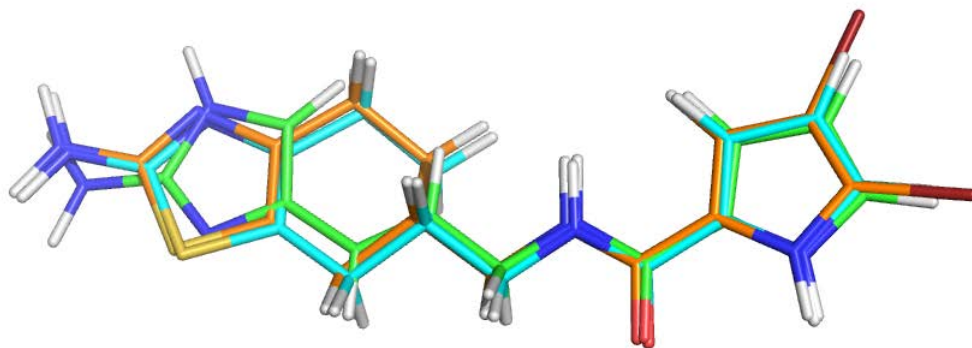


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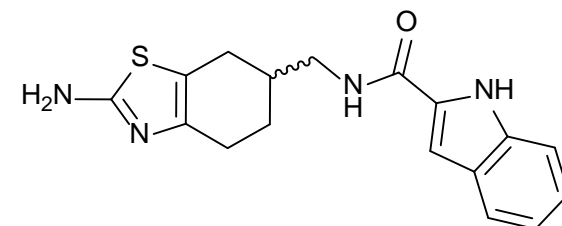
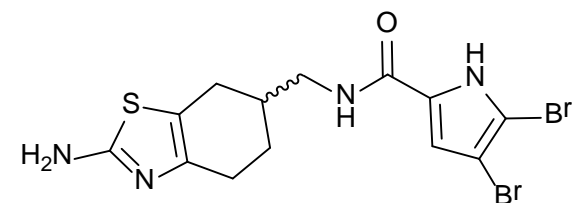
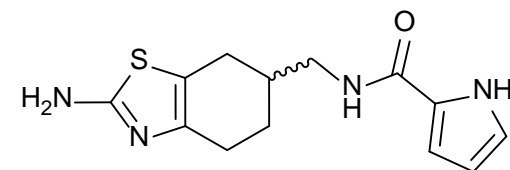
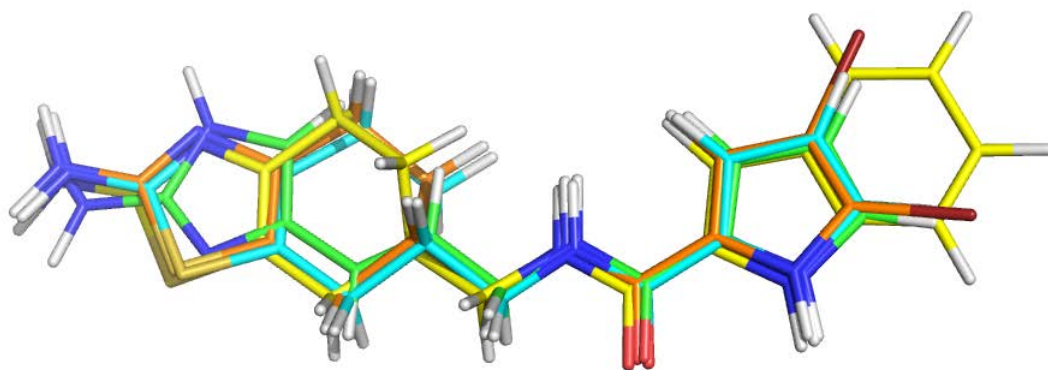




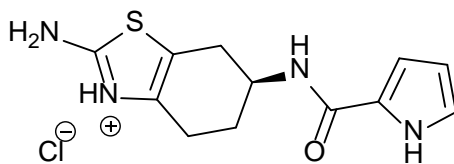
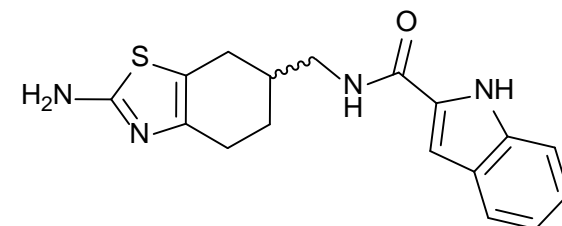
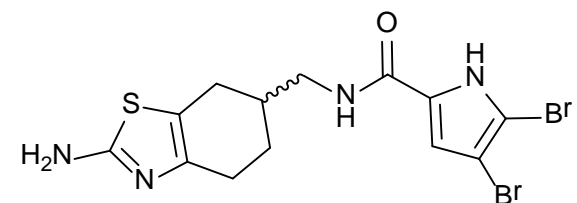
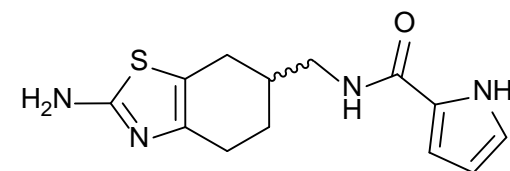
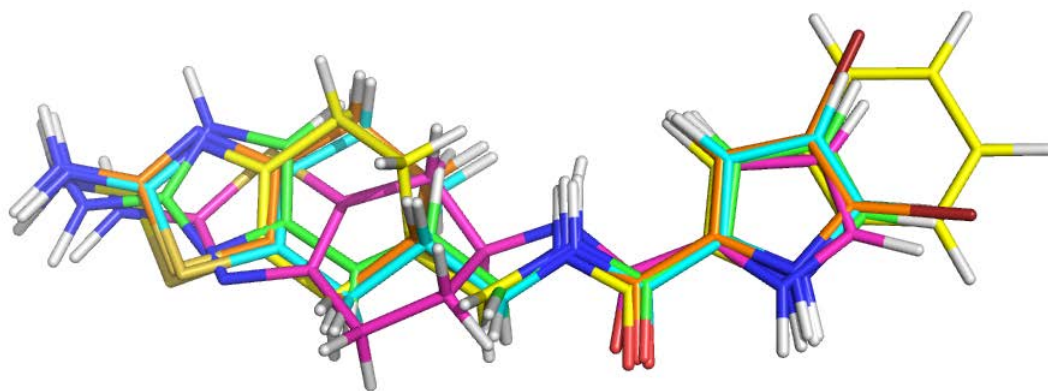
# Izvor ideje - molekula oroidina



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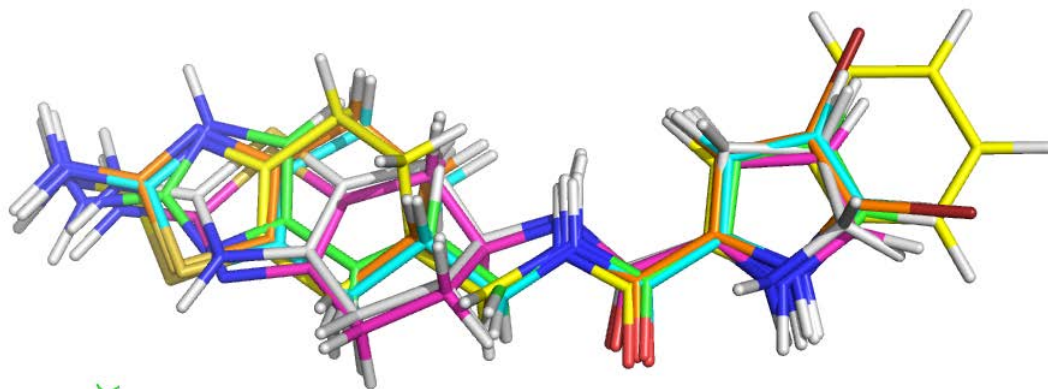


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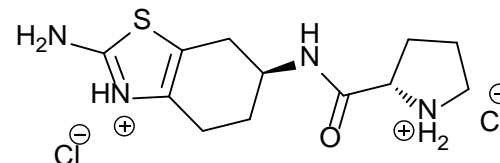
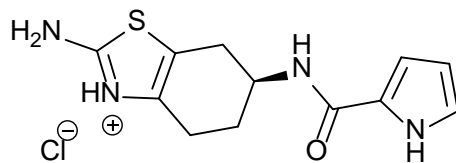
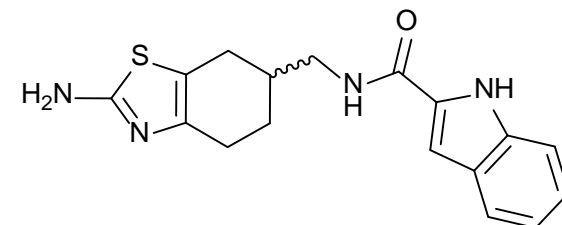
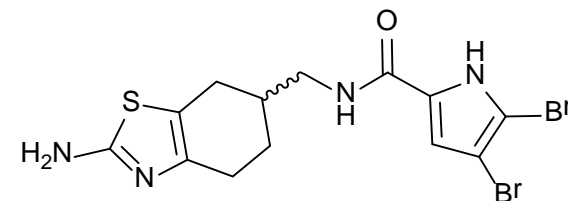
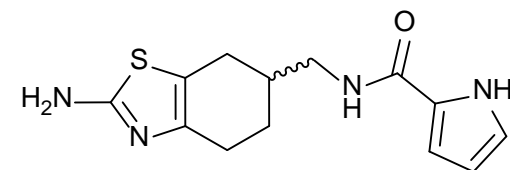


# Izvor ideje - molekula oroidina



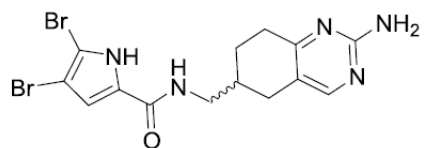
X

X



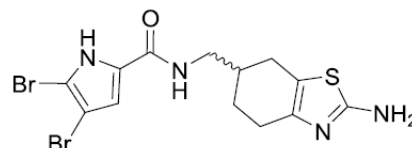
# Prvi zadetki, nato optimizacija

knjižnica 120 analogov oroidina  $\xrightarrow{\text{sidranje}}$  20 najboljših spojin



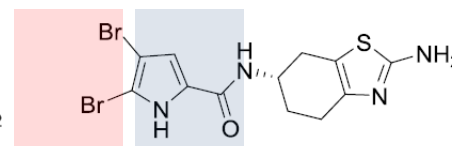
1

*E. coli* GyrB IC<sub>50</sub> = 167 μM



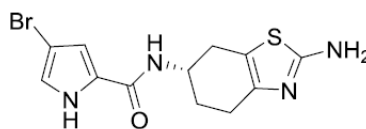
2

*E. coli* GyrB IC<sub>50</sub> = 125 μM



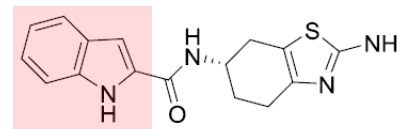
3

*E. coli* GyrB IC<sub>50</sub> = 11.7 μM



4

*E. coli* GyrB IC<sub>50</sub> = 520 μM



5

*E. coli* GyrB IC<sub>50</sub> = 21.0 μM

sidranje & načrtovanje

sinteza

testiranje



# Kristalna struktura

Compound	IC <sub>50</sub>
UL-KMG-9	<b>83 nM</b>

