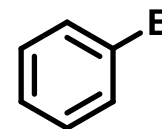
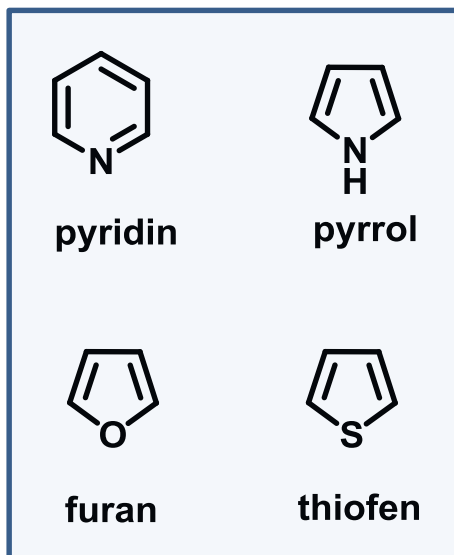
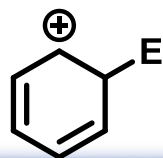


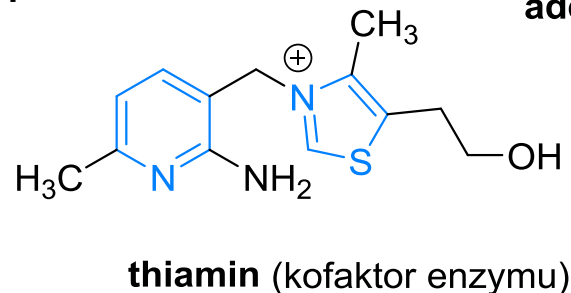
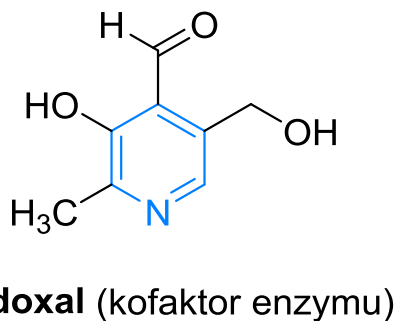
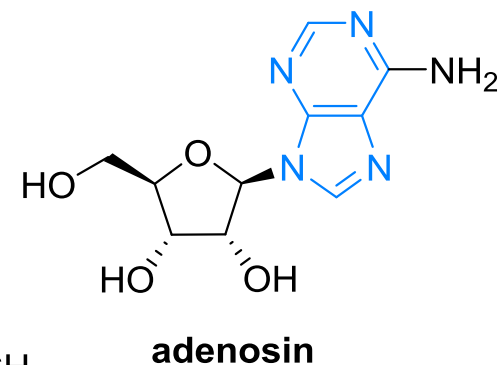
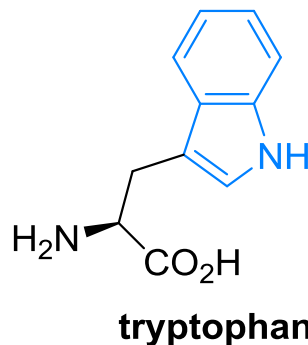
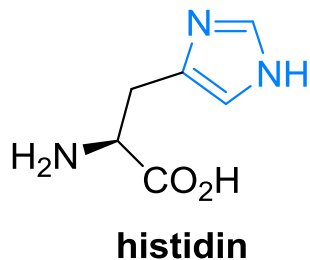


7. Areny

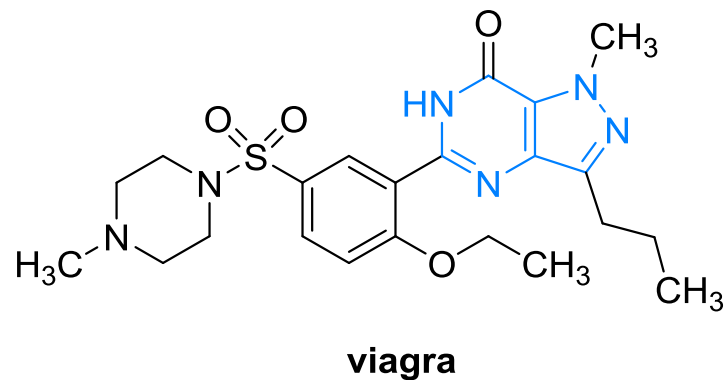
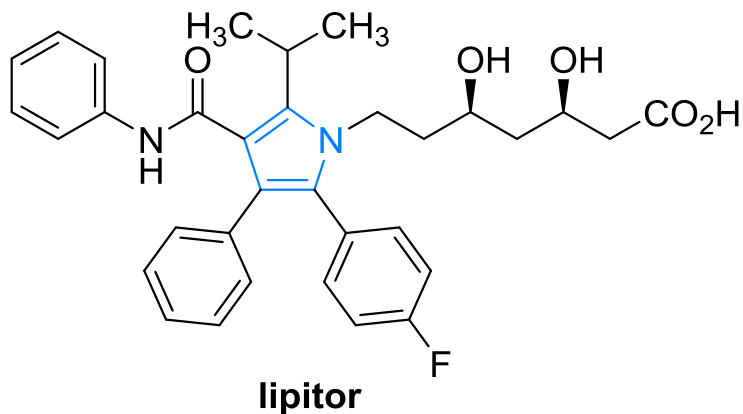




- důležité strukturní a funkční elementy biomolekul (enzymy, DNA, RNA ...)

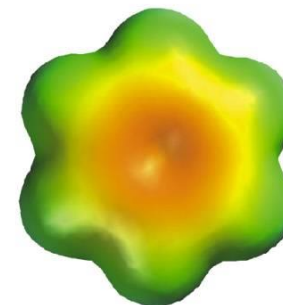
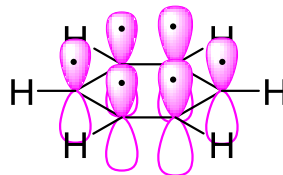
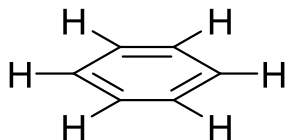
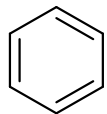


- běžná součást léčiv

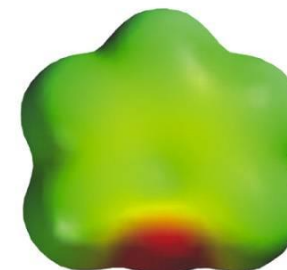
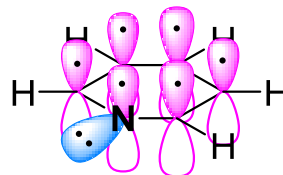
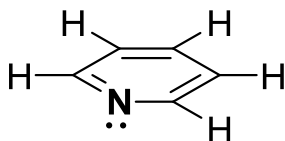
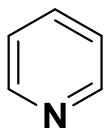




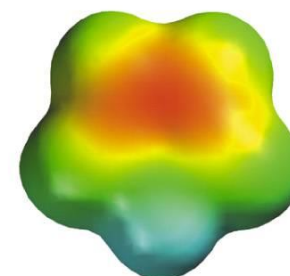
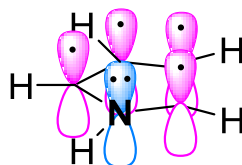
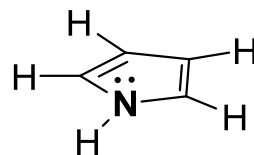
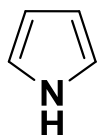
- Srovnání struktury benzenu, pyridinu, a pyrrolu



benzene



pyridine



pyrrole

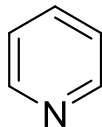
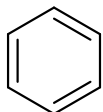
Q: jaký vliv budou mít tyto rozdíly na reaktivitu?





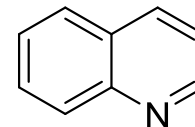
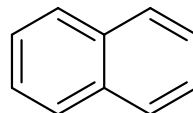
- přítomnost heterocyklického motivu často významně ovlivňuje:

rozpuštnost ve vodě



benzen
1,79 g/l H₂O

pyridin
rozpuštný v H₂O

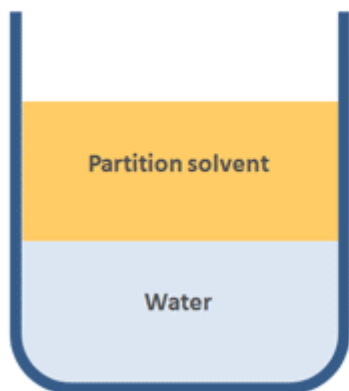


naftalen
0,03 g/l H₂O

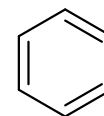
chinolin
6,65 g/l H₂O

hydrofilní vs lipofilní vlastnosti: velmi důležitý parametr při optimalizaci léčiv

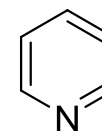
$P = \text{Partition Coefficient} = \frac{\text{Concentration dissolved in partition solvent}}{\text{Concentration dissolved in water}}$



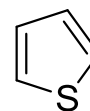
Conditions:
The solvents are "immiscible"
The system must be at equilibrium
All the solute must be dissolved
Temperature should be constant



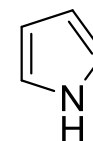
log P = 2.12



log P = 0.65



log P = 1.79

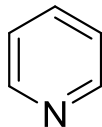
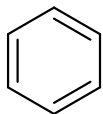


log P = 0.75



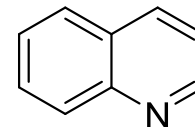
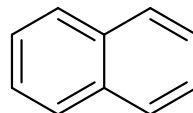
- přítomnost heterocyklického motivu často významně ovlivňuje:

rozpustnost ve vodě



benzen
1,79 g/l H₂O

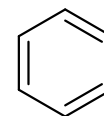
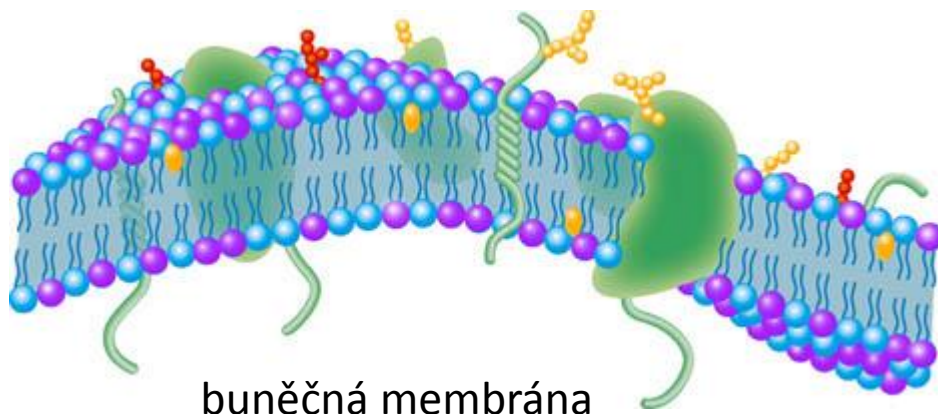
pyridin
rozpustný v H₂O



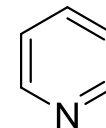
naftalen
0,03 g/l H₂O

chinolin
6,65 g/l H₂O

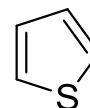
hydrofilní vs lipofilní vlastnosti: velmi důležitý parametr při optimalizaci léčiv



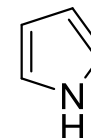
log P = 2.12



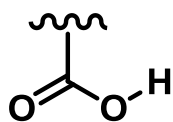
log P = 0.65



log P = 1.79

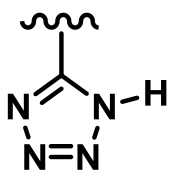
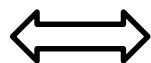
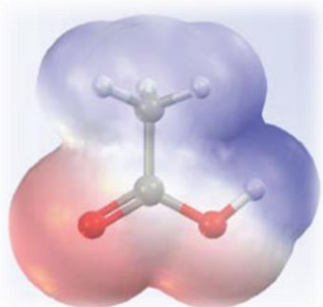


log P = 0.75



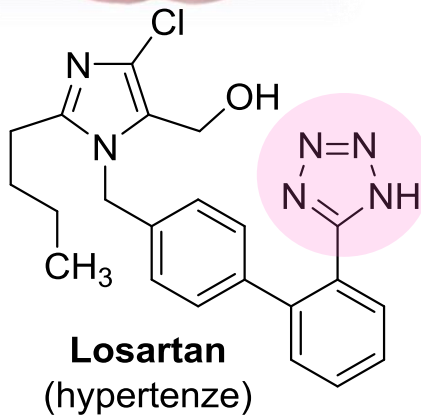
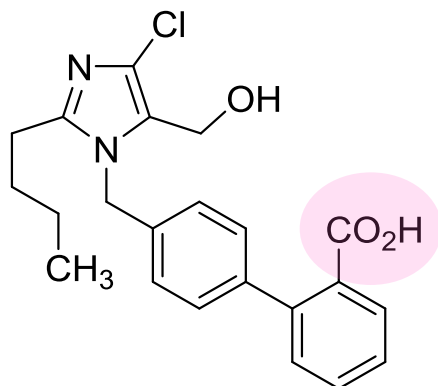
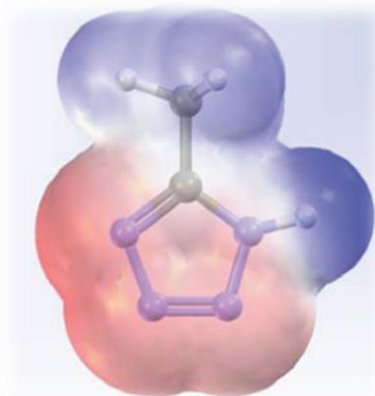
karboxylová
skupina

pKa = 4.5



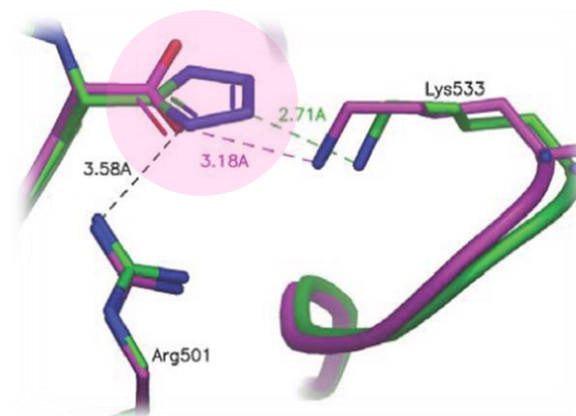
tetrazol

pKa = 4.75

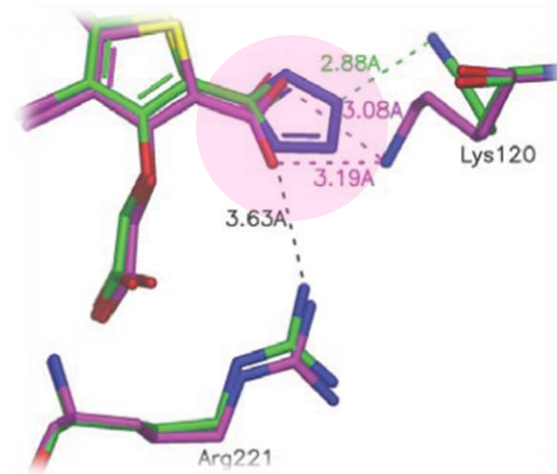


Analogická interakce s proteiny

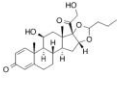
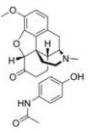
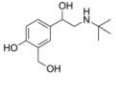
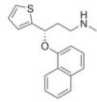
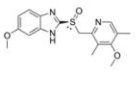
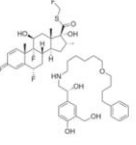
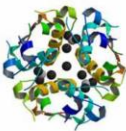
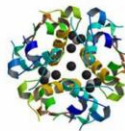
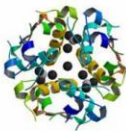
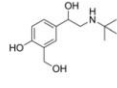
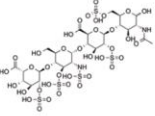
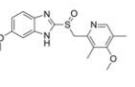
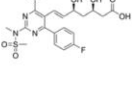
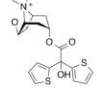
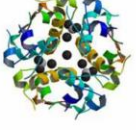
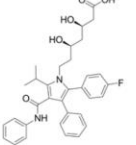
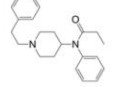
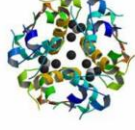
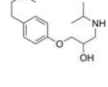
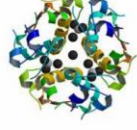
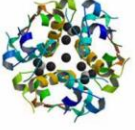
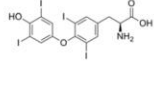
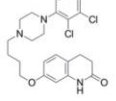
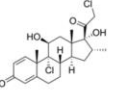
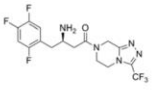
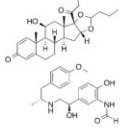
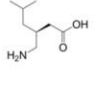
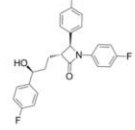

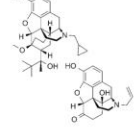
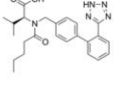
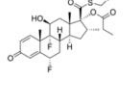
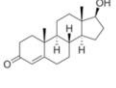
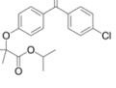


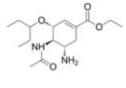
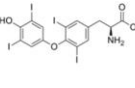
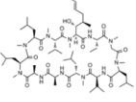

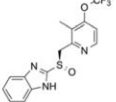
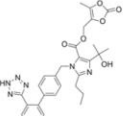
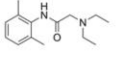
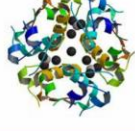
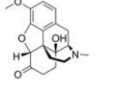
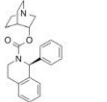
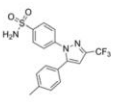
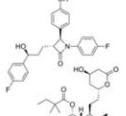

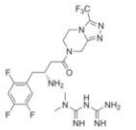
Ilustrace 1



Ilustrace 2





<p>1 Budesonide (Budesonide)</p>  <p>ALM DER RES Approved 1997</p>	<p>2 Hydrocodone/APAP (Hydrocodone & Acetaminophen)</p>  <p>Nervous System Approved 1982</p>	<p>3 Proair HFA (Salbutamol)</p>  <p>Respiratory System Approved 2004</p>	<p>4 Cymbalta (Duloxetine)</p>  <p>Nervous System Approved 2004</p>	<p>5 Nexium (Esomeprazole)</p>  <p>Alimentary Tract & Metabolism Approved 2001</p>	<p>6 Advair Diskus (Fluticasone Propionate & Salmeterol)</p>  <p>Respiratory System Approved 2000</p>	<p>7 Lantus (Insulin Glargine)</p>  <p>Endocrine System Approved 2000</p>	<p>8 Lantus SoloSTAR (Insulin Glargine)</p>  <p>Endocrine System Approved 2000</p>	<p>9 OneTouch (Insulin Glargine)</p>  <p>Endocrine System Approved 2006</p>	<p>10 Ventolin HFA (Salbutamol)</p>  <p>Respiratory System Approved 2001</p>
<p>11 Enoxaparin (Enoxaparin)</p>  <p>BBO MSK Approved 1993</p>	<p>12 Omeprazole (Omeprazole)</p>  <p>Alimentary Tract & Metabolism Approved 1989</p>	<p>13 Crestor (Rosuvastatin)</p>  <p>BBO CAR Approved 2003</p>	<p>14 Spiriva (Tiotropium)</p>  <p>Respiratory System Approved 2004</p>	<p>15 Levemir (Insulin Detemir)</p>  <p>Endocrine System Approved 2005</p>	<p>16 Atorvastatin (Atorvastatin)</p>  <p>BBO CAR Approved 1996</p>	<p>17 Fentanyl (Fentanyl)</p>  <p>NER ONC Approved 1968</p>	<p>18 NovoLog FlexPen (Insulin Aspart)</p>  <p>Endocrine System Approved 2000</p>	<p>19 Metoprolol (Metoprolol)</p>  <p>Cardiovascular System Approved 1978</p>	<p>20 NovoLog (Insulin Aspart)</p>  <p>Endocrine System Approved 2000</p>
<p>21 Humalog (Insulin Lispro)</p>  <p>Endocrine System Approved 1996</p>	<p>22 Synthroid (Levothyroxine)</p>  <p>Endocrine System Approved 2002</p>	<p>23 Abilify (Aripiprazole)</p>  <p>Nervous System Approved 2002</p>	<p>24 Nasonex (Mometasone)</p>  <p>Respiratory System Approved 1997</p>	<p>25 Januvia (Sitagliptin)</p>  <p>Endocrine System Approved 2006</p>	<p>26 Symbicort (Budesonide & Formoterol)</p>  <p>Respiratory System Approved 2006</p>	<p>27 Lyrica (Pregabalin)</p>  <p>MSK NER Approved 2004</p>	<p>28 Zetia (Ezetimibe)</p>  <p>BBO CAR Approved 2002</p>	<p>29 Namenda (Memantine)</p>  <p>Nervous System Approved 2003</p>	<p>30 Suboxone (Buprenorphine & Naloxone)</p>  <p>Nervous System Approved 2002</p>
<p>31 Diovan (Valsartan)</p>  <p>CAR END Approved 1996</p>	<p>32 Flovent HFA (Fluticasone Propionate)</p>  <p>Respiratory System Approved 1996</p>	<p>33 AndroGel (Testosterone)</p>  <p>Genito-Urinary & Sex Hormone Approved 2000</p>	<p>34 Fenofibrate (Fenofibrate)</p>  <p>BBO CAR END Approved 1993</p>	<p>35 Remicade (Infliximab)</p>  <p>END MSK Approved 1998</p>	<p>36 OneTouch Ultra</p>  <p>Endocrine System Marketed 2006*</p>	<p>37 Tamiflu (Oseltamivir)</p>  <p>Anti-Infective Approved 1999</p>	<p>38 Levothyroxine (Levothyroxine)</p>  <p>Endocrine System Approved 2000</p>	<p>39 Restasis (Cyclosporine)</p>  <p>Sensory Organ Approved 2002</p>	<p>40 Lovaza (Omega 3-Acid Ethyl Esters)</p>  <p>Cardiovascular System Approved 2004</p>
<p>41 Dextilant (Dexlansoprazole)</p>  <p>Alimentary Tract & Metabolism Approved 2007</p>	<p>42 Benicar (Olmesartan)</p>  <p>CAR END Approved 2002</p>	<p>43 Lidoderm (Lidocaine)</p>  <p>CAR DER NER RES SEN Approved 1948</p>	<p>44 Humalog KwikPen (Insulin Lispro)</p>  <p>Endocrine System Approved 1996</p>	<p>45 Oxycontin (Oxycodone)</p>  <p>END MSK Approved 2010</p>	<p>46 VESicare (Solifenacin)</p>  <p>Genito-Urinary & Sex Hormone Approved 2004</p>	<p>47 Celebrex (Celecoxib)</p>  <p>MSK ONC Approved 1998</p>	<p>48 Vytorin (Ezetimibe & Simvastatin)</p>  <p>BBO CAR Approved 2004</p>	<p>49 Enbrel (Etanercept)</p>  <p>Musculo-Skeletal System Approved 1998</p>	<p>50 Janumet (Metformin & Sitagliptin)</p>  <p>Alimentary Tract & Metabolism Approved 2007</p>