Common enzyme-inhibiting Drugs

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20 common amino acids
Enzymes have immense catalytic power (but they cannot alter reaction equilibria)
Enzymes are highly specific
The catalytic activities of many enzymes are highly regulated
Enzymes accelerate reactions by stabilizing transition states

For example, 1 molecule of carbonic anhydrase carries out the following reaction on 100,000 molecules of CO$_2$ per second

$$\text{CO}_2 + \text{H}_2\text{O} = \text{HCO}_3^- + \text{H}^+$$
V = V_{max} \frac{S}{(S + K_m)}

Competitive inhibition
Non-competitive inhibition
Why inhibit enzymes?

• Certain disease states may be caused by the product of an enzyme catalysis

• Drugs can target enzymes which are present in pathogens but not in the host
The Shikimate Pathway

glucose

\[ \text{EPSP synthase} \]

EPSP

\[ \text{EPSP} \]

\[ \text{prephenate} \]

\[ \text{chorismate} \]

phenylalanine

tyrosine

tryptophan

S-3-P
Anti hypertensive agents

Angiotensin-I

\[ \text{H}_2\text{N-Asp-Arg-Val-Tyr-Ile-His-Pro-Phe}^\beta\text{His-Leu-CO}_2\text{H} \]

Antihypertensive agents

Captopril

\( \text{HS-} \)

Enalapril

\( \text{EtO-} \)

ACE

Angiotensin-II

Smooth muscle contracton

Aldosterone secretion

Increased peripheral resistance

Increased extracellular fluid volume

Na-retention

Hypertension
Penicillins and the bacterial cell-wall biosynthesis

D-ala-D-ala
pentaglycine

carbohydrate chain
Figure 8-29
The conformation of penicillin in the vicinity of its reactive peptide bond (A) resembles the postulated conformation of the transition state of R—d-Ala—d-Ala (B) in the transpeptidation reaction. [After B. Lee. J. Mol. Biol. 61(1971):464.]
Thymidylate synthase

\[ \text{dihydofolate} \xrightarrow{\text{DHF reductase, NADPH, H}^+} \text{tetrahydrofolate} \]

\[ \text{N}^5\text{-N}^{10}\text{-methylene-THF} \]

\[ \text{sugar} \rightarrow \text{methylerited sugar} \]
Inhibits blood DOPA decarboxylase
Does NOT cross the blood-brain barrier
Reduces DOPA intake by 75%
HGPRTase

AMP

hypoxanthine

allopurinol

aloxanthine

xanthine oxidase

GMP

uric acid
The metabolic pathways involved in the inflammation process

Phospholipids (cell membrane) → arachidonic acid

**Inflammatory pathway 1**
- 5-lypoxigenase
- 5-HPETE
  - Leukotriene A4 (LTA4)
  - Leukotriene C4
  - Leukotriene D4
  - Leukotriene E4

**Inflammatory pathway 2**
- Cyclo-oxygenase
- Endoperoxides
- Prostaglandin G2 and H2
- Prostaglandins I2, E2, F2

Arachidonic acid
COX inhibitors

celecoxib

rofecoxib
www.lyprinol.com

“natural” lipoxygenase inhibitor

Principal Ingredients

Natural mono-unsaturated Olive oil – 100 mg
Lyprinol GLM pat. lipids (Eicosatetraenoic acid) – 50 mg
Vitamin E (D-alpha-Tocepherol) as antioxidant - 0.225 mg.

Perna Canaliculus