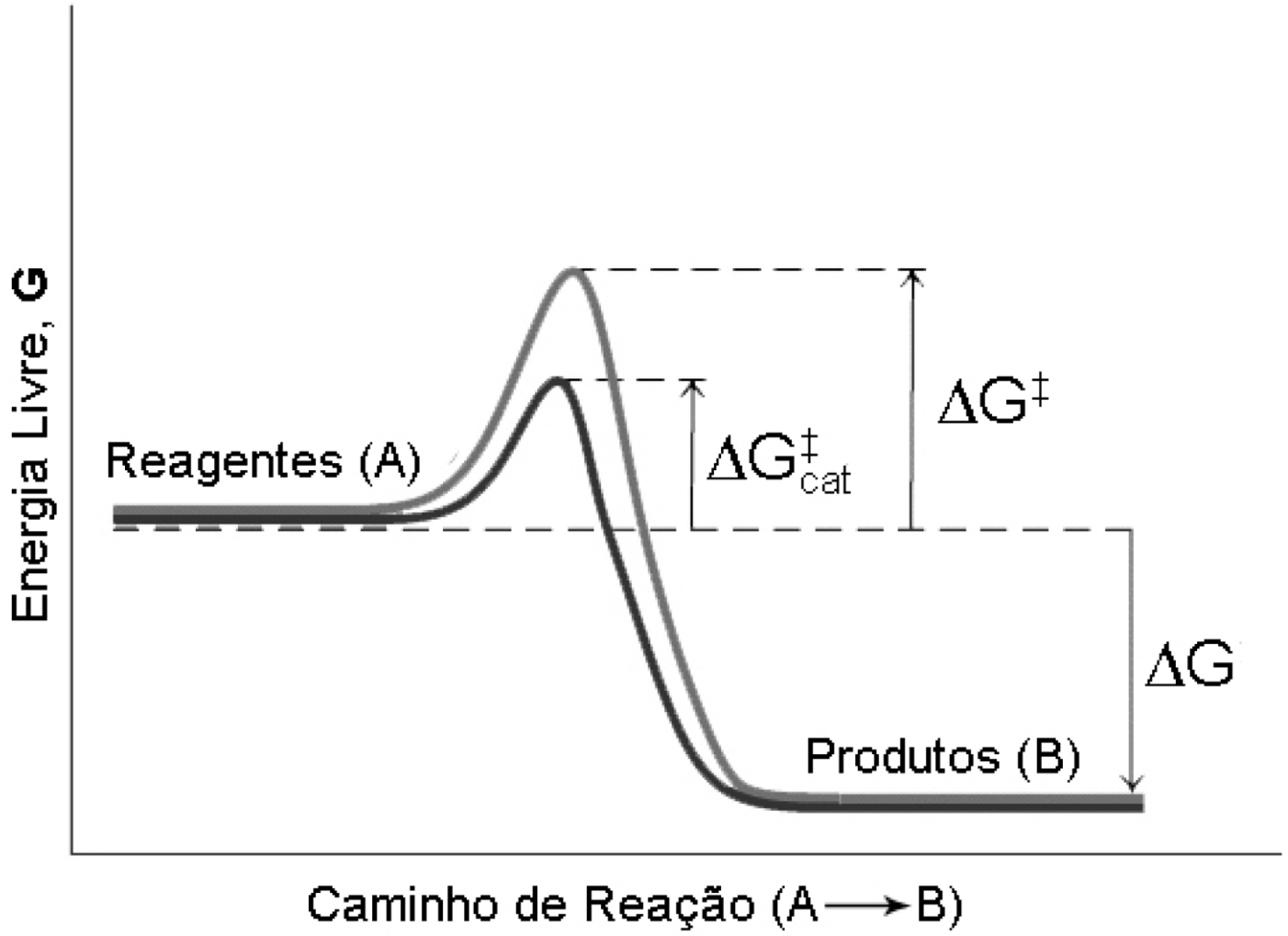
Química Medicinal

Prof. Dr. Andrei Leitão

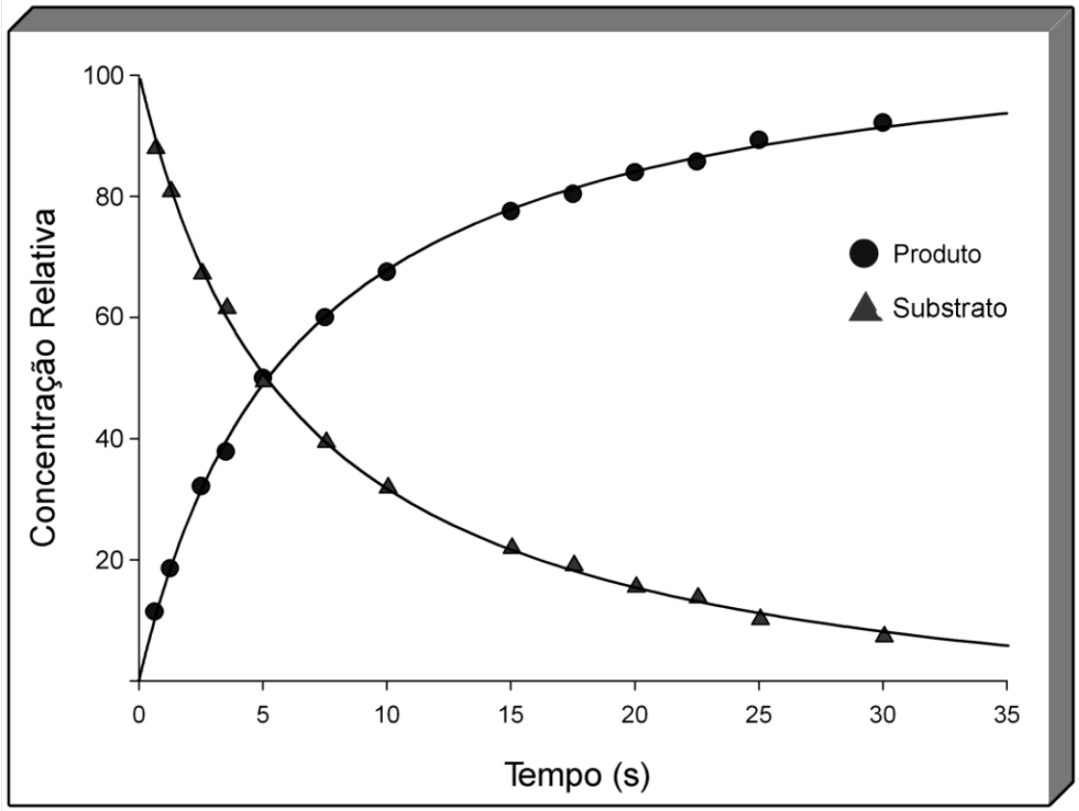
Ensaios bioquímicos - enzimas



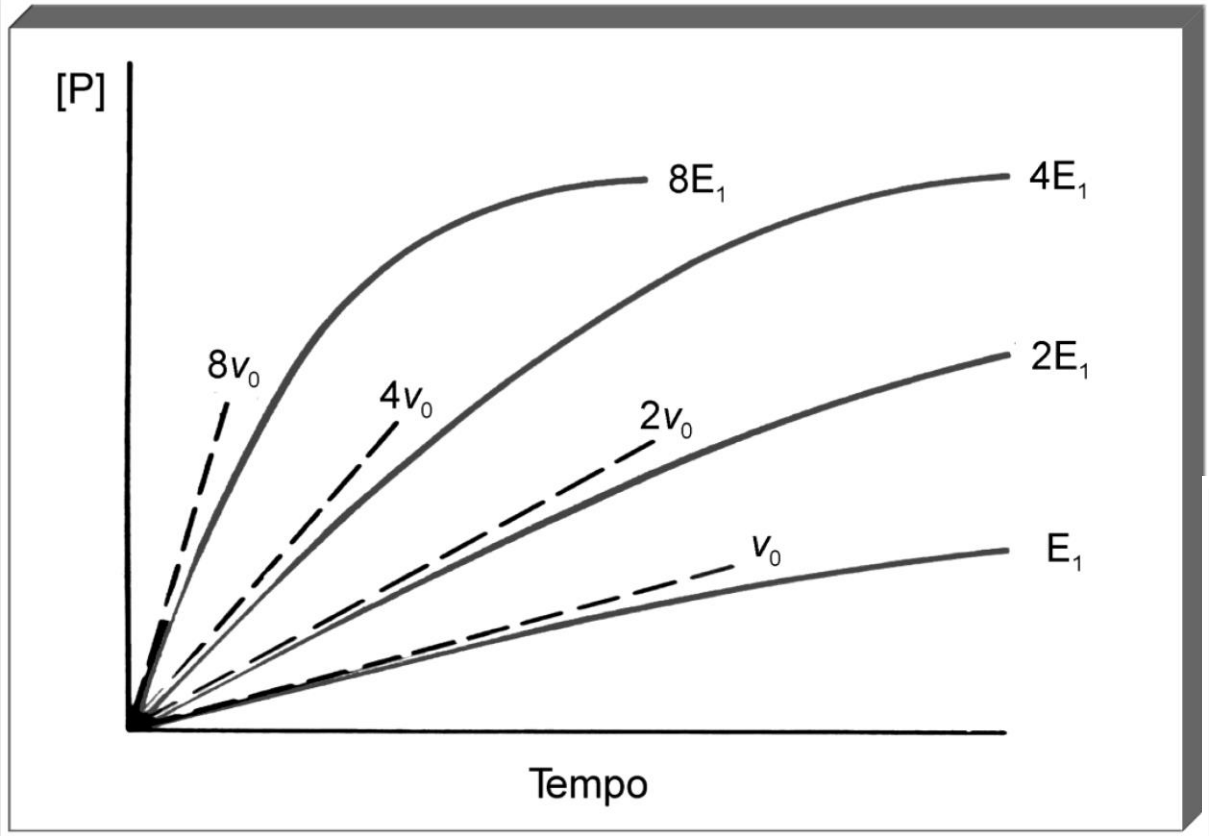
Slides baseados no capítulo 14 *In*: Química Medicinal - Carlos A. Montanari (ed.), EDUSP, 2011.

Enzima & catálise

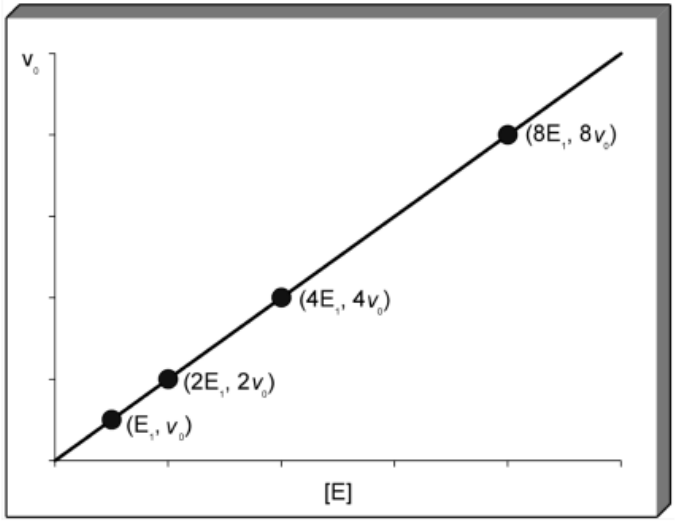
$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P$$



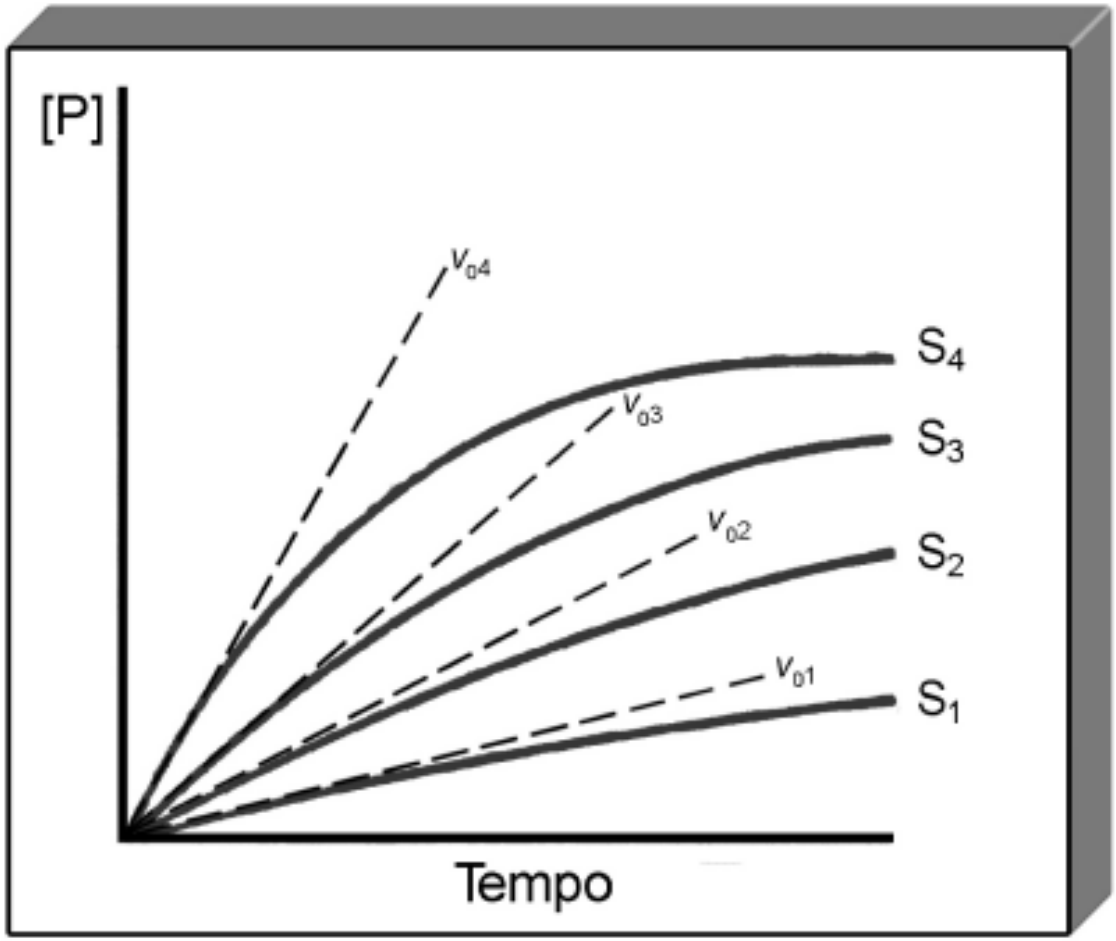
Formação de produto e concentração de enzima



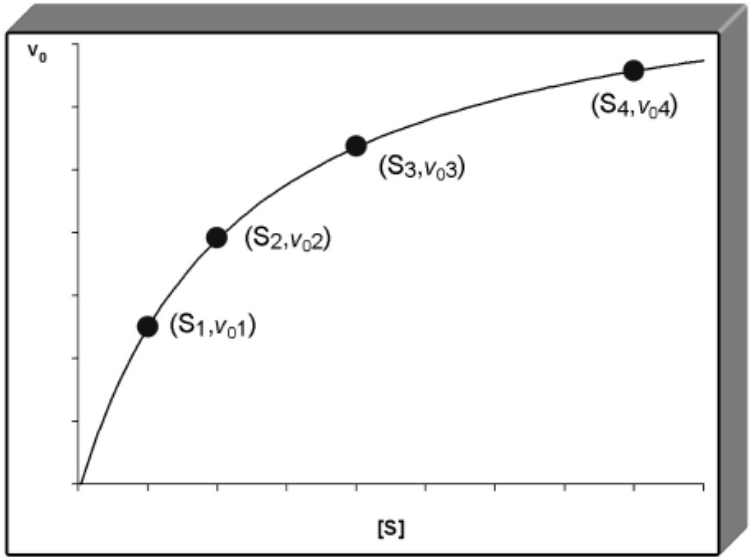
$$v_0 = -\frac{\Delta S}{\Delta t} = \frac{\Delta P}{\Delta t}$$



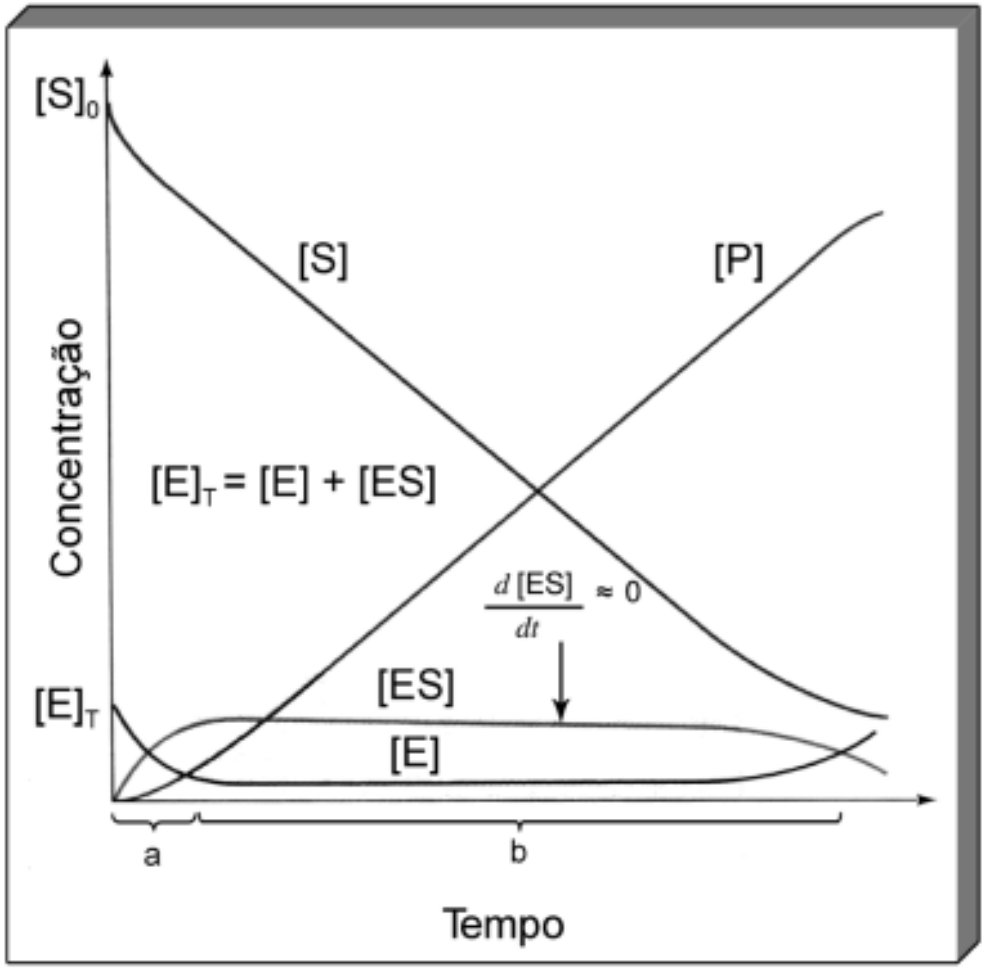
Formação de produto e concentração de substrato



$$v_0 = -\frac{\Delta S}{\Delta t} = \frac{\Delta P}{\Delta t}$$



O estado estacionário

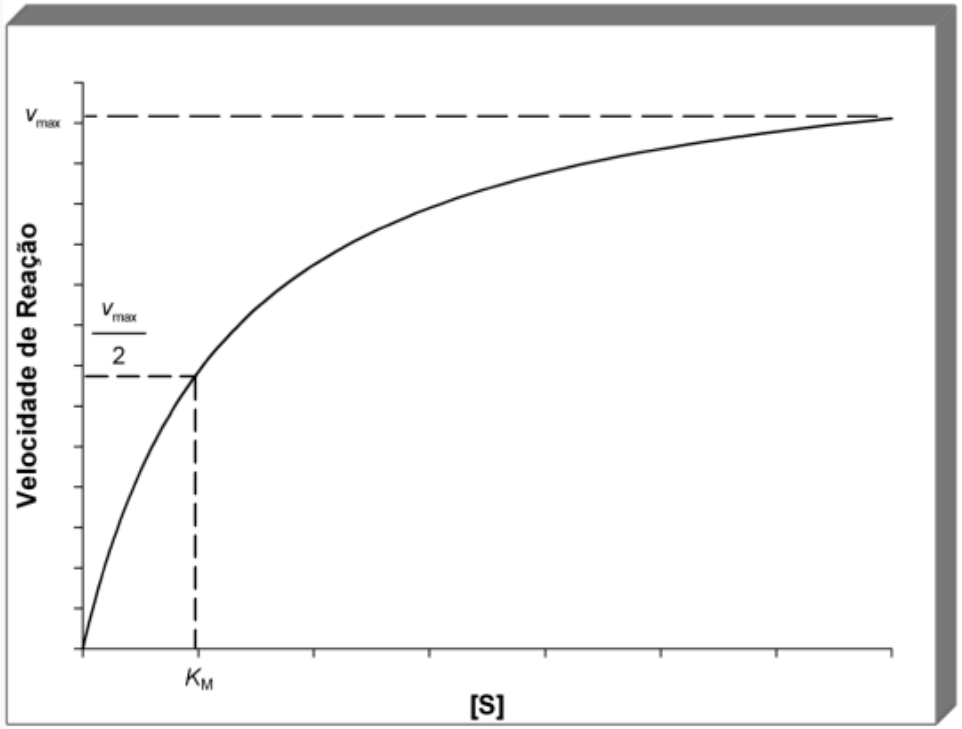


(**a** corresponde ao período de indução e **b** a v_0)

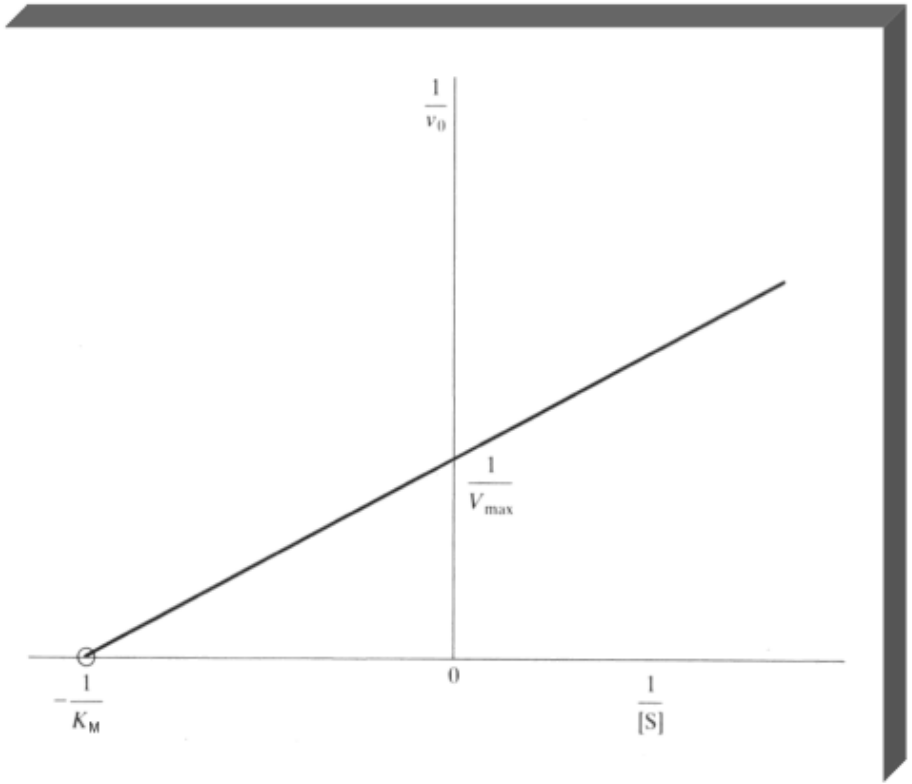
Michaelis-Menten

$$v = \frac{V_{max}[S]}{K_M + [S]}$$

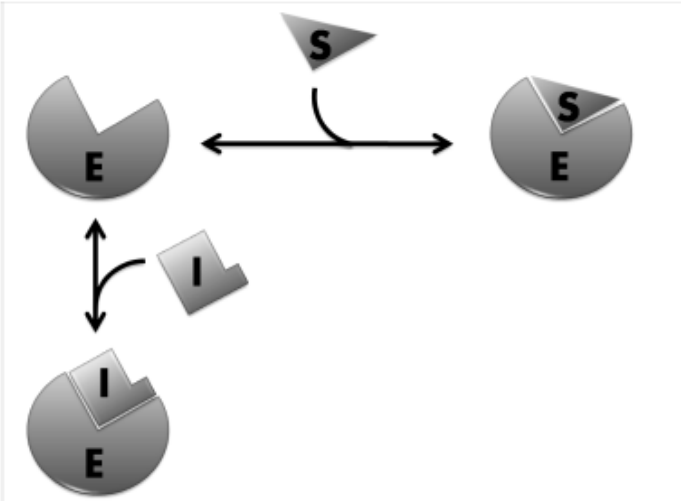
Determinação de K_M e V_{max}

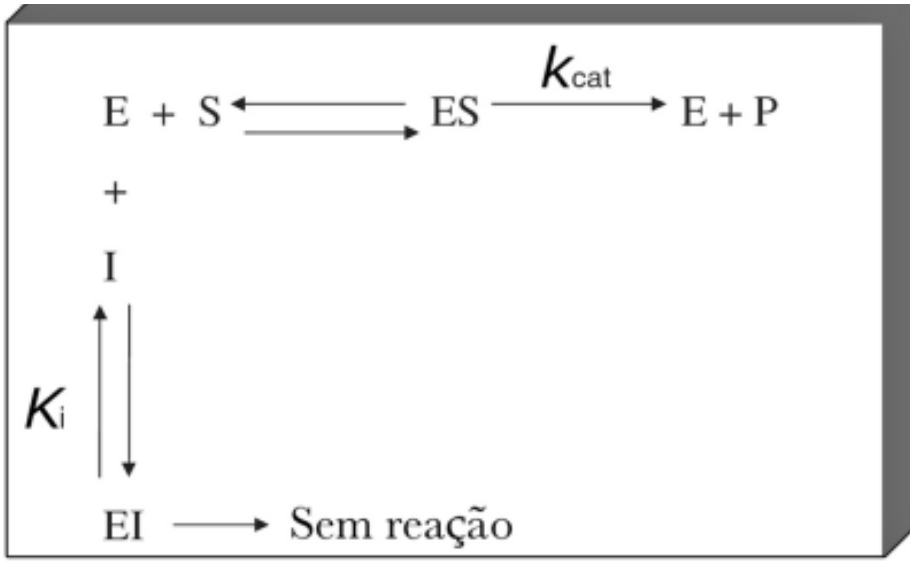


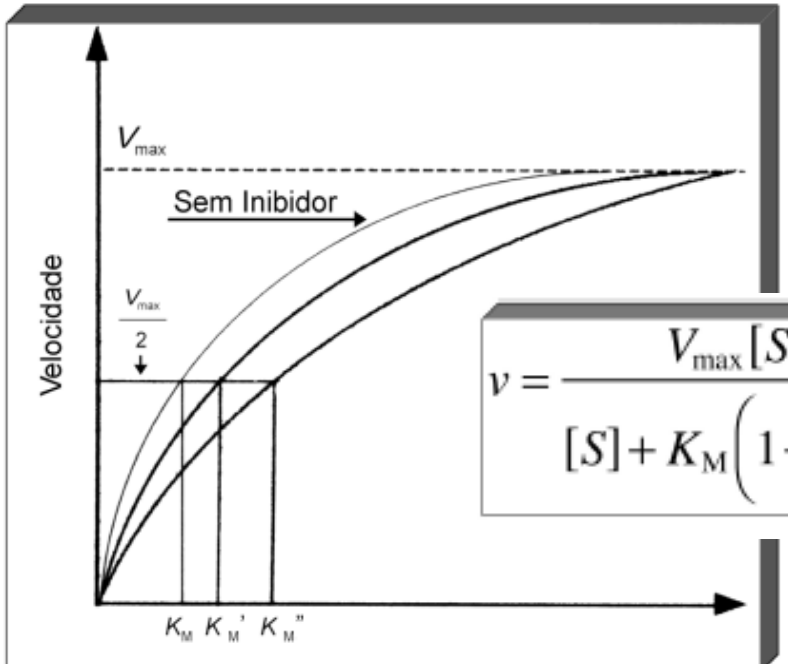
$$\frac{1}{v} = \left(\frac{K_M}{V_{max}} \bullet \frac{1}{[S]}\right) + \frac{1}{V_{max}}$$



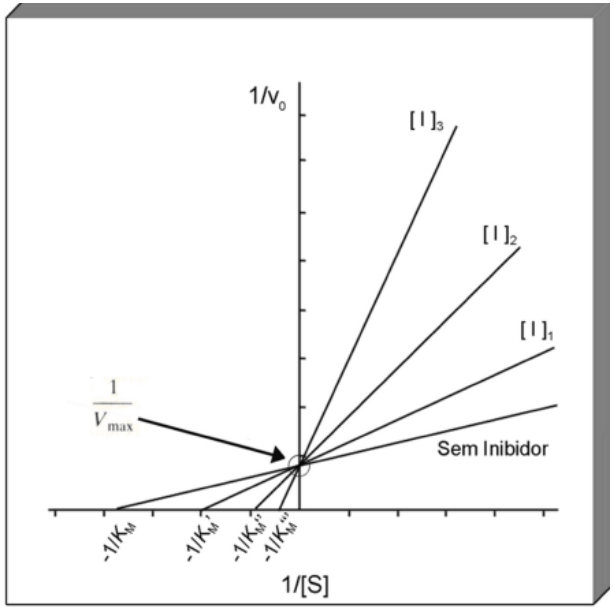
Inibição enzimática competitiva



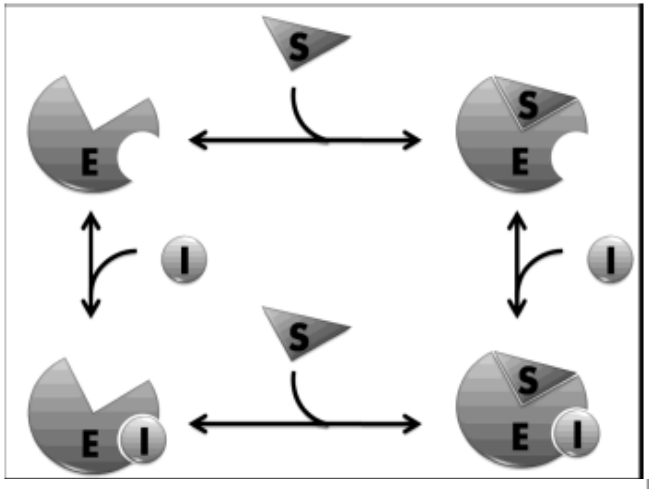


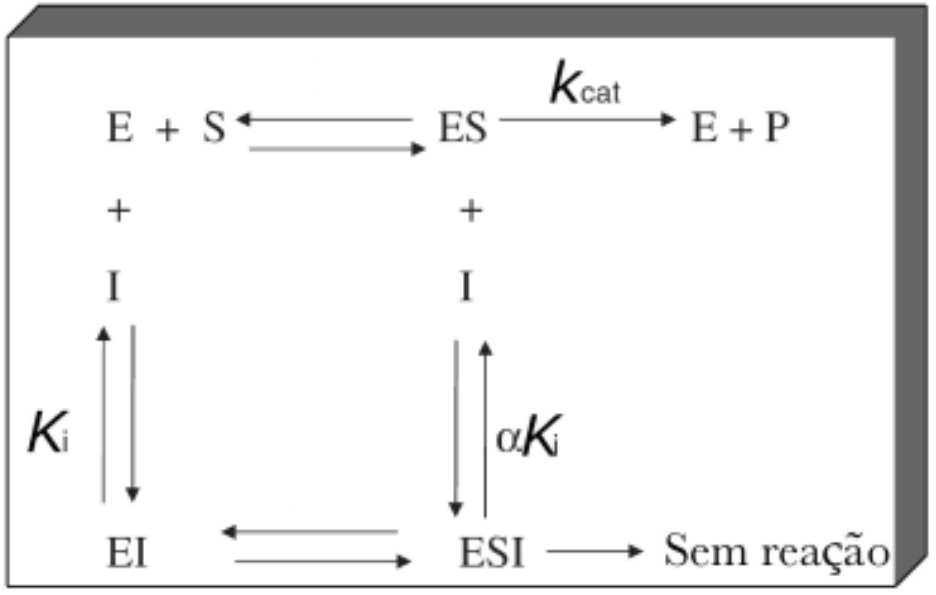


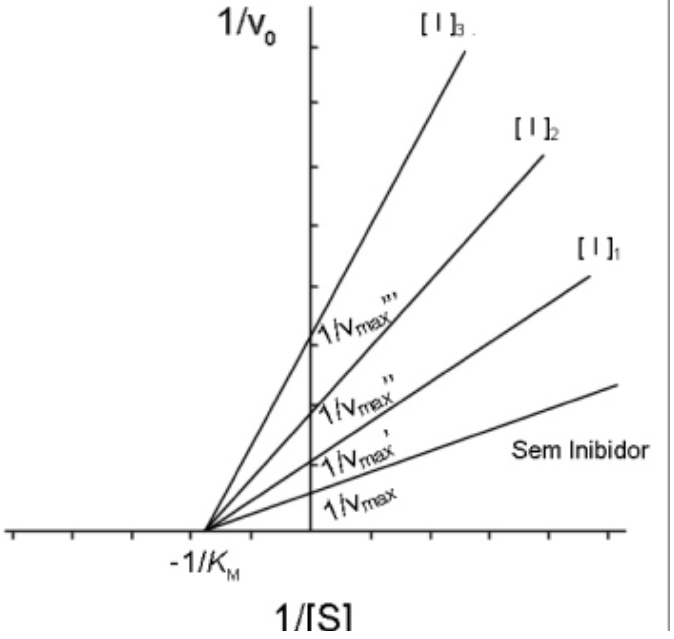
$$v = \frac{V_{max}[S]}{[S] + K_M\left(1 + \frac{[I]}{K_i}\right)}$$



Inibição enzimática não competitiva

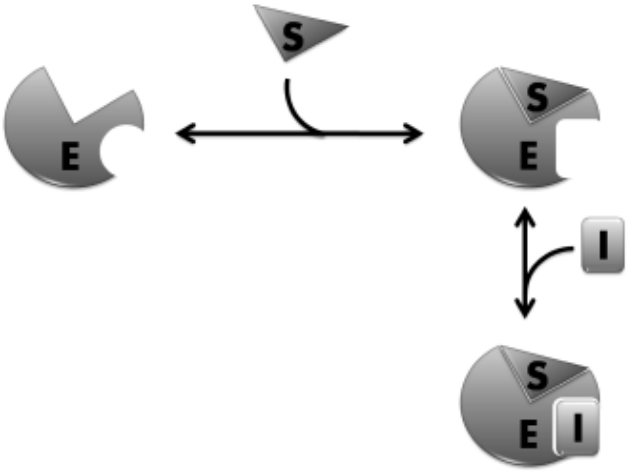


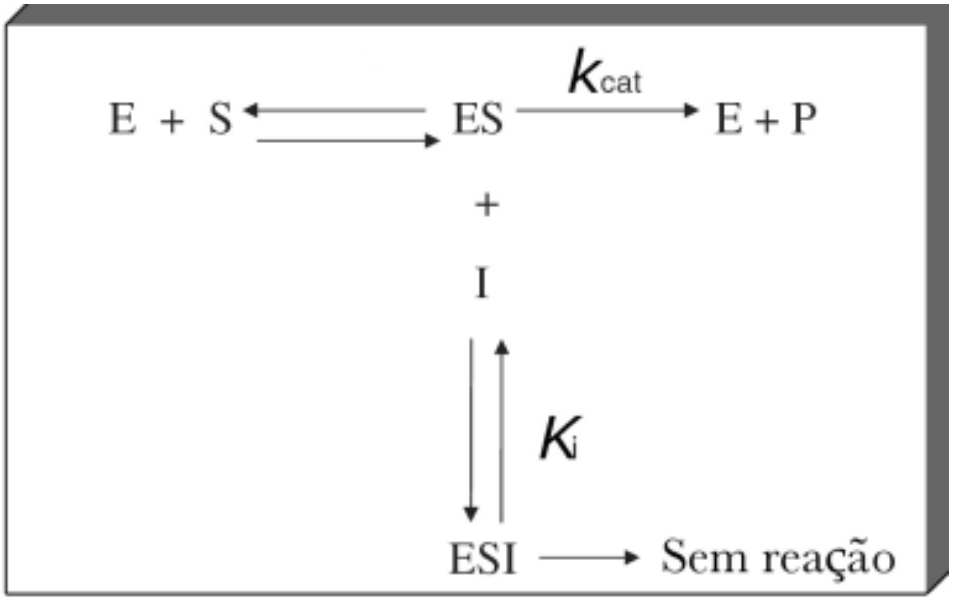


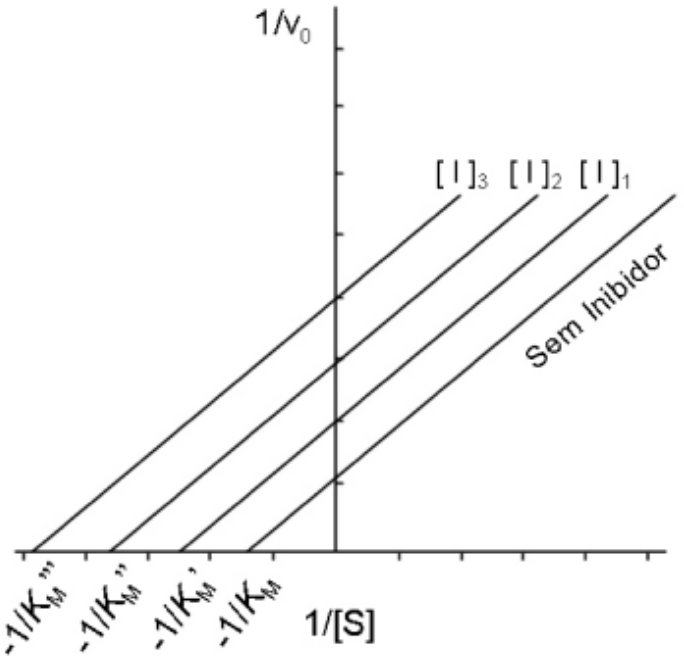


$$v = \frac{V_{max}[S]}{([S] + K_M)\left(1 + \frac{[I]}{K_i}\right)}$$

Inibição enzimática incompetitiva



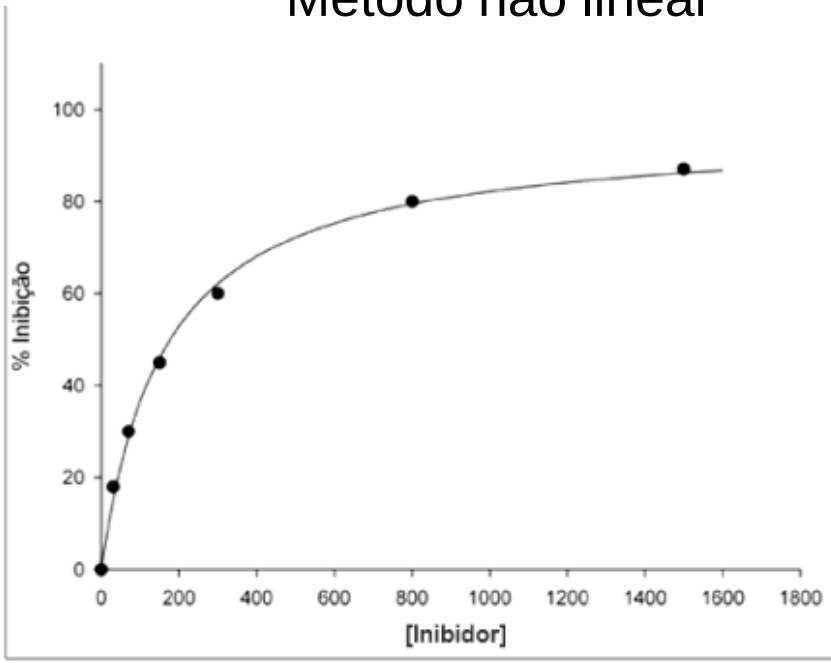




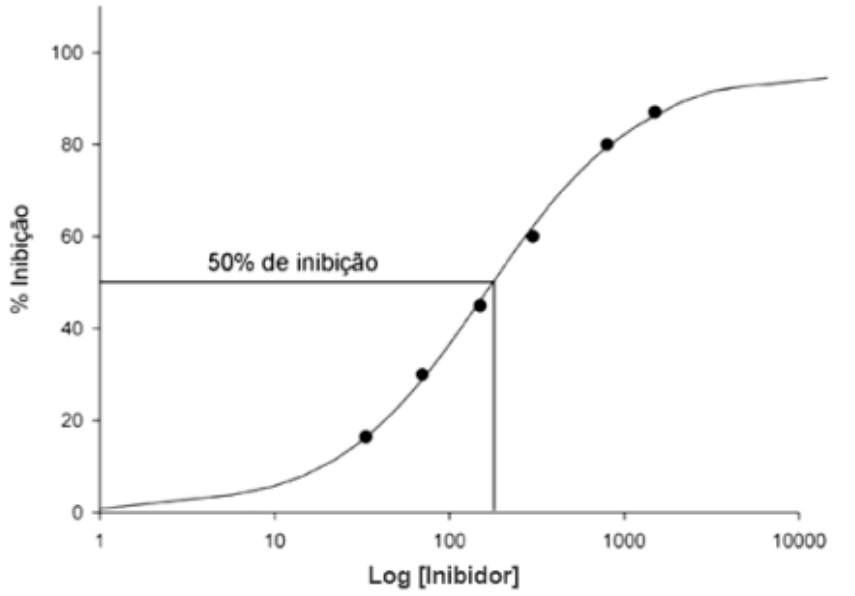
$$v = \frac{V_{max}[S]}{[S]\left(1 + \frac{[I]}{\alpha K_i}\right) + K_M}$$

Determinação de IC_{50}

Método não linear



Semi-logarítmico

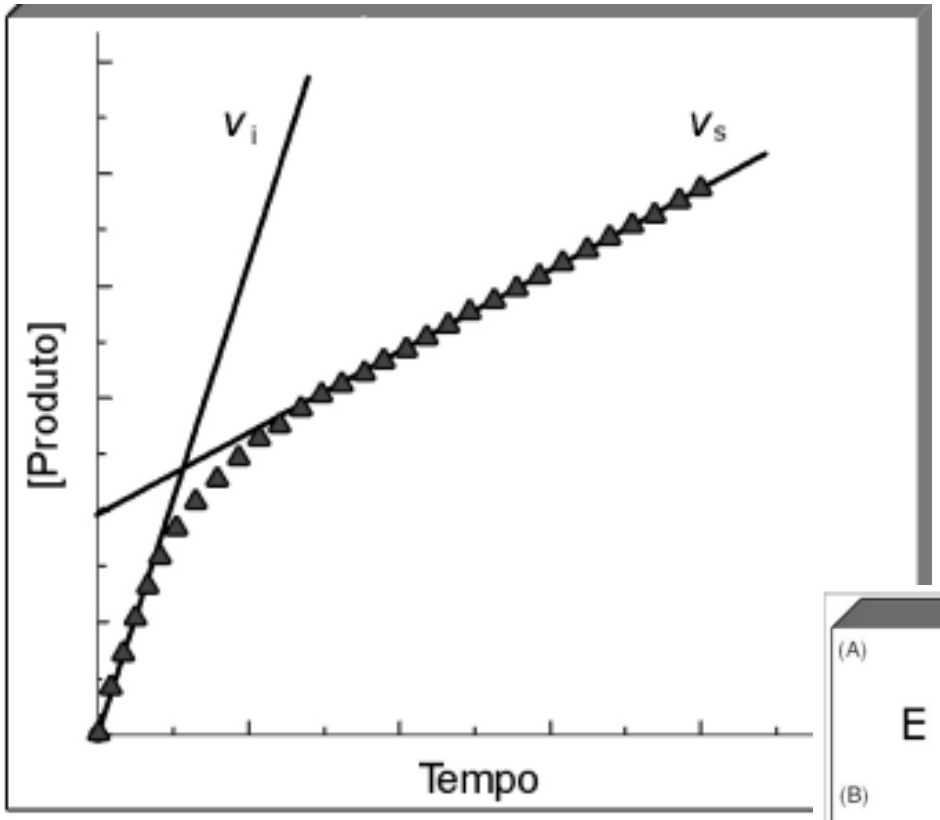


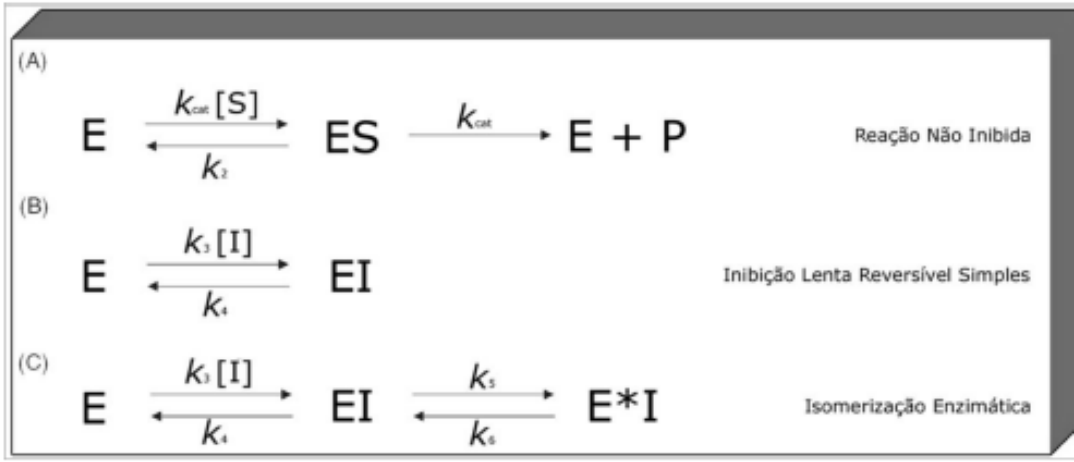
$$IC_{50} = K_i\left(1+\frac{[S]}{K_M}\right)$$ Mecanismo Competitivo

$$IC_{50} = \frac{[S]+K_M}{\frac{K_M}{K_i}+\frac{[S]}{\alpha K_i}}, \quad \text{quando } \alpha = 1, IC_{50} = K_i$$ Mecanismo Não-Competitivo

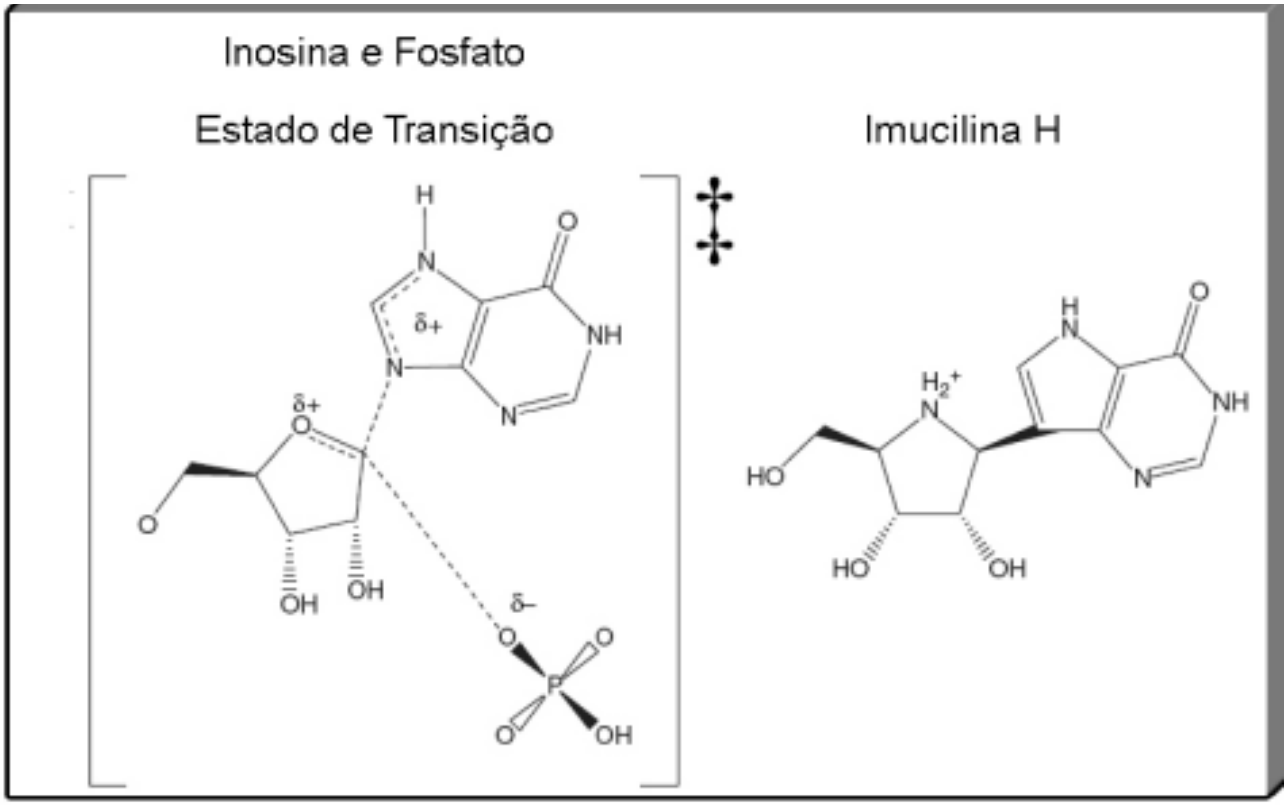
$$IC_{50} = \alpha K_i\left(1+\frac{K_M}{[S]}\right)$$ Mecanismo Incompetitivo

Ligação lenta do inibidor

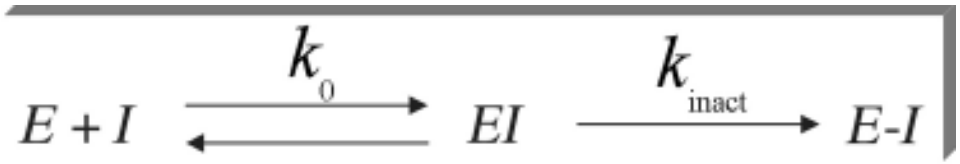




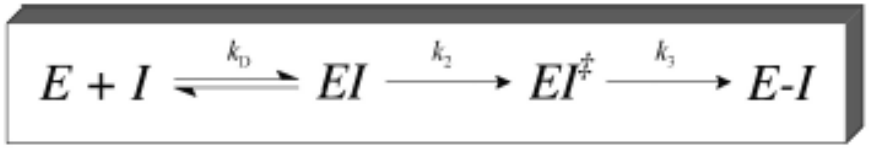
Inibidor baseado no estado de transição



Inibidor irreversível



Mecanismo de inativação enzimática com base no mecanismo



Suicida