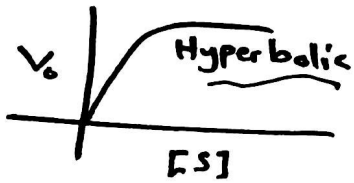
Enzymes/Proteins

2 types

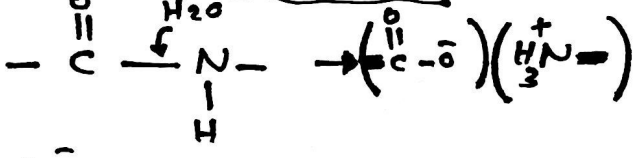
Non-allosteric
لا تتأثر بالعوامل الخارجية Not 4



as Myoglobin Protiens

Ex:- Chemotrypsin

- Secreted by pancrease
- Break peptide Bond

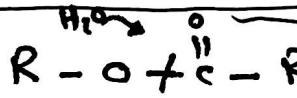


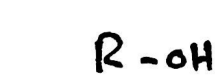
تتخصص عند aromatic amino-acids

to lesser extent at بنسبة أقل

His , leu , Gln

→ also break Ester-Bond

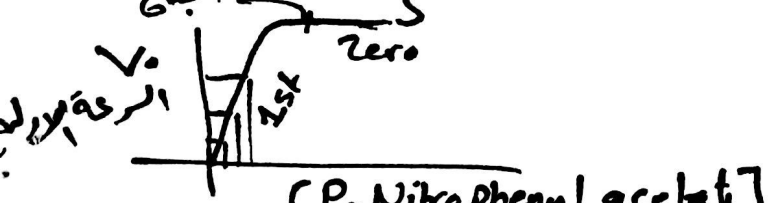


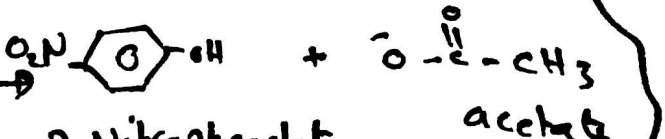


* الأدوية المستخدمة لهذه الإنزيم

P-Nitro-phenyl acetate

الأدوية المضادة





P-Nitrophenolate
اصفر

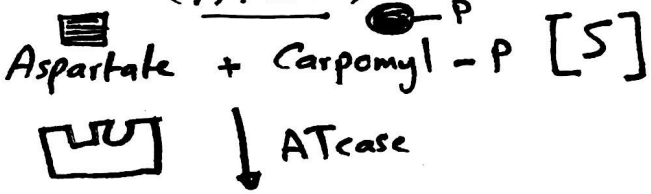
acetate

النواتج

Allosteric
تتأثر بالعوامل الخارجية 4

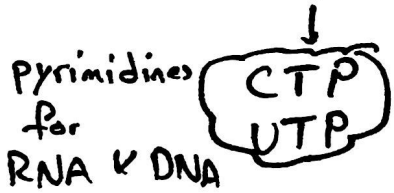
as Hemoglobin Protiens

Ex:- Asparbate trans Carbomylase (ATcase)



Carbomyl-Aspartate

النواتج



كلما زاد Carbomyl-P ثابت وطبيعي

(1)

mportant Notes

* allosteric Enzymes all are Quaternary proteins and show cooperativity [Cooperative Kinetic]

* Non-allosteric Enzymes are not Quaternary proteins and does NOT show cooperativity [simple Kinetic]

Q: In reaction catalyzed by chemotrypsin, agraph in which the rate is plotted against the concentration of substrate :-

a. is sigmoidal, characteristic of an allosteric Enzyme
b. shows that cooperative kinetics are observed
c. shows that the reaction is zero order
d. is hyperbolic, characteristic of a non allosteric Enzyme

Q:- The reaction catalyzed by ATcase is :-

a. the first step in the synthesis of amino-acids
b. the first step in the synthesis of Fatty acid
c. the first step in the synthesis of CTP and UTP
d. part of glycolysis

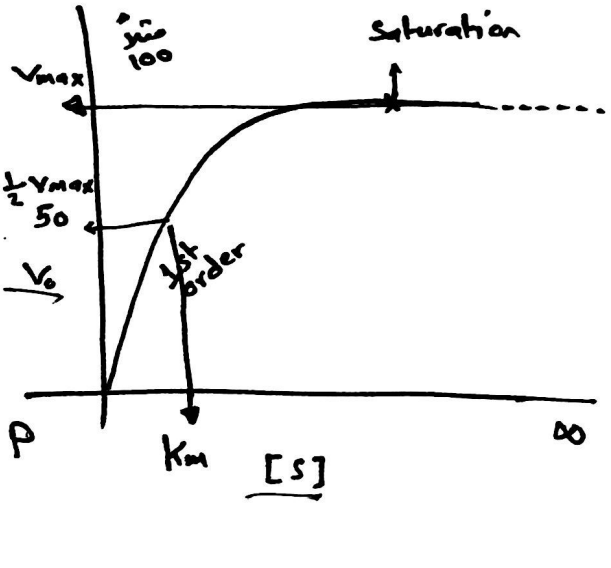
Q:- Myoglobin is a non-allosteric enzyme showing simple kinetics

True False

Michealis - Menten Equation

M - M equation

* For Non-allosteric Enzyme
* Relation العلاقة [S] Vs V_o السرعة الابتدائية



$$E + S \underset{K_{-1}}{\overset{K_1}{\rightleftharpoons}} E\text{-}S \text{ complex} \xrightarrow{K_2} E + P$$

* هنا نفترض ان Products don't Converted back to substrate لا تعود لانه [P] في بداية التفاعل قليل جداً حيث انتا نحسب السرعة الابتدائية في بداية التفاعل

K_1 : rate Constant for E-S complex formation from E and S

K_{-1} : Rate constant for E-S complex dissociation to E and S

K_2 : rate Constant for E-S complex dissociation to E + P

$$V_o = \frac{V_{max} * [S]}{K_m + [S]}$$

M-M equation

Micheal's Constant

$$K_m = \frac{K_{-1} + K_2}{K_1}$$

السرعة الابتدائية V_o عندما $[S] = \infty$

* من الصعب في الاعلى لا على نحدد V_{max} او K_m بدقة

اشتقاق معهم

فرضاً

$[S] = K_m$

$$V_o = \frac{V_{max} \cdot [S]}{K_m + [S]}$$

$$V_o = \frac{V_{max} \cdot [S]}{[S] + [S]} \Rightarrow V_o = \frac{V_{max} \cdot \cancel{[S]}}{2\,\cancel{[S]}}$$

$$V_o = \frac{V_{max}}{2} = \frac{1}{2} V_{max}$$

~~إذاً إذا كان $K_m = [S]$ عندها السرعة الابتدائية $= \frac{1}{2} V_{max}$~~

إذاً يمكن تعريف K_m هو تركيز $[S]$ الذي عنده نصل الى نصف السرعة العظمى V_{max}

Enzyme A $K_m = 500$ ماذا تعني ← $[S] = 500$ ← نصل $\frac{1}{2} V_{max}$

Enzyme B $K_m = 1000$ ماذا تعني ← $[S] = 1000$ ← نصل $\frac{1}{2} V_{max}$

↑ K_m ↓ affinity الحب بين الأنزيم والمادة المتفاعلة

Unit of Km is mM millimolar

سؤال مهم

إذا كان

$[S] = 2\,Km$

ما العلاقة بين V_o و V_{max}

$$V_o = \frac{V_{max} \cdot [S]}{Km + [S]}$$

$$V_o = \frac{V_{max} \cdot 2\,Km}{Km + 2\,Km} \Rightarrow V_o = \frac{V_{max} \cdot 2\,\cancel{Km}}{3\,\cancel{Km}}$$

إذا

$$V_o = \frac{2}{3} V_{max}$$

سؤال: وإذا كانت

$$V_o = \frac{1}{3} V_{max}$$

ما العلاقة بين Km و $[S]$

$$V_o = \frac{V_{max} \cdot [S]}{Km + [S]}$$

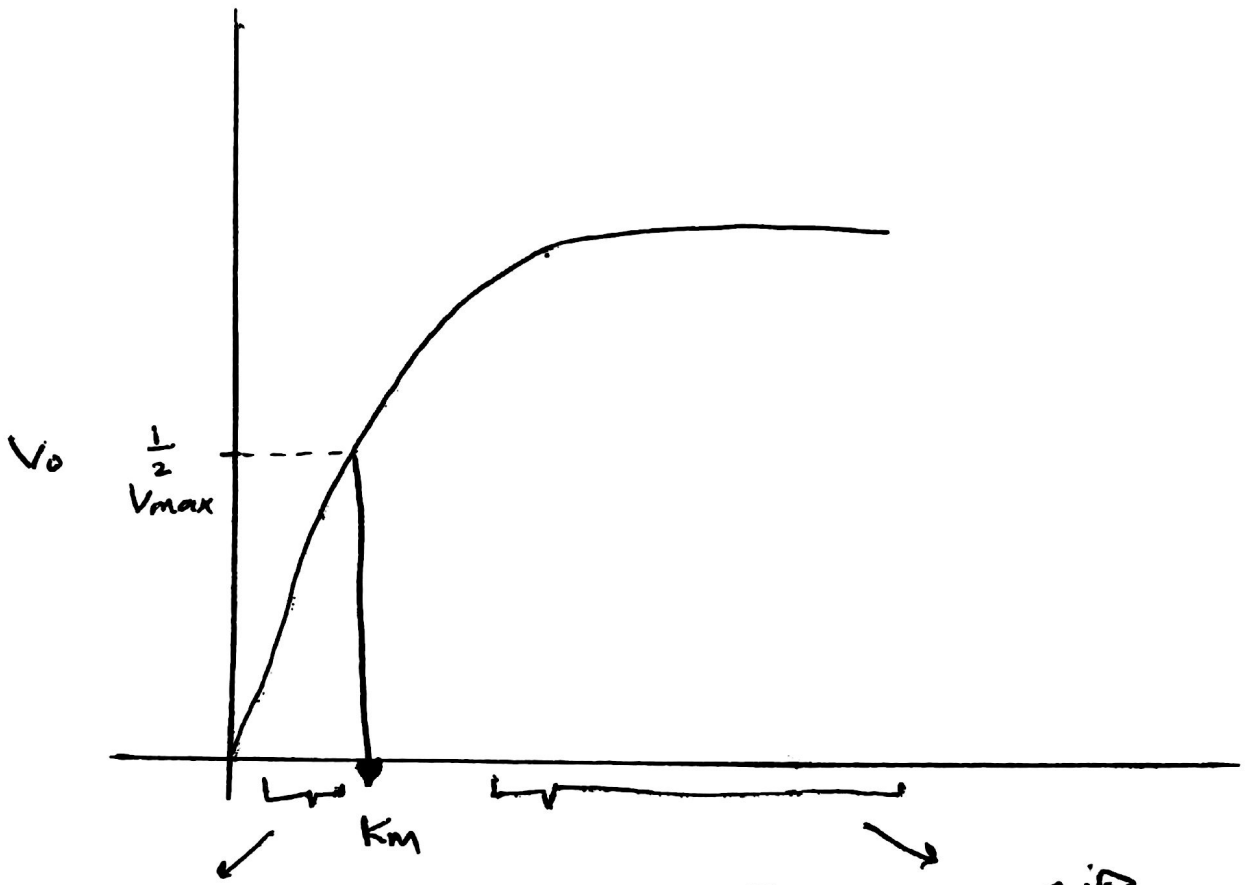
$$\frac{1}{3}\cancel{V_{max}} = \frac{\cancel{V_{max}} \cdot [S]}{Km + [S]}$$

$$3[S] = Km + [S]$$

$$2[S] = Km$$

$$[S] = \frac{1}{2} Km$$

Notes



low substrate concentration

[S] < Km

في التفاعل

First order

الدرجة الأولى

Linear

High substrate concentration

[S] >> Km

في التفاعل

Zero Order

: The E-S complex :-

a. always proceed to form product rapidly

b. always breaks down to form Free enzyme and S

c. always breaks down to form Free enzyme and product

d. may break down to form free enzyme and S or free enzyme and product.

Q:- The Michaelis-Menten approach to describe the Kinetic of an enzyme Catalyzed reaction, make which of the following assumptions about the Conversion of product to Substrate :-

a. The product bind reversibly to the enzyme in order to be converted to Substrate

b. The product is not converted to Substrate to any appreciable extent

c. product is converted to Substrate following simple first order Kinetic

d. product is converted to Substrate following simple second order Kinetic

Q: The initial rate of an enzymatic reaction is usually determined in order to assure that :-

a. the enzyme is active

b. there is no reverse reaction of product to E-S complex

c. the Substrate is not used up

d. the experiment Can be completed quickly

most enzyme reactions display first order Kinetics for the individual substrate when the substrate concentration is Low

True False

Q: which of the following statements regarding the Michaelis constant (K_m) is false ?-

a. It's similar to affinity concentration between the enzyme and substrate

b. the dimension for Km is concentration such as molarity

c. the Km determines the Vmax

d. it's the substrate concentration necessary to reach $\frac{1}{2} V_{max}$

Q: The Km of hexokinase for Glucose = 0.15 mM and for Fructose = 1.5 mM, which is the preferred Substrate?-

a. Glucose

b. Fructose

c. Neither Substrate is preferred over the other

d. you cannot tell from the data given

e. none of these answers is correct

Linearizing M. M equation

تحويل معادلة M-M الى معادلة خطية

$$V_o = \frac{V_{max} \cdot [S]}{K_m + [S]}$$

المقلوب للطرفين Reciprocal

الهدف تحديد V_{max} و K_m بدقة

هذه معادلة خطية مهمة

$$\frac{1}{V_o} = \frac{K_m}{V_{max}}\left(\frac{1}{[S]}\right) + \frac{1}{V_{max}}$$

اسمها lineweaver-Burk double reciprocal Equation

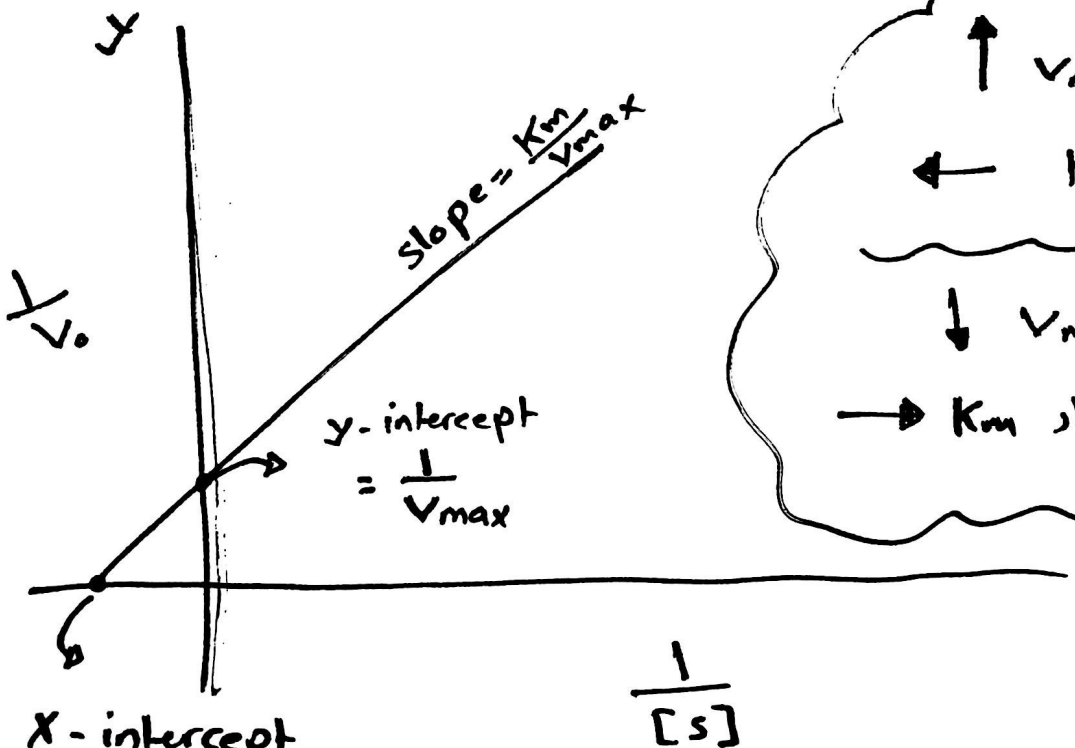
المعادلة الخطية

$$y = a\,x + b$$

- y محور y = $\frac{1}{V_o}$
- a slope الميل = $\frac{K_m}{V_{max}}$
- x محور x = $\frac{1}{[S]}$
- b y-intercept نقطة التقاطع مع محور y = $\frac{1}{V_{max}}$

علاقة س

$\frac{1}{[S]}$ Vs $\frac{1}{V_o}$



↑ V_{max} تقل

← K_m تقل / ↑ affinity

↓ V_{max} تزداد

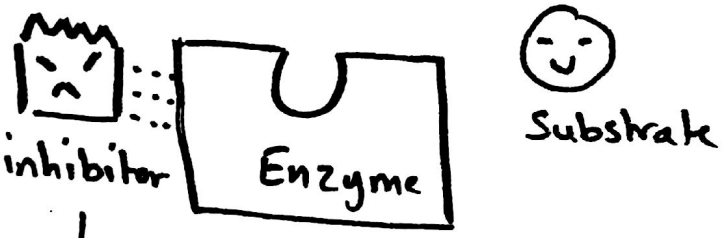
→ K_m تزداد / ↓ affinity

Inhibitors مواد تمنع عمل الانزيم

نوعين

↓ rate

عكسي Reversible



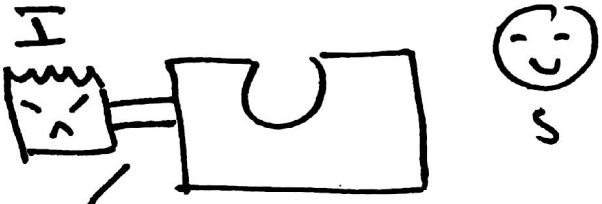
يرتبط By Non-Covalent Bonds

لذلك Bind & Break

⇒ Normal Enzyme Can be regenerated

يولد من جديد

غير عكسي Irreversible



يرتبط By Covalent Bond

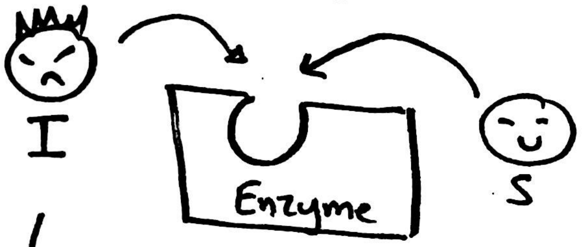
⇒ Normal Enzyme Can NOT be regenerated.

ترتبط بروابط غير تساهمية

Reversible Inhibitors

نوعين اساسية

تنافسي
Competitive



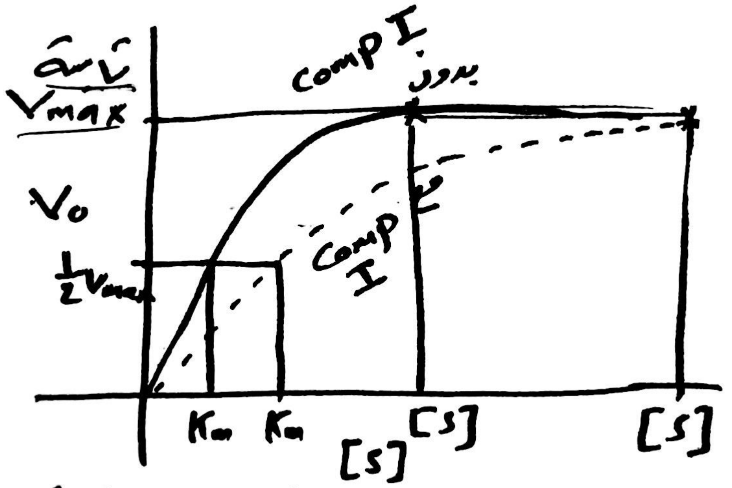
→ has similar Structure to Normal Substrate and bind to the Same site (active Site)

ترتبط فقط مع Free enzyme

ولا ترتبط مع E-S complex

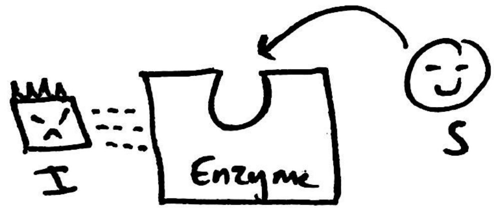
Vmax Constant

Km increase



يمكن التغلب عليها عن طريق زيادة [S]

غيرتنافسي
Non-compititive

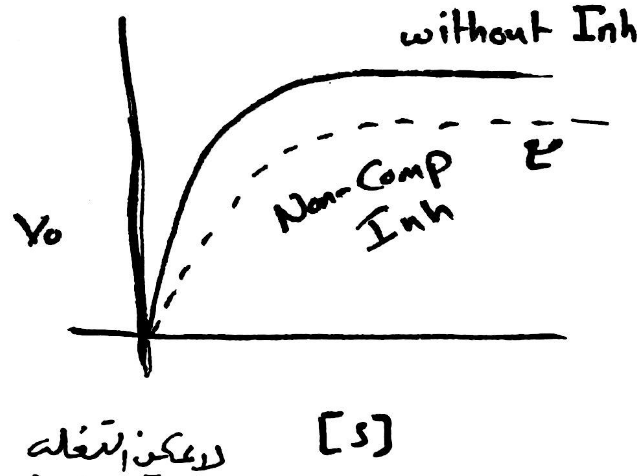


* Inhibitor differ from Substrate
* Bind to other site

Non-comp Inhibitors ترتبط مع Free-Enzyme and E-S complex

↓ Vmax

Km Constant

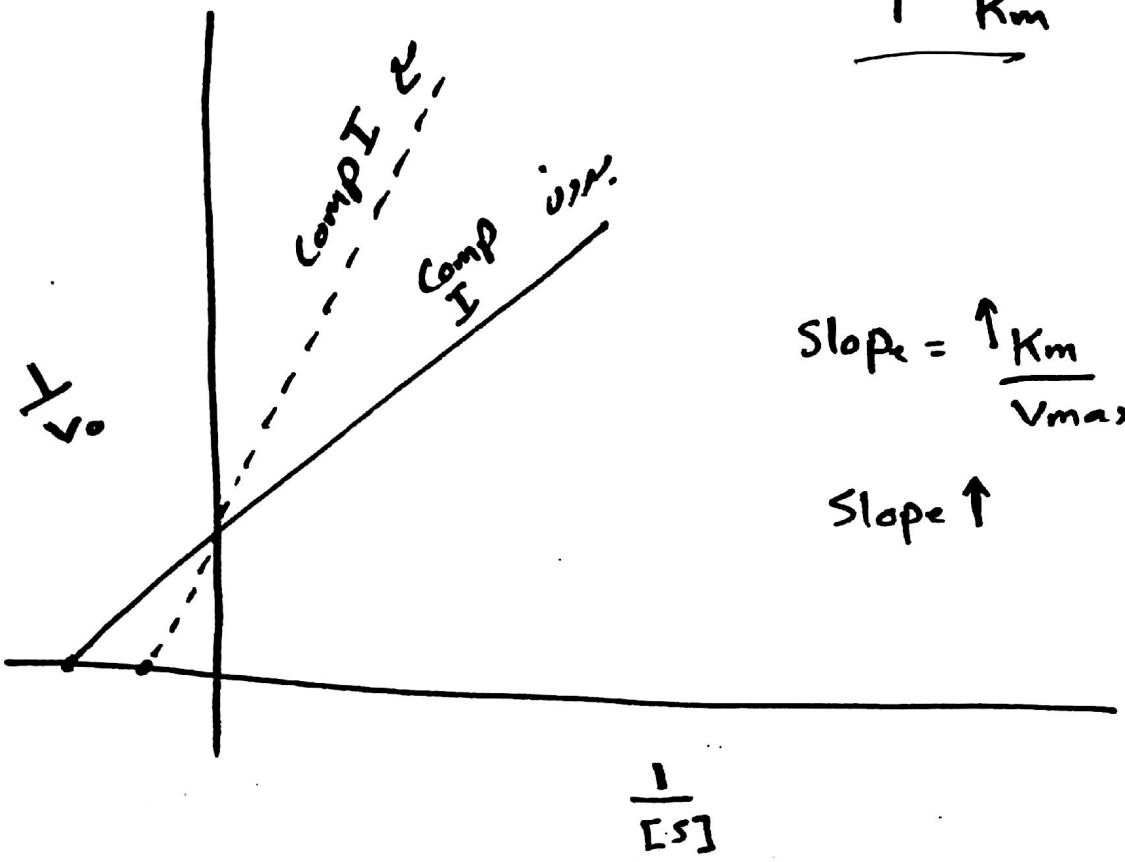


لا يمكن التغلب عليها بزيادة [S]

Competitive Inhibitors

V_{max} Constant

↑ Km



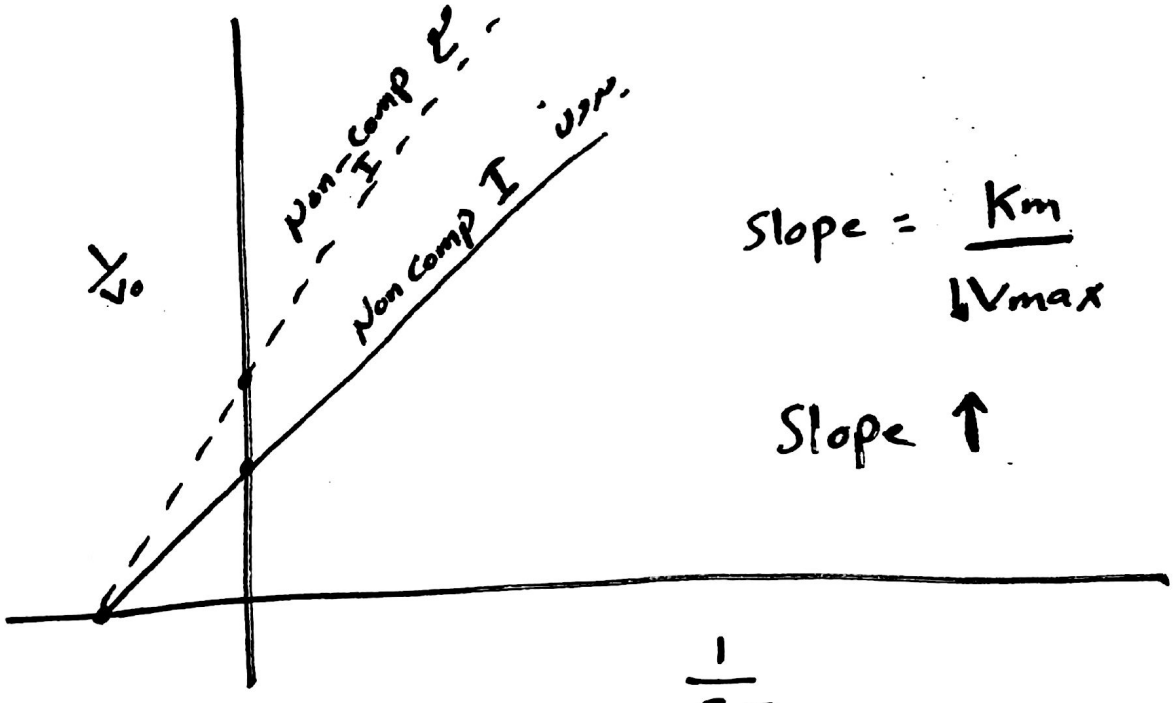
Slope = $\frac{\uparrow Km}{Vmax}$

Slope ↑

Non-Competitive Inhibitors

↓ Vmax

Km Constant

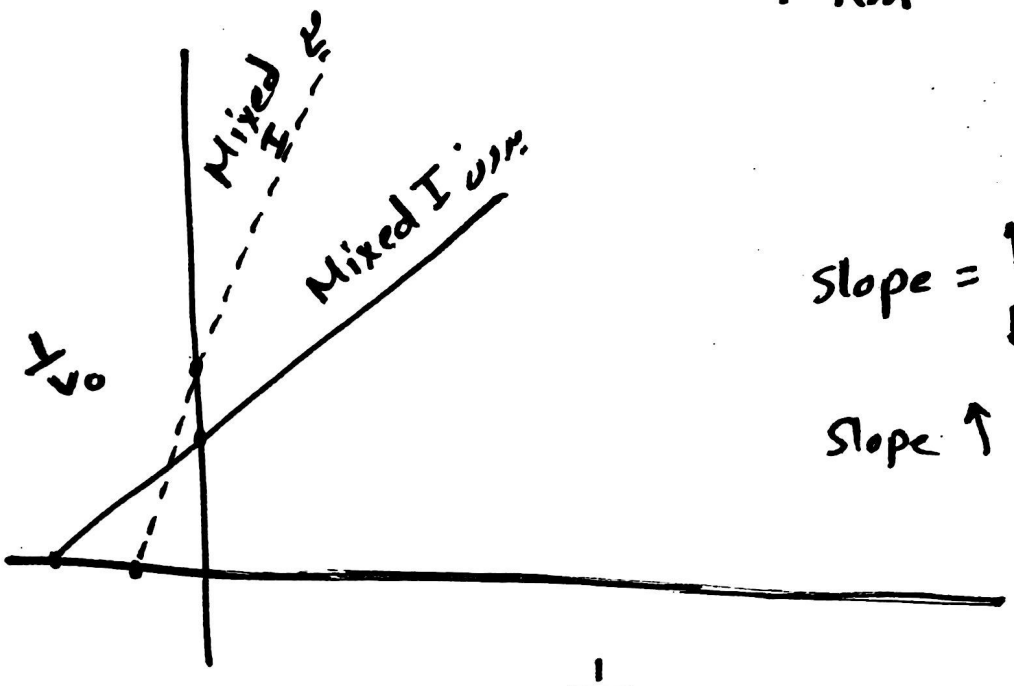


Slope = $\frac{Km}{\downarrow Vmax}$

Slope ↑

Mixed Inhibitors

↑ Km ↓ Vmax



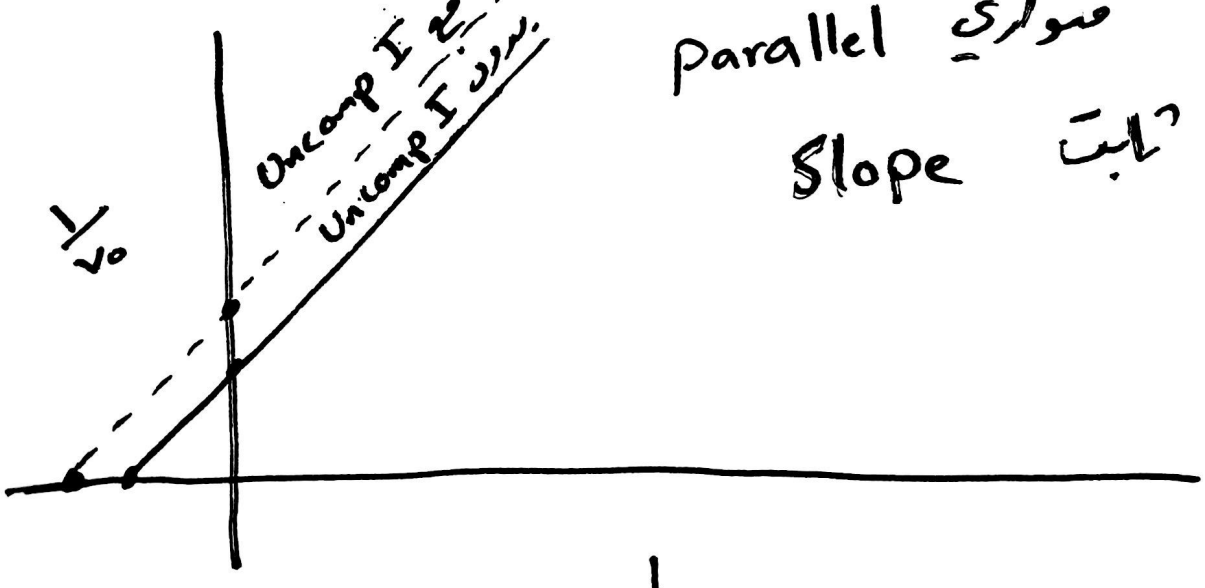
$$Slope = \frac{\uparrow Km}{\downarrow Vmax}$$

Slope ↑

Uncompetitive Inhibitors

↳ Bind to E-S complex Not to Free Enzymes

↓ affinity ↓ Km ↓ Vmax



parallel متوازي

Slope ثابت

Turnover #: Kcat or Kp

is numbers of moles of substrate react per second

عدد مولات الـ S التي تتفاعل في الثانية

Unit: per sec (sec^{-1})

↑ Kcat ↑ Efficiency of the enzyme

Table 6.2

Turnover Numbers and Km for Some Typical Enzymes

Enzyme	Function	k_{cat} = Turnover Number*	K_M**
Catalase	Conversion of H_2O_2 to H_20 and O_2	4×10^7	25
Carbonic Anhydrase	Hydration of CO_2	1×10^6	12
Acetylcholinesterase	Regenerates acetylcholine, an important substance in transmission of nerve impulses, from acetate and choline	1.4×10^4	9.5×10^{-2}
Chymotrypsin	Proteolytic enzyme	1.9×10^2	6.6×10^{-1}
Lysozyme	Degrades bacterial cell-wall polysaccharides	0.5	6×10^{-3}

* *The definition of turnover number is the moles of substrate converted to product per mole of enzyme per second. The unites are sec^{-1}.

* **The units of KM are millimolar.

Michaelis-Menten equation فرضيات معادلة خلال اشتقاق

at steady state

Rate of E-S complex formation = Rate of E-S complex Breakdown

* Very little E-S complex present, but it's concentration stay the same at steady state

- $V_{max} = K_2 [E]$ هذا يعني ان Vmax تعتمد على تركيز الانزيم
- $K_m = K_{eq}$ only when $K_{-1} \gg K_2$