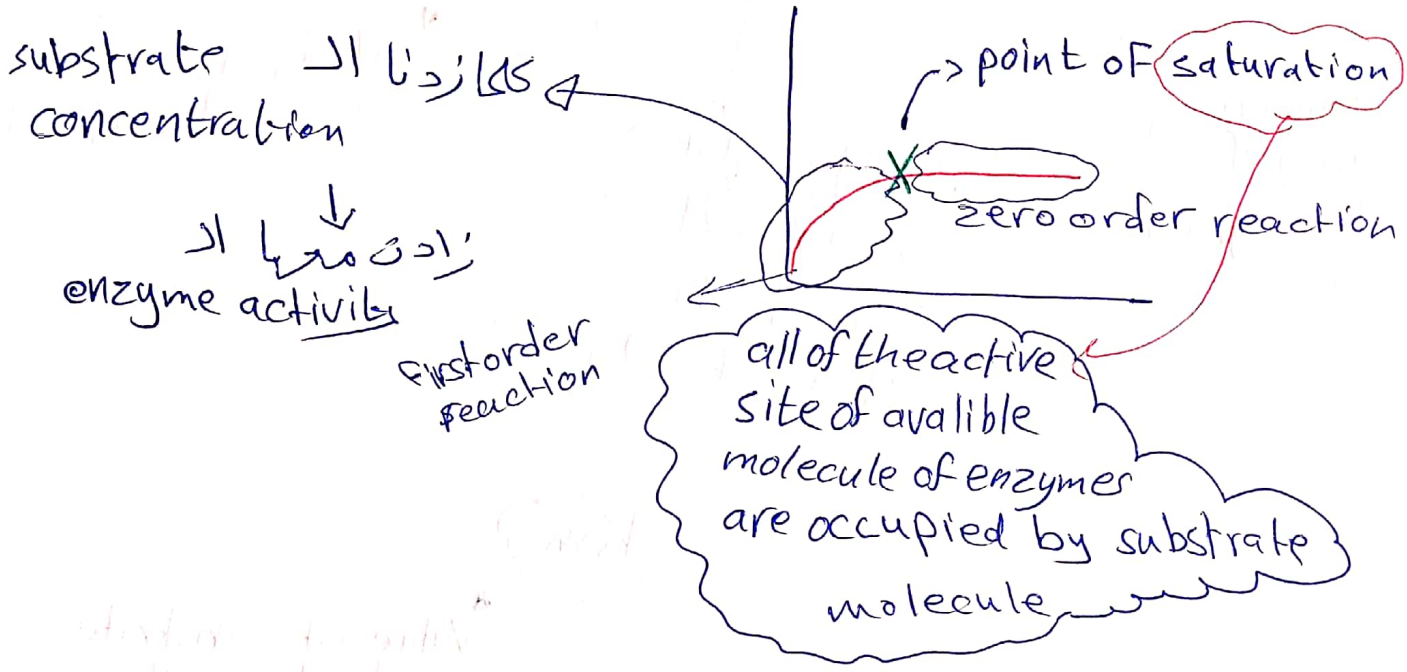
⊕ رح نحكي أولاً عن [Effect of subtrate concentration]

*) hyperbolic curve ← هو الكيرف اللي بيبين العلاقة بين [rate of enzyme activity] و [subtrate concentration]

← سبب الحنية :

consisted of two portion

→ first part of curve in which there is a direct relation between the activity of enzyme and subtrate concentration



zero order reactions : its show no relationship between substrate concentrate and activity of enzyme

Michaelis - Menten equation (Kinetics)

توضيح لاحقاً

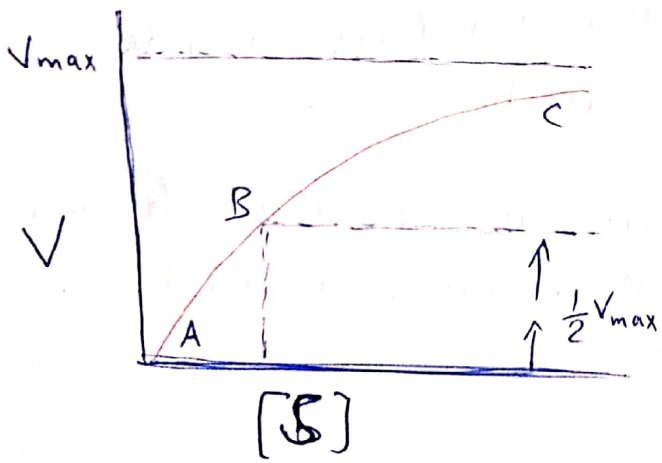
quantative description of the relationship between substrate concentration and rate of the enzymatic activity

انزيمنوا → each enzyme molecule is going to catalyze one reaction

each enzyme molecule is going to convert one substrate molecule into one product

$$V_1 = \frac{V_{max}[S]}{K_m + [S]}$$

- V_{max}: maximum activity of the enzyme
- K_m: حاصل جمع كل الثوابت الي كنا (٤) (K1) - (K-1) (K2) - (K-2)
- $[S]$: substrate concentration



Km → Value of substrate concentration when the activity of the enzyme is half the max.

← عندي ٣ فرضيات للكيرف السابق :

1) ٧ [S] < Km

[S] أقل من K

نعمل ignoring لل [S] لأنه
very little compared to the Km

$$V_1 = \frac{V_{max}[S]}{K_m} \rightarrow V_1 = K_1 [S]$$

constanant ← V_1 / K_m

2) [S] is very big compared to the Km

نعمل ignoring لل Km

$$V_1 = \frac{V_{max}[S]}{[S]} \Rightarrow V_1 = V_{max}$$

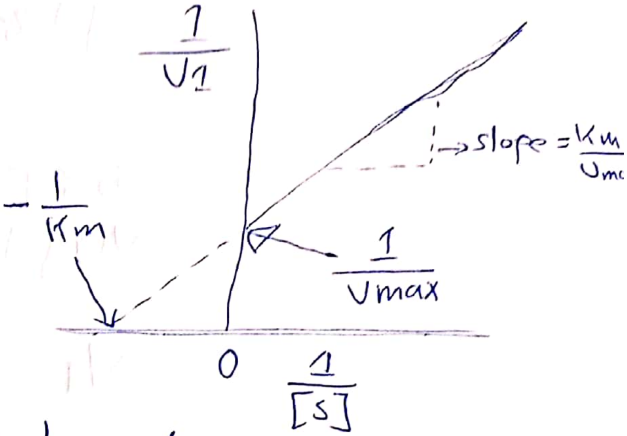
point of saturation يعني

3) [S] = Km

$$V_1 = \frac{V_{max}[S]}{2[S]} \Rightarrow V_1 = \frac{V_{max}}{2}$$

Lineweaver- Burk plot

types of curves :



1) linear

كل ما يزيد متغير يزيد المتغير التابع له

2) hyperbolic → ~~zero~~ first order reaction
→ zero order reaction

3) s-shaped curve (sigmoidal curve) : يكون زي حرف ال (S)

→ at point of saturation we can't take any value.

Lineweaver : inversion of equation

~~$Vi = \frac{Vmax[S]}{...}$~~

$$\hookrightarrow Vi = \frac{Vmax[S]}{Km+[S]} \xrightarrow{invert} \boxed{\frac{1}{Vi} = \frac{Km+[S]}{Vmax[S]}}$$

factor ↓

$$\boxed{\frac{1}{Vi} = \frac{Km}{Vmax[S]} + \frac{[S]}{Vmax[S]}}$$

simplify ↓

$$\boxed{\frac{1}{Vi} = \left(\frac{Km}{Vmax}\right)\frac{1}{[S]} + \frac{1}{Vmax}}$$

ما بيعمل ignore لأي
قيمة كانت غير منطقية
متطابقة

تذكير

Km : substrate concentration when the activity of enzyme is half Vmax

ما أهميته

1) specific and constant for a particular enzyme

* لو قسنا Km لكل انزيم رح نلاقي لكل انزيم Km خاصة فيه

* متى مثلاً لو عندنا [two enzyme acting on the] same substrate

under defined شرط واحد : conditions of time ~~understan~~ temperature and pH

2) determines the affinity of an enzyme for its substrate

يعني what is the amount of substrate needed to give the enzyme in x maximum activity

← كلما كانت كمية ال (substrate) المطلوبة كي أتوصل ال enzyme لـ maximum activity كلما كانت أقل affinity أعلى

علاقة عكسية بين substrate و affinity

*) by the knowledge of the Km we can detect a particular enzyme and we can detect particular substrate → [Km is constant and specific]

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*Enzyme inhibition → don't mean ~~that~~ stopen the activity of enzyme

* it's means reducing the activity of enzyme by chemical molecule

inhibitor

Irreversible

if the inhibitor is binding to a functional group in the active site of the enzyme by covalent bond or noncovalent bond stoping the activity of enzyme

reversible

binding with loosly bonds

washed away from solution.

*) inhibitors can be classified according to 3 bases:

A) whether they modified the enzyme chemically or not

B) site of action of inhibitor

C) kinetic parameters to be affected by inhibitors

- Vmax
- Km
- Vmax / Km

→ We have six different types of inhibitors

* competitive
* Non competitive
* uncompetitive
* suicidal
* Allosteric
* feed back

→ Competitive enzyme Inhibition

* competition between substrate and inhibitors

→ where the inhibitor is going to bind ? to active site

← عشان نحكي انه هذا ال [inhibitors] من نوع [competitive inhibitor]

↳ must be similar to the shape of substrate and both can bind to the active site

← مين غير رح يكون binding ؟

→ the higher concentration the easy to bind to the active site.

← كان في تفاعل هنا وال [substate] ثابك ال [active site] وال enzyme activity ثابتة . وبعدين اضفنا inhibitor شبيه تركيب ال substrate وكان تركيز inhibitors أعلى من تركيز substate ← رح يعمل ايه ؟؟؟؟

it will displace the substrate from the active site and the activity of the enzyme going down gradually

في حال صار تركيز substrate أعلى من تركيز inhibitor
رح يصير ايش ؟؟!!!

it will displace the inhibitor from the active site and going up with the reaction again

where they will be bind ← (الصراع عاشو)

صاحب التركيز الأعلى هو اللي رح يكسب التنافس

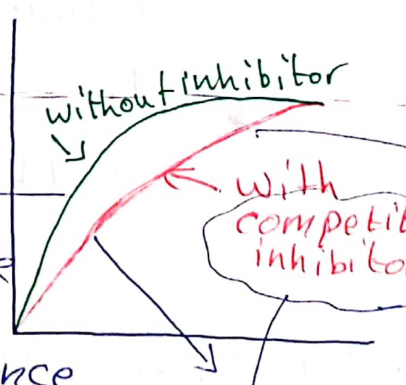
ملاحظة ← عشان نحكي انه في عنا [competitive inhibitor]
لازم يكون اله صفات عندنا

- similar to the structure of substrate
- they are both binding to the active site but not in the same time

الي تركيزه أعلى هو الي خابط ال active site

→ which type of kinetics will be affected?

Km



inhibitor ما في
→ so, there is increase on the activity of the enzyme and responce to the increase of substrate concentration

going down with the activity of the enzyme

acting on one kinetic

Km with inhibitor > Km without inhibitor

* سواء في inhibitor أو ما في inhibitor
the reaction will go to the same Vmax

*) the precense of inhibitor
is decrease the affinity of enzyme
to its substrate

رح يحتاج الكـ concentration أكثر من الـ substate

(why) ↳ to go back to the original activity

(راجع الجدول الموجود الي بالسلايد)

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*) Non competitive enzyme inhibition

→ no similarity and the structure between
inhibitor and substrate

* where the inhibitor is going to bind?
another site

كيف بشتغل الـ inhibitor ؟

→ decreasing the affeciency
of the enzyme to convert
substrate into product

→ will not affect to [Km]

* uncompetitive inhibition

→ no similarity between inhibitor and the substrate

↳ the inhibitor is not going to bind in the active site and going to bind on the another site

* where the inhibitor is going to binding?

→ very close to the active site

← ارتباط ال substrate ك ال active site في حالة ~~uncompetitive~~

uncompetitive inbitor is very difficult

← كما يتحول ال substrate الى product في هذا النوع

من ال Inhibitor ← it is not easy to be released from the active site

هذا النوع inhibitor ← is not binding to enzyme alone

راجع الرسمة الموجودة بالسلايدات

انتحاري

*) suicidal inhibition

inhibitor الي بعمل enzyme ← بتتعب

inhibition → not active

activation بعمل enzyme ال

naive enzyme

بتحول inhibitor بتحول

not active → active (irreversable)

medical application:

→ difluormethyl ornithine : used for suicidal inhibition of ornithine decarboxylase enzyme

- stop cell division → antiparasite طفيلي
- essential for cell division

→ Allopurinol : treatment for gout التهاب المفاصل

*) coffee and tea are cause gout

*) Aspirin

acetylate group → ترتبط مع serine in the active site of the cyclo-oxygenase enzyme → تعمل acetylation

↳ antiflammatory

*) Disulfiram : treatment of alcoholism

اسيلك مشكلة الاشخاص اللي بشربو الخمور ؟ وليش بصير معهم cancer liver

← لانه المادة الفعالة في ال alcohols هي ال ethanol

↳ after drinking alcohols will go to liver عشان تتحول ل acetaldehyde

↳ no inhabitory effect on central nervous system

1) fatty liver
2) transformation of cell
3) cancer liver

الحل: نوقف oxidation of aceteldehyde by using disulfram