two Diagrams present

Moderate level

1) Valproic Acid is a Short chain fatty acid, used in psychiatric Disorders

It Acts on GABA levels in the Brain, Blocks Histone deacytlase inhibitor, and Blocks Voltage gated ion channels.

GABA is formed from αKG in the TCA cycle. Valproic Acid inhibits GABA transaminase and succinate semialdehyde Dehydrogenase, which Degrades GABA

Valproic Acid Also has Anti-epileptic properties By Blocking Voltage gated Sodium & Ca^{2+} channels, To Decreasing the Freqency of firing of neurons
It has Also Been shown to inhibit HDAC1 which increases the expression of Apoptosis and anti tumor action.

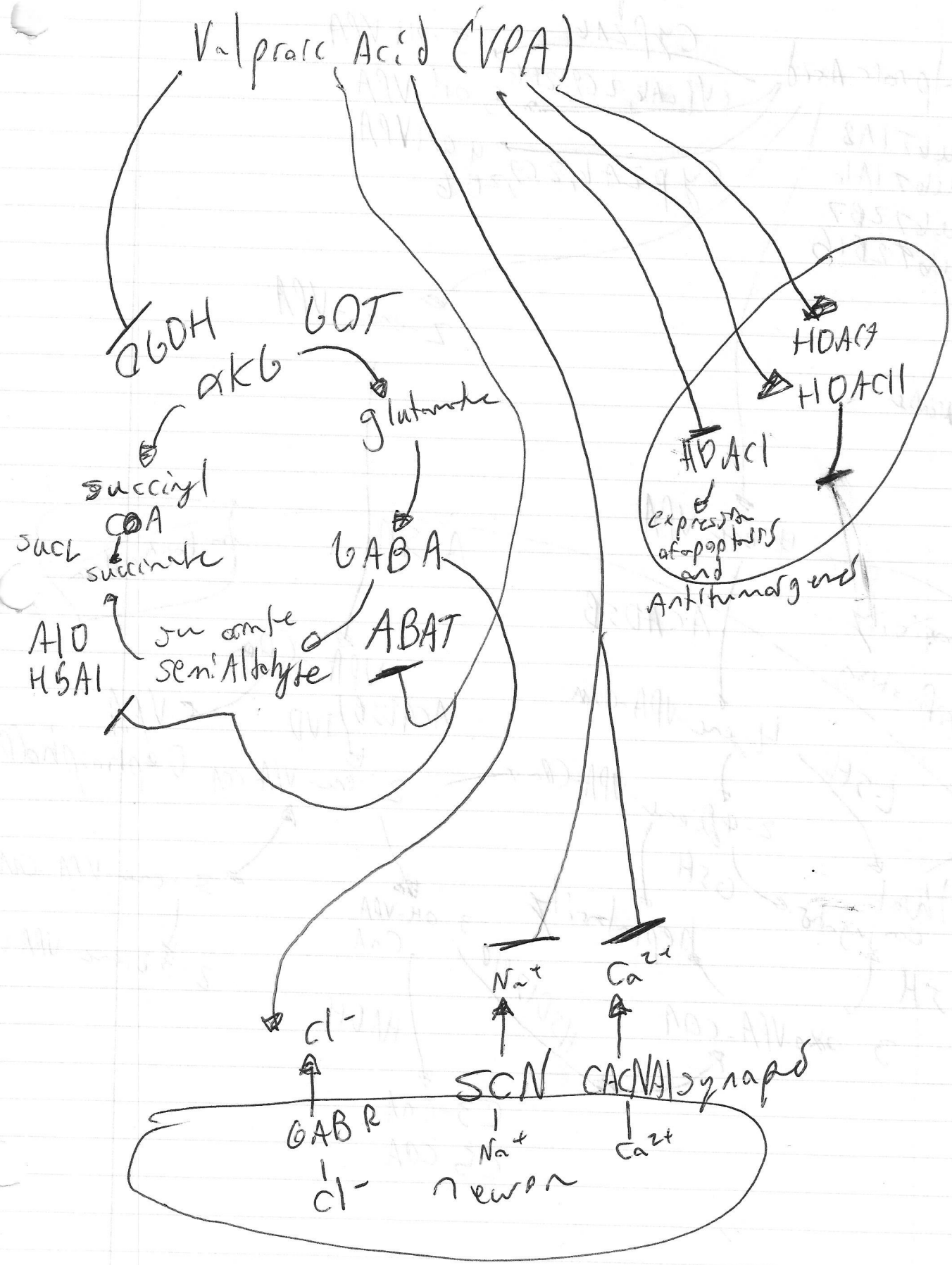
knows VPA is a highly (87-95%) Bound protein Resulting in low clearance.

3 Mechanisms for metabolism, Glucoronidation, Beta oxidation in the mitochondria and Cyp450 mediated oxidation (this is minor role however).

The Valproate Glucoronide is the major Metabolite 30-50% excreted in the urine.

It also can Be brought into the liver w a carnitine shuttle. Then through Beta oxidation it is Broken Down to several metabolites,
A slow hydrolysis by an Acyl CoA thioesterase creates 3-oxo-VPA which is ~~an endproduct~~ then used By a thiolase which turns it into a thial conjugate

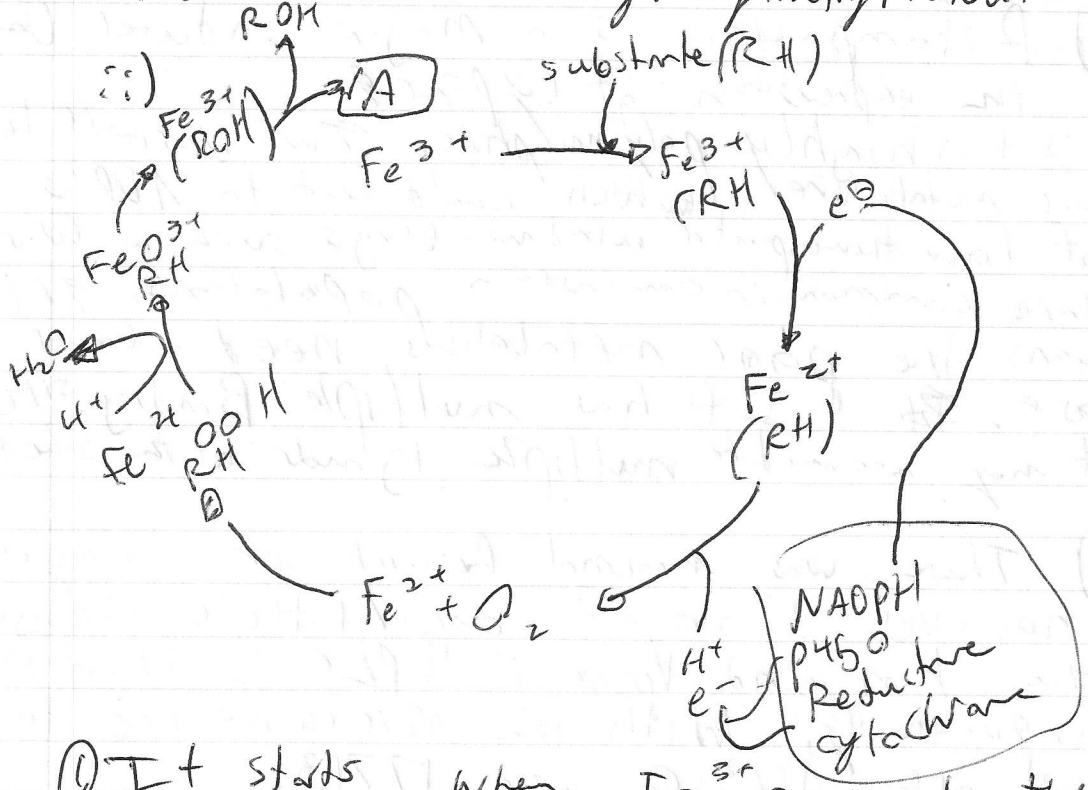
pharmacodynamics



Cyp 2C9

(2)

:) It is a phase I drug metabolizing cytochrome P450 enzyme isaform that is primarily expressed in the liver and has the 2nd highest expression of all CYP isaforms. It is Responsible for 15-20% of all Drugs in the phase I of Detoxification. It is known to metabolize Tolbutamide to hydroxymethyltolbutamide.



(1) It starts when Iron 3+ Binds to the Iron the Iron Becomes Reduced to Fe^{2+}.

(2) O_2 then Binds to the enzyme

(3) O_2 is then Activated in a 1 electron Reduction A single O_2 Atom is Dissociated with an Oxidation of Iron and protonation of complex involves H_2O leaving

The Remaining O Atom is highly energetic and Reacts with substrate, which then leaves

3) Aminoglycosides and Nephrotoxicity.

The Dose are several Days of 10 to 20mg/kg of Body weight is the therapeutic Dose They change the lysosomes of the proximal tubule. This effects the Reabsorption of many minerals such as Mg^{2+} Ca^{2+}, K^{+} and also CASTS, phospholipid, and glucose in excretion, If continued Daily use occurs then it can lead to Acute Renal failure.

If high Doses of 40mg/kg Are achieved then Cortical necrosis and Renal dysfunction occur Rapidly.

While tubular Necrosis is evident the Mechanism of how it happens is unknown though several mechanisms are found potentially to be the source. The Damage is usually Reversed After it has Been Done, as toxicity is achieved Rapidly

As stated it would greatly Decrease the Reabsorption in the proximal tubules leading to Dehydration, polyuria, hypotension, Nausea, Fatigue, weakness. This is because the Blood volume is Decreasing Dramatically and you are losing sugar cells, Blood, and Ions. These are all Crucial for function Due to 90% of Reabsorbtion occuring at the proximal convoluted tubule it will cause large Distress.

It is largely eliminated By glomerular filtration.

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