# Carbonic anhydrase the fastest enzyme biology essay

Design

Carbonaceous anhydrase, abbreviated as CA, is the first identified Zn incorporating enzyme, ( CA ; carbonate hydro-lyase, EC 4. 2. 1. 1 ) It is an enzyme that catalyzes the reversible hydration and desiccation of C dioxide to organize carbonaceous acid, bicarbonate ions and protons.

Bing one of the fastest enzyme known, it is believed that one molecule of CA can treat one million molecules of C dioxide per second. The basic molecular construction of CA includes specific amino acerb threonine 199, glutamate 106, histidine 64 and histidine residues viz. His 93, His 95, and His 118. The manner of ordinance of CA is being inhibited by assorted medically prescribed substances that act as non competitory inhibitors, an illustration is Acetazolamide. CA plays a major cardinal function in the fluid balance and regulative of pH in different parts of the organic structure therefore, Mutation of this enzyme may take to several diseases.

( 1 )

# CARBONIC ANYHYDRASE

## THE START: Breathing, a cardinal map in life

The air that we breathe in has some valuable O, an of import molecule wherein it helps the dislocation of fats and sugars in our cells. From the blood, O diffuses so binds with the haemoglobin to be transported in the cells of our organic structure. A by merchandise of sugar and fat dislocation in cells is called Carbon dioxide CO2 ) . It is a cardinal metabolite in all life being and it needs to be removed from our organic structure. Carbon dioxide is diffuse out of the cells and transported in the blood in different ways to acquire to the lungs. CA is transported in legion signifiers, chiefly as

hydrogen carbonate, HCO3- . Bicarbonate is a CO2- with an affiliated OH group. When the HCO3- reaches the lungs, it is transformed back to a CO2, so it can be exhaled from the organic structure.

The transition of hydrogen carbonate to carbon dioxide facilitates its conveyance into the cell ; while the transition of C dioxide to bicarbonate aids trap the C dioxide in the cell. This interconversion of C dioxide and hydrogen carbonate develop at a slow physiological pH hence being tend to bring forth an enzyme to rush the procedure. This enzyme responsible for the velocity up interconversion, which can be found in the ruddy blood cells, is called carbonaceous anhydrase. Although the interconversion of hydrogen carbonate to carbon dioxide can go on without the enzyme, CA can great increase the rate of the transitions up to a 1000000s of crease. ( 2 )

## Structure

The CA molecule in general has ellipsoidal form with the estimated dimension 4. 1 ten 4. 1 ten 4. 7 nanometer.

The active site is situated in a pit holding an about conelike form. The pit is assessed 1. 5 thousand broad at the manner in and about 1. 6 nm deep attaining about the centre of the molecule. The Zn ion is following to the extremum of the cone and liganded into 3 imidazole groups. Figure 1. Calcium Structure ( 2 )Figure 1. shows the construction of CA.

Taken as a whole, is composed of 10-stranded anti-parallel beta-sheet enclosed with assorted elements of other secondary construction. The 6 alpha-helices and 10-beta sheets make up the secondary construction of

carbonaceous anhydrase. The basic map of CA is fundamentally to modulate the O and C dioxide content of the blood that is needed in a human organic structure.

As the map suggests, the chemical construction of CA highly lies with the presence of Zn that lies deep within its active site. Its common amino acerb composing includes threonine, glutamate and histidine. The specificity of these 3 amino acids ( threonine 199, glutamate 106, and histidine 64 ) plays a critical function in relation to the presence of Zn by bear downing it with a hydroxyl ion. The Zn cation is associated with three histidine residue protein anchor viz. : His93, His95, and His118. As stated, zinc plays a major function in the reaction of CA. The Zn nowadays in the active side of CA is being bound to H2O to be able to disassociate it into a proton and hydroxyl ion. The hydroxyl ion is being stabilized by the positively charged Zn, in this manner ; the hydroxyl ion is being prepared to assail the C dioxide inside the RBC.

A closer expression with CA can be seen in the figure below where the amino acid ironss in the active site together with the Zn are apparent. The function of the Zn fundamentally includes the bid of directional transportation of the edge hydroxyl to the C dioxide to be able to organize bicarbonate ion. From the figure, it shows that the intermediate construction where the hydrogen carbonate ion is still attached to the enzyme. The alanine replicated the side concatenation for amino acid 199 in this agreement. Histidine 64 swings in the way of and off from the Zn ion in every rhythm of enzyme action although it is assisting the Zn to reload with a fresh hydroxyl ion. The two

locations of this residue, revealed in the bottom right figure, typify its motion throughout the action of enzyme. Almost instantly as the Zn is reloaded with an original H2O molecule together with the release of hydrogen carbonate ion, the enzyme is set for another action on some new C dioxide molecule.

( 3 )

## MECHANISM OF CATALYSIS

The rate of contact action of the CA is extremely pH dependant. It means that, the higher the pH, the contact action is faster and as the pH reduces, the velocity of the reaction falls down. The average pH of this passage is near pH 7. ( 5 )Figure 2.

Mechanism of CA contact action ( 6 )Figure 2. 0 shows the mechanism of CA contact action. A Zn atom which is by and large bound to four or more ligands differs in CA. In CA, three locations are occupied by imidazole ring of three histidine residues and an extra site is occupied by a H2O molecule. Thus the geometry signifier of the active site is tetrahedral.

The Zn atom plays an of import function in the mechanism of CA contact action because it is responsible for the release of a proton H+ from a H2O molecule, which so generates a nucleophilic hydrated oxide ion. Then the C dioxide substrate will attach to the active site of the enzyme to respond with the ion of hydrated oxide. The zinc-bound OH- onslaughts the C of CO2 therefore change overing it into a bicarbonate ion. This occurs since the Zn ion has the +2 charge, which attracts the O of H2O. It so deprotonates the

H2O, therefore, change overing it into a better nucleophile so that the freshly converted hydroxyl ion can assail the C dioxide.

After the nucleophilic onslaught of Zn bound OH- , add-on of H2O molecule displaces the hydrogen carbonate ion from the metal ion. The CA is so ready for another rhythm of contact action. ( 7 )

## KINETICS OF REACTIONS

CA inhibitors are category of pharmaceuticals that control the activity of carbonaceous anhydrase.

It is inhibited by two categories of compounds, a metal complex forming anions and others are isosteres and sulfa drugs. Inhibitors ionize upon adhering with the enzyme to give manner an NH- group that relocates the Zn hydrated oxide ions and portions a H bond. There are approximately 25 clinically used CA inhibitors as a drugs. It is chiefly established as antiglaucoma drugs, water pills, hypotensive agents, antiepileptics, anticancer agents, anticonvulsants, with extra usage in the direction of duodenal and stomachic ulcers, osteoporosis and neurological upset. ( 8 )AcetazolamideMethazolamideDorzolamideTopiramateFigure 3. Illustrations of some CA inhibitors ( 9 )Figure 3. 0 shows some CA inhibitors like Acetozolamide which acts as a mild diuretic. It cures glaucoma, height illness, and some benign intracranial high blood pressure.

Methazolamide treats glaucoma nowadays in Canis familiariss which is called Open-angle glaucoma. While Topiramate which is a weak inhibitor, alleviate epilepsy, lennox gastuat syndrome and megrim concerns. And another CA

inhibitor is the, Dorzolamide or sulphonamide which dainty optic high blood pressure or open-angele glaucoma. ( 10 )CA activator regulates the proton transportation processes between the active site and the dissolver system. It besides binds at the entryway of the enzyme of the active site. One of the strong activator of CA is Histidine. Some aminoalkanes and aminic acids like l-Trp ( tryptophan ) , l-Phe ( Phenylalanine ) , d-DOPA ( D- 3, 4-dihydroxyphenylalanine ) , l-Tyr ( Tyrosine ) , 4-amino-l-Phe besides works as activators of CA.

These CA activators are potentially aim for drug development that can be utile as a derived function for the sweetening of synaptic efficaciousness which can be able to handle assorted conditions like, depression, alzheimer ' s disease, ageing, spacial acquisition and memory therapy foil. ( 11 )

## MODE OF REGULATION: Acetazolamide Inhibitor

In instance of inordinate contents of CA in blood and peripheral countries of the lungs, proper ordinance and suppression is needed. Acetazolamide is a non competitory inhibitor that is effectual in giving control with the catalytic reaction of the enzyme. This chemical complex substance is medically used o dainty different conditions of moderate up to severe metabolic or respiratory alkalosis. Alkalosis may go on if extra CA is being reacted with the hydrogen carbonate and C dioxide ions in the RBC, doing utmost soaking up of hydrogen carbonate therefore giving the red blood cell more basicity instead than holding adequate and sufficient pH degree. Acetazolamide action is explained by interfering with hydrogen carbonate ( HCO3- ) resorption in the kidneys, thereby giving adequate sourness in the RBC, and

farther consequences to alkalinising the piss. The action of suppression consequences further to reduced synthesis of aqueous wit of the oculus and causes the lowering of intraocular force per unit area. The interaction of Acetazolamide with CA does non happen with the active site, merely near or remote to the active site.

The net consequence of this inhibitor fundamentally changes the form of CA that evidently leads to the inability of the substrate to adhere decently, consequences to no catalytic reaction. ( 12 )

## CARBONIC ANHYDRASE IN HEALTH AND DISEASE:

Carbonaceous Anhydrase is found in legion topographic points in the organic structure, including in the cerebro-spinal fluid, cytosol of some cells and chiefly in the ruddy blood cells. Since CA generates and utilizes protons and hydrogen carbonate ions, it plays a major cardinal function in the fluid balance and regulative of pH in different parts of the organic structure. Absence or mutant of the CA enzyme may take to several diseases.

Besides, CA inhibitor contributes to several interventions of diseases. One of the linked diseases of CA is the Osteopetrosis with intellectual calcification and nephritic acidosis. It is a syndrome deficient with CA in the organic structure normally called as Marble encephalon disease.

This happens because sulfonamide inhibitor of CA can bring forth metabolic acidosis and have shown that CA inhibitors blocks the parathyroid hormone-induced the release of Ca bone which causes bone reabsorption. And since CA is present in the encephalon and CA inhibitors inhibits the production of

intellectual spinal fluid, mutant of CA lead to intellectual calcification. Other disease associated with the lack of specific type of CAIII is the Myastenia gravis. It is an autoimmune neuromuscular upset that consequences to a weak musculus of a individual. Defects in CA IV can do retinitis pigmentosa, a devolution of retinal photoreceptor, which a patient experiences dark vision sightlessness and loss of midperipheral ocular. ( 13 )Glaucoma, a status wherein a physique up of fluid in the eyes occurs and this presses the ocular nervus that caused harm, is treated with the usage of CA inhibitors like acetazolamide, brinzolamide, dorzolamide, and methazolamide.

These inhibitors lessen the sum of fluid in the oculus quickly by 40 % to 60 % therefore take downing the force per unit area inside the oculus of a individual with glaucoma. It now lessens the hazard of ocular nervus harm which promote vision loss. But prolong usage of this drug affects the same enzyme in the tissue and may take to kidney and liver harmThe CA besides plays an of import function in the secernment of acid through the catalyzed hydration of excreted CO2 in the tummy liner which is chiefly responsible in digestion of nutrient. It helps to do pancreatic juice alkaline and our saliva impersonal. In drumhead, CA performs different function and maps at their specific locations. ( 14 )