Metabolism of carbohydrates

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- Advantages of metabolism:

(1) To provide energy as ATP

(2) Number of intermediate of glucose metabolism utilized in the synthesis of another compounds (amino acids or lipid)

(3) Glucose is utilized in the synthesis of other compound (polysaccharide or fructose)

(4) To generate NADPH as a reducing agent to synthesize another compound such as (lipid , nucleic acid)

Digestion of Carbohydrates

Dietary carbohydrates principally consist of the polysaccharides: starch and glycogen. It also contains disaccharides: sucrose, lactose, maltose and in small amounts monosaccharides like fructose and pentoses. Liquid food materials like milk, soup, fruit juice escape digestion in mouth as they are swallowed, but solid food stuffs are masticated thoroughly before they are swallowed.

1. Digestion in Mouth

Digestion of carbohydrates starts at the mouth, where they come in contact with saliva during mastication.

Saliva contains a carbohydrate splitting enzyme called salivary amylase (ptyalin).

Action of ptyalin (salivary amylase)

It is α - amylase, requires Cl- ion for activation and optimum pH 6-7. The enzyme hydrolyzes α-(1,4) glycosidic linkage at random from molecules like starch, glycogen and dextrins, producing smaller molecules maltose, glucose and maltotriose.

Ptyalin action stops in stomach when pH falls to 3.0

Starch or glycogen —α –*Amylase*→ Glucose, Maltose and maltotriose

2. Digestion in Stomach

No carbohydrate splitting enzymes are available in gastric juice. HCl may hydrolyze some dietary sucrose to equal amounts of glucose and fructose.

3. Digestion in Duodenum

Food reaches the duodenum from stomach where it meets the pancreatic juice. Pancreatic juice contains a carbohydrate-splitting enzyme pancreatic amylase.

Action of pancreatic Amylase

It is also an α - amylase, optimum pH 7.1. Like ptyalin it also requires Cl- for activity. The enzyme hydrolyzes α-(1,4) glycosidic linkage situated well inside polysaccharide molecule.

Other criteria and end products of action are similar of ptyalin.

1. Digestion in Small Intestine

Action of Intestinal Juice

a. pancreatic amylase:

It hydrolyzes terminal α-(1,4), glycosidic linkage in polysaccharides and Oligosaccharide molecules liberating free glucose molecules.

b. Lactase

It is a β- glycosidase, its pH range is 5.4 to 6.0. Lactose is hydrolyzed to glucose and galactose.

Lactose $\xrightarrow{lactase}$ *Glucose* + *Galactose*

Lactose Intolerance

Lactose is hydrolyzed to galactose and glucose by lactase in humans (by β- Galactosidase in Bacteria).

Some adults do not have lactase.Such adults cannot digest the sugar.It remains in the intestines and gets fermented by the bacteria.

The condition is called as Lactose intolerance.

Such patients suffer from watery diarrhea, abnormal intestinal flow and pains. They are advised to avoid the consumption of Lactose containing foods like Milk.

C. Maltase

The enzyme hydrolyzes the α -(1,4) glycosidic linkage between glucose units in maltose molecule liberating two glucose molecules. Its pH range is 5.8 to 6.2.

Maltose ***Maltase*** Glucose +Glucose

….. ……..

D. Sucrase

PH ranges 5.0 to 7.0. It hydrolyzes sucrose molecule to form glucose and fructose.

Sucrose ***Sucrase*** ***Glucose + Fructose***

.....

Absorption of Carbohydrates

Products of digestion of dietary carbohydrates are practically completely absorbed almost entirely from the small intestine.

Absorption from proximal jejunum is three times greater than that of distal ileum. It is also proved that some disaccharides, which escape digestion, may enter the cells of the intestinal lumen by "pinocytosis" and are hydrolyzed within these cells.

No carbohydrates higher than the monosaccharides can be absorbed directly in to the blood stream.

Mechanism of Absorption

Two mechanisms are involved:

1. Simple Diffusion

This is dependent on sugar concentration gradients between the intestinal lumen. Mucosal cells and blood plasma. All the monosaccharides are probably absorbed to some extent by simple 'passive' diffusion.

2. “Active “Transport Mechanisms

• Glucose and galactose are absorbed very rapidly and hence it has been suggested that they are absorbed actively and it requires energy.

• Fructose absorption is also rapid but not so much as compared to glucose and galactose
but it is definitely faster than pentoses. Hence fructose is not absorbed by simple
diffusion alone and it is suggested that some mechanism facilitates its transport, called as” **facilitated transport”.**

Digestion and absorption

- The source of the diet of carbohydrates, starch , glycogen as polysaccharide . Fructose , glucose as monosaccharide. Lactose , sucrose & maltose as disaccharides.
- In the mouth there is an enzyme called salivary amylase catalyze hydrolysis of starch and glycogen to produce disaccharide (maltose) .

- In the stomach there is no digestion for carbohydrates takes place because PH=(1-2) which inhibits the activity of salivary Amylase (due to changes in PH in stomach)
- In small intestine and due to the secretion of pancreatic enzyme (pancreatic Amylase) which catalyze hydrolysis of the starch and glycogen to convert it in to maltose.

- The maltase, iso maltase , sucorase & lactase hydrolyze disaccharides
- After the action of all these enzymes on the CHO ,the CHO converted into monosaccharide mainly as glucose in addition to galactose & Fructose..

Absorption

- The glucose unit is absorbed passively into portal vein to the Liver which represent the major site for metabolism of CHO.

Metabolism of glucose:

- Fructose and lactose in their metabolism converted into glucose . After glucose ingestion blood glucose circulation was elevated and this lead stimulated the Beta cell of pancreas to secrete (Insulin)
- One of the mechanism of the Insulin action is to increase the uptake of glucose by tissues. The tissues and organs need Insulin are : Adipose tissue & lens of the eye , Aorta , Skeletal muscle , Lactic gland ; while in RBCS , Brain & Liver act without Insulin

GLYCOLYSIS

Oxidation of glucose or glycogen to pyruvate and lactate is called glycolysis.

It occurs virtually in all tissues. Erythrocytes and nervous tissues derive its energy mainly from glycolysis.

This pathway is unique in the sense that it can utilize O2 if available (‘aerobic’) and it can function in absence of O2 also (‘anaerobic’)

Aerobic Phase

Aerobic phase includes the conversion of glucose to pyruvate

Oxidation is carried out by dehydrogenation and reducing equivalent is transferred to NAD.

NADH + H+ in presence of O2 is oxidized in electron-transport chain producing ATP.

- **Anaerobic Phase**

This phase includes the conversion of Glucose to lactate

NADH cannot be oxidized, so no ATP is produced in electron transport chain. But the NADH is oxidized to NAD+ by conversion of pyruvate to Lactate, without producing ATP.

Anaerobic phase limits the amount of energy per molecule of glucose oxidized. Hence, to provide a given amount of energy, more glucose must undergo glycolysis under anaerobic as compared to aerobic.

A. Enzymes

Enzymes involved in glycolysis are present in cytoplasm.

Glycolysis

- A series of reactions in which the glucose is converted to pyruvate (pyruvic acid) and lactate (lactic acid)
- ATP is released and the glycolysis occurs even in absence of oxygen (an aerobically)

{1} **Glucose + ATP** $\xrightarrow[Mg^{+2}\ (\text{Co –factor})]{\textbf{Hexo kinase(HK)}}$ **g.6.p+ADP** (-1 mole of ATP)

- This reaction is irreversible to reverse it by using of (g.6.p ase) enzyme that bring out the ‘p’ to give free glucose.
- Explain Why the body convert glucose into g.6.p???
- The benefit of this reaction is to generate g.6.p that is impermeable of cell membrane as well as to activate glucose.

- In heavy exercise an aerobic glycolysis occur??
- Because there is not enough oxygen.
- Another enzyme called “GK” (glucokinase) catalyze hydrolyze the same reaction N1 but there is some differences between “GK” & “HK”

- GK is present in Liver .
- HK is present in all tissue including the Liver.
- HK has high affinity and low Km (constant).
- GK has low affinity and high Km value

Note: low affinity means it acts with increased glucose concentration

- . Substrate specifity of GK is extremely high because it acts only on glucose
- HK acts on glucose and another hexose (galactose,fructose) so less specific.
- HK is inhibited by excess amount of ATP and g.6.p.

- G.6.p is channeled in their metabolism to give:

→ F.6.P → Glycolysis

(2) transfer → g.1.p → Glycogen synthesis

(3) oxidize → Gluconlacton .6.p → Pentose (pentose pathway)

(4) (g.6.p) → Free glucose

(In the Liver)

(2) g.6.p $\underset{\longleftarrow}{\xrightarrow{\text{isomerase}}}$ F.6.p { 0 mole ATP}

(3) F.6.P+ ATP $\xrightarrow[\text{Mg+2}]{\text{P.F.K(phospho-fructokinase)}}$ F.1,6.diphosphate+ADP {-1 mole ATP}

#This reaction is irreversible control glycolytic pathway and it is the slowest reaction , also it is rate limiting step.

#P.F.K is inhibited by excess of ATP ,ADP and citrate, however it is stimulated by AMP.

to reverse this reaction by F.1,6 diphosphatase

#if the glucose not used , it will be convert to glycogen to be stored

(4) F.1,6biphosphate $\xrightleftharpoons{\text{Aldolase}}$ Dihydroxy aceton phosphate (D.H.A.P) +

Glycero aldehyde 3 phosphate(G.A.3.P)

ATP= 0 mole

why in insulin deficiency citric acid cycle inhibited??

A// due to less amount of oxalo acetate

Glucose → pyruvate → oxalo acetate

(5) D.H.A.P $\xrightleftharpoons{\text{phosphotriose isomerase}}$ G.A.3.P

ATP= 0 mole

(6) G.A.3.P+H3PO4+NAD$^+$ $\xrightleftharpoons{\text{dehydrogenase}}$ 1,3 diphospho glyceric acid + NADH + H +ATP

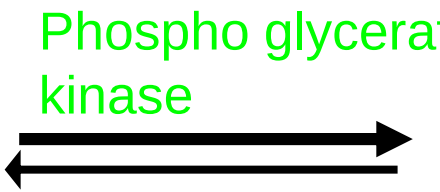
2 or 3 mole ATP $\longrightarrow$ X2=4 or 6 ATP aerobic

This reaction is very important in aerobic but can not happened with out oxygen

- Inhibited by iodo acetate
- Occur in present of phosphate.
- In present of Arsenic , this reaction inhibited
- Important from this reaction if we re-oxidize the NADH by FAD we generate 2 mole of ATPx2 =4 mole. But if we oxidize by NAD we generate 3ATPx2=6 mole of ATP.

- Each molecule of CoA oxidized in citric acid cycle generate 12 mole ATPx2=24 from acetyl CoA

(7) 1,3 diphospho glyceric acid + ADP



ATP + 3 phospho glyceric acid + 1 mole ATPx2

This is the first reaction that generate free energy as ATP (an aerobic)

Phospho glycerate Mutase

(8) 3 p .glyceric acid ⇌ 2.p.glyceric acid

ATP = 0 mole

Enolase

(9) 2.p.glceric acid ⇌ Phospho enol pyruvate (P.E.P)

Mg+2

Mn+2

ATP= 0 mole

#This enzyme is inhibited by fluoride because F form a complex with Mg^{+2} to give MgFP complex

(10) P.E.P + ADP $\xrightarrow[\text{Mg+2}]{\text{Pyruvate kinase}}$ Pyruvic acid + ATP

1 mole ATP x 2 =2 ATP (an aerobic)

(11) Pyruvate + NADH + H^+ $\xrightarrow{\text{LDH}}$ Lactate + NAD^+

- Muscle does not give us the glucose because it has no g.6.p ase. But the liver can do that because it has g.6.p ase
- The importance is to generate NAD & recycle the reaction No.6
- Muscle gives lactate to the circulation
- Liver takes lactate and convert it to pyruvate.
- Net energy = +2 mole ATP

- This reaction occur (an aerobic) inside the muscle gives us an explanation that is the glucose is converted to lactose, secreted from the muscle and taken up by the liver and then in the liver converted into pyruvate.

(12) Pyruvate + CoA -SH + NAD^+ —(T.P.P complex enzyme / dehydrogenase)→

Acetyl CoA + CO_2 + NADH + H + 3mole ATP

X2 = 6 mole ATP (aerobic)

(13) Acetyl CoA + oxalo acetate $\xrightleftharpoons{\text{Citrate synthase}}$ Citrate (C.A.C) + CoA-SH

0 mole ATP

Products of pyruvate :

Metabolize into (1) lactate (2) Alanine (3) oxalo acetate (4) malate

(5) Acetyl CoA-SH

After formation of Acetyl CoA it will

enter in a series of reactions

inside the mitochondria in aerobic conditions & within a cycle called citric Acid cycle.

Entry of fructose in to glycolysis:

Liver contains specific enzymes fructokinase. It converts fructose to fructose 1 phosphate in the presence of ATP. In liver fructose1-phosphate is split to glyceraldehyde and dihydroxy acetone phosophate by AldolaseB.

Glyceraldehyde enters glycolysis, when it is phosphorylated to glyceraldehyde-3-P by triose kinase.

Dihydroxy aceton phosphate and glyceraldehyde-3-P may be degraded via glycolysis or may be condensed to form glucose by aldolase.

Lack of fructose kinase leads to fructosuria.
Absence of aldolaseB leads to hereditary fructose intolerance. If fructose 1, 6 bisphosphatase is absent, causes fructose induced hypoglycemia.
The reason being high concentration of Fructose 1 phosphate and fructose 1, 6 bis phosphate inhibit Liver phosphorylase by allosteric modulation.
As in case of Galactose, fructose intolerance can also lead to cataract formation.