Introduction to Biochemistry

Biochemistry is the application of chemistry to study of biological processes at the cellular and organisms, with their chemical reactions.

It emerged as a distinct discipline around the beginning of the 20th century when scientists combined chemistry and biology to investigate the chemistry of living systems.

Carbohydrates: Chemically defined as neutral compounds of carbon, hydrogen and oxygen. Carbohydrates used as energy sources (calories) by the body. Large carbohydrate molecules called polysaccharides consist of many small ring-like sugar molecules (carbon atoms bound to hydroxyl groups, Empirical formula $C_n(H_2O)n$, these sugar monomers are attached to one other by glycosidic bonds in a linear or branched array to form the sugar polymer.

Carbohydrates are aldehyde (CHO) or ketone (C=O) compounds with multiple hydroxyl groups (Carbon-oxygen double bonds make the sugars reactive).

Importance of Carbohydrates

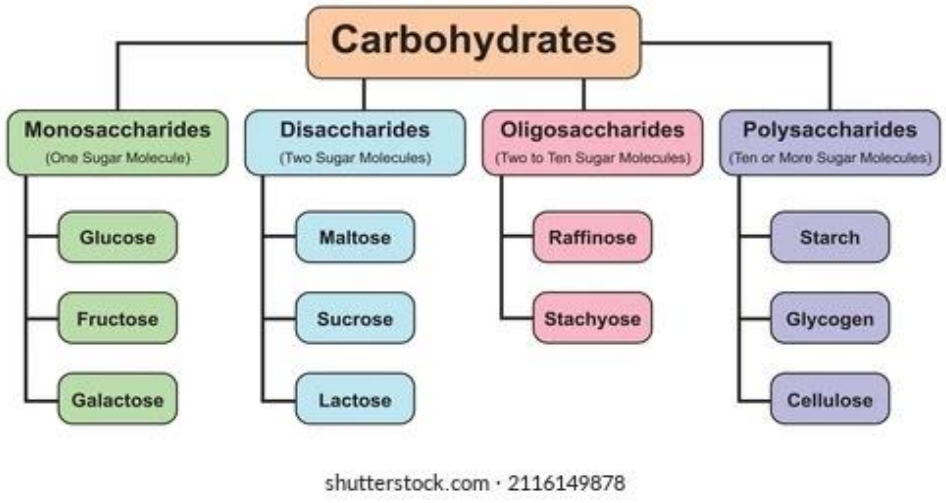
- Carbohydrates serve as energy store and metabolic intermediates.
- Ribose and deoxyribose sugars form part of the structural framework of RNA and DNA.
- Carbohydrates are important for tissue formation.
- Carbohydrates form the basis of human blood groups.
- Carbohydrates are linked to many proteins and lipids, where they play key roles in mediating interactions among cells and interactions between cells and other elements in the cellular environment.

Several Classifications of Carbohydrates:

Basics	Types
Complexity	***Simple Carbohydrates***: *monosaccharaides* ***Complex Carbohydrates***: *disaccharides, oligosaccharides & polysaccharides.*
Size	***Tetrose***: C_4 *sugars,* ***Pentose***: C_5 *sugars* ***Hexose***: C_6 *sugars* ***Heptose:*** C_7 *sugars, Etc.*
C=O Function	***Aldose***: *sugars having an aldehyde function or an acetal equivalent.* ***Ketose:*** *sugars having a ketone function or an aketal equivalent.*
Reactivity	***Reducing:*** *sugars oxidized by Tollens' reagent (or Benedict's or Fehling's reagents).* ***Non-reducing***: *sugars not oxidized by Tollens' or other reagents.*

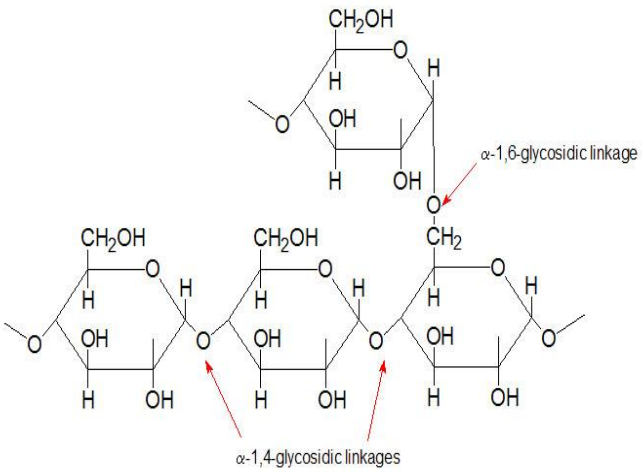
Carbohydrates can be classified according to no. of sugar units into:

- **Monosaccharaides:** 1 sugar unit e.g. glucose, fructose, galactose, ribose.
- **Disaccharides:** 2 sugar units e.g. sucrose (glucose + fructose), lactose (galactose + glucose), maltose (glucose + glucose).
- **Oligosaccharides:** 3-10 units.
- **Polysaccharides:** more than 10 units



Glycogen Metabolism

- Glycogen is the major storage form of glucose, mainly in the liver and muscle.
- The concentration of liver glycogen (up to 6%) is greater than in muscle tissues (1%). However, because muscle tissue comprises a large mass, its total capacity to storage is three to four times that of the liver.
- The synthesis (glycogenesis) and degradation (glycogenolysis) occur via different pathways.



Glycogenesis

Glycogenesis is the pathway for the formation of glycogen from glucose. This process requires energy, supplied by adenine triphosphate (ATP) and uridine triphosphate (UTP). It occurs in muscle and liver.

Reactions of Glycogenesis

1. Phosphorylation of glucose to form glucose-6-phosphate catalyzed by hexokinase in muscle and glucokinase in liver..
2. Conversion of glucose-6-phosphate to glucose-1-phosphate.
3. Formation of uridine diphosphate glucose (UDP-Glc) from glucose-1-phosphate.
4. Glycogen synthesis initiated by UDP-Glc, forming glycosidic bonds with pre-existing glycogen.
5. Establishment of α-1,4 linkages between glucose residues.
6. Branching enzyme formation of α1,6-linkages, creating branching points in the glycogen molecule.

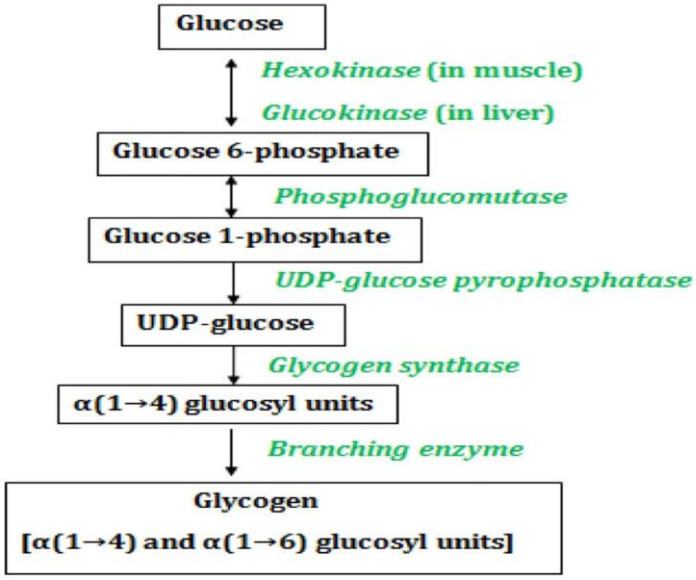


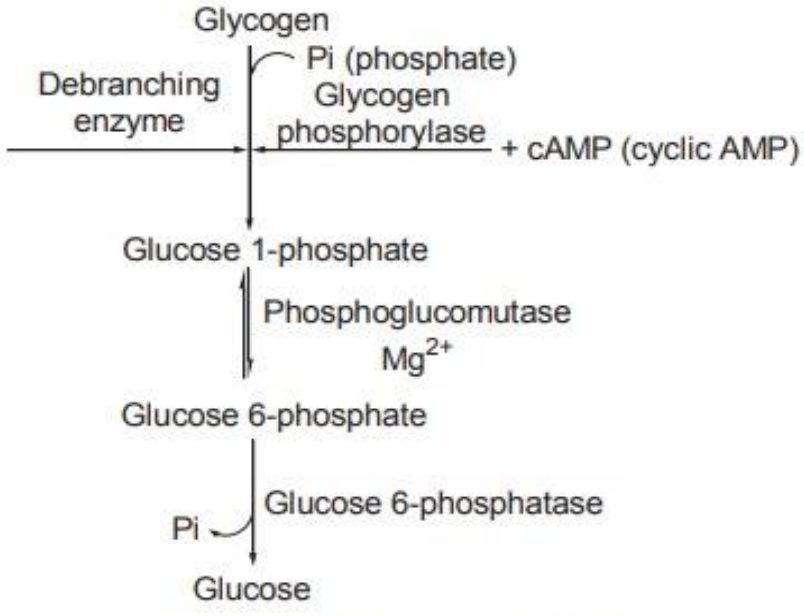
Diagram: Steps of glycogenesis

Glycogenolysis

Glycogenolysis is the degradation of glycogen to glucose-6-phosphate and glucose, in muscle and liver respectively.

Reaction of Glycogenolysis:

1. Phosphorolytic breaking of α-1,4 glycosidic bonds by glycogen phosphorylase, yielding glucose-1-phosphate.
2. Removal of branches by the debranching enzyme through glucan transferase and 1,6-glucosidase activities, releasing free glucose.
3. Conversion of glucose-1-phosphate to glucose-6-phosphate by phosphoglucomutase.
4. Conversion of glucose-6-phosphate to glucose by glucose-6-phosphatase in the liver, allowing glucose release into the bloodstream. This enzyme is absent in muscle, preventing muscle from providing glucose to maintain blood glucose levels.



The Significance of Glycogenolysis and Glycogenesis Can be Understood as Follows:

In the liver:

- After a meal, excess glucose is stored as glycogen through glycogenesis.
- During fasting, when blood glucose levels drop, glycogenolysis releases glucose from liver glycogen, helping to maintain normal blood glucose levels.

In muscle:

- Muscle glycogen serves as a rapid source of glucose during muscle contraction.
- Unlike the liver, muscle lacks glucose-6-phosphatase, preventing the release of glucose into the bloodstream from muscle glycogen.

- Therefore, muscle glycogen stores are exclusively used by the muscle itself to meet its energy needs during exercise or other activities.

Epinephrine and Glucagon play key roles in regulating Glycogen metabolism in response to changes in energy demands:

****Epinephrine**** This hormone is released during times of stress or physical activity. When epinephrine binds to receptors in the liver and muscle:

- It activates glycogen phosphorylase, promoting glycogenolysis (breakdown of glycogen into glucose) to provide glucose for immediate energy needs.
- It inhibits glycogen synthase, which reduces glycogenesis (formation of glycogen from glucose), preventing storage of glucose as glycogen. This ensures that glucose is available for immediate energy use rather than being stored.

****Glucagon**** Produced by the pancreas, glucagon is released in response to low blood glucose levels, signaling the body to increase glucose production.

- In the liver, glucagon activates glycogen phosphorylase, promoting glycogenolysis to release glucose into the bloodstream.
- It also inhibits glycogen synthase, reducing glycogenesis, and favoring the release of glucose rather than its storage.

In summary, epinephrine and glucagon act as signals to mobilize glucose from glycogen stores to meet immediate energy demands during stress, physical activity, or fasting periods, while simultaneously inhibiting the storage of glucose as glycogen to ensure its availability for energy production.

Regulation of Glycogenesis and Regulation of Glycogenolysis

There are differences in the regulation of glycogenesis (glycogen synthesis) and glycogenolysis (glycogen breakdown):

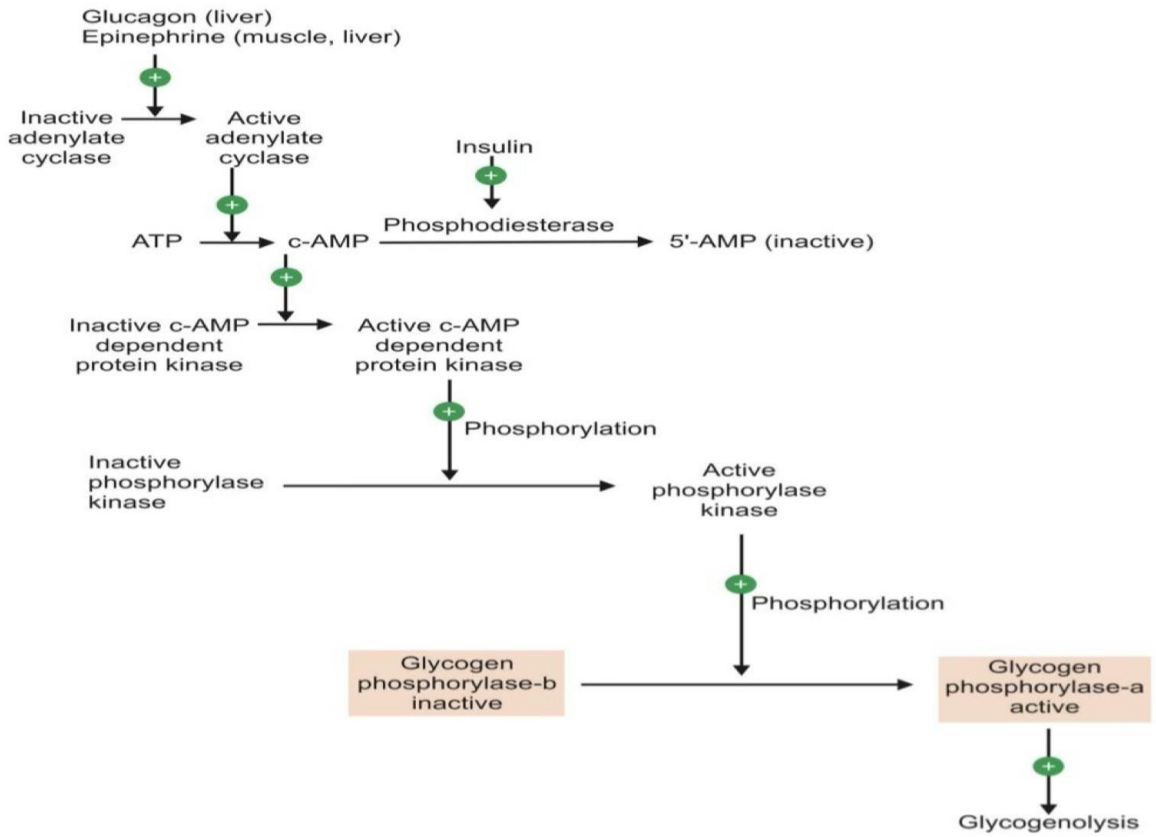
1. **Regulatory Enzymes:**
   - For glycogenesis, the regulatory enzyme is glycogen synthase, which exists in (a) active form and (b) inactive form, based on its phosphorylation status.
   - For Glycogenolysis, the regulatory enzyme is glycogen phosphorylase, also existing in (a) active form and (b) inactive form based on its phosphorylation status.

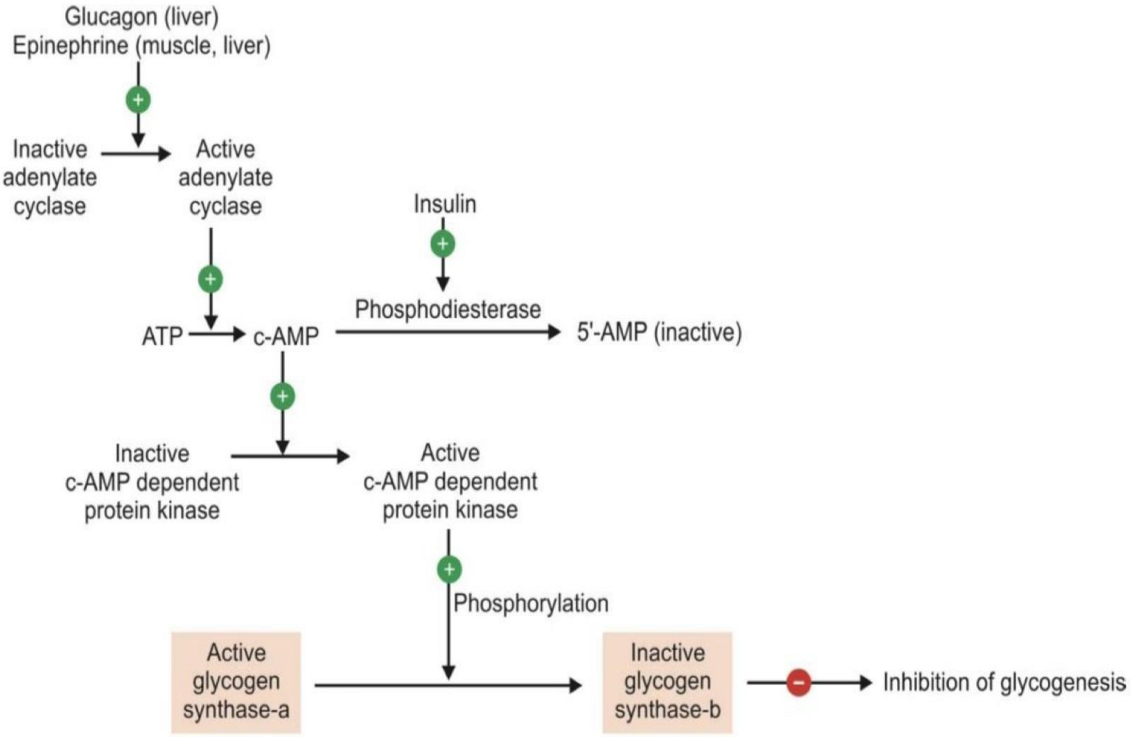
2. **Triggering Hormones:**

- Glycogenesis is inhibited by hormones like glucagon and epinephrine, which activate CAMP production and subsequently phosphorylate glycogen synthase, inhibiting its activity.
- Glycogenolysis is stimulated by hormones like epinephrine (in muscle) and glucagon (in liver) which activate adenylate cyclase, leading to increased CAMP levels and phosphorylation of glycogen phosphorylase, activating it.

3. **Role of Insulin:**

- Insulin opposes the actions of glucagon and epinephrine by reducing CAMP levels.




Glucagon (liver)
Epinephrine (muscle, liver)
Inactive adenylate cyclase
Active adenylate cyclase
Insulin
Phosphodiesterase
ATP
c-AMP
5'-AMP (inactive)
Inactive c-AMP dependent protein kinase
Active c-AMP dependent protein kinase
Phosphorylation
Active glycogen synthase-a
Inactive glycogen synthase-b
Inhibition of glycogenesis