STUDY MATERIAL

VIVEKANANDA COLLEGE
THAKURPUKUR

NAAC ACCREDITED GRADE – 'A'

BIOCHEMISTRY

(HONOURS)

Blood Glucose Homeostasis

Dr. Kakali Roy

Blood glucose Homeostasis

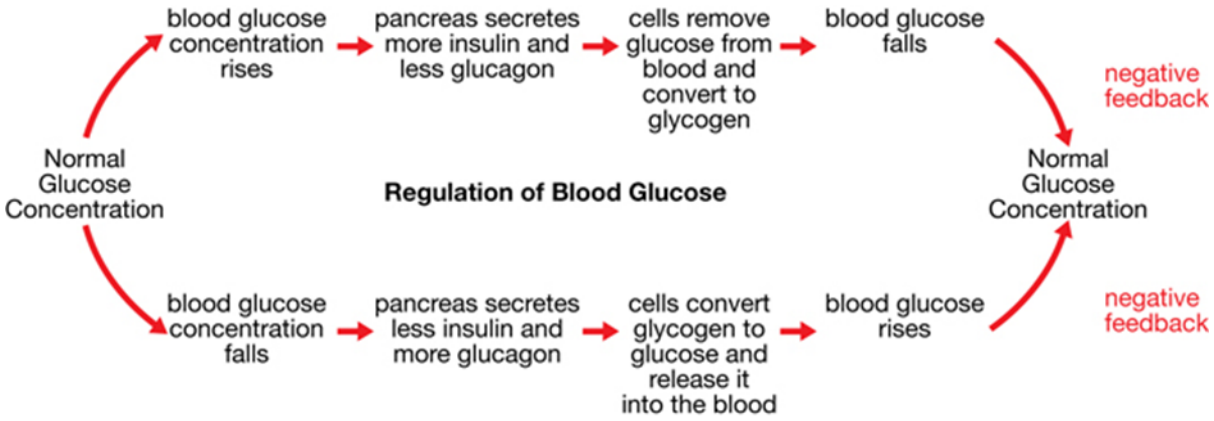
Blood sugar regulation is the process by which the levels of blood sugar, i.e. glucose are maintained by the body within a narrow range, called glucose homeostasis which is the balance of insulin and glucagon hormone to maintain blood glucose.

Blood Glucose Concentration : Hypoglycemia (<70mg/dl)

(in fasting condition) Normal (70-110mg/dl)

Hyperglycemia (> 110mg/dl)

Glucose control has been shown to be very important in helping prevent particular diseases, especially diabetes. In the long term, poor control of blood sugar levels in diabetic patients leads to both heart and blood vessel disease, kidney failure, nerve damage, eye problems and heart disease.

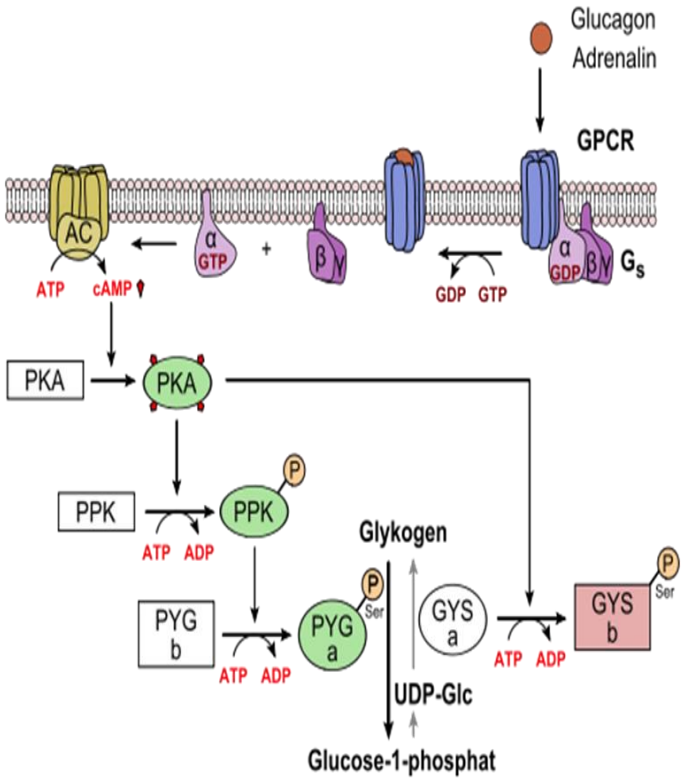


Hormone	Target Organ	Effect
Insulin	Muscle	stimulates glucose transport, increases glycogenesis and glycolysis
	Adipose	stimulates glucose transport
	Liver	induces glucokinase, increases glycogenesis and glycolysis
Glucagon	Liver	promotes glycogenolysis, gluconeogenesis

Effect of Glucagon Hormone

- Glucagon is a non steroid peptide hormone containing 29 amino acids. It is produced by α-cells of the islets of Langerhans of Pancreas.
- Glucagon elevates the concentration of glucose in the blood by promoting gluconeogenesis and glycogenolysis.
- Its effect is opposite to that of insulin, which lowers the extracellular glucose.

Metabolic Regulation of Glycogen by Glucagon

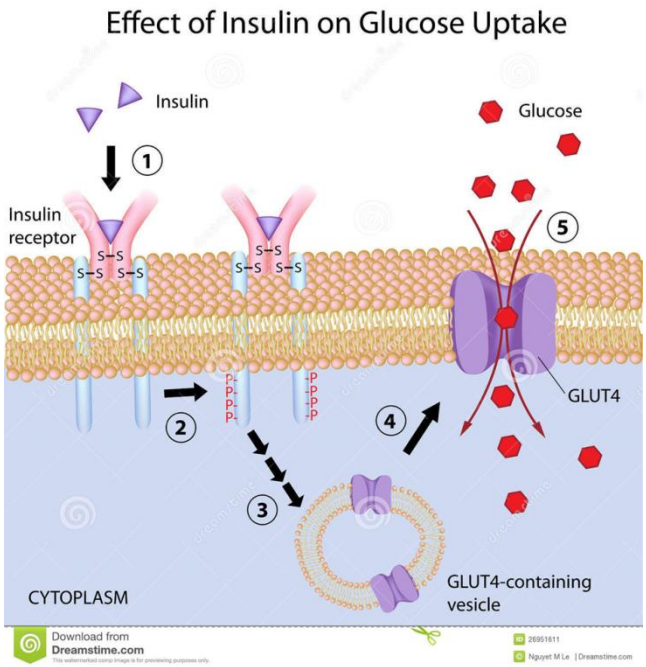


- Glucagon binds to the glucagon receptor, which is a G-protein coupled receptor (GPCR), located in the plasma membrane. The conformational change of the receptor activates G-proteins (α, β and γ subunits), a heterotrimeric protein to bind with GTP. The bound α-subunit-GTP complex then activates adenylate cyclase. Adenylate cyclase (AC) produce c-AMP from ATP, which activates protein kinase A (PKA).

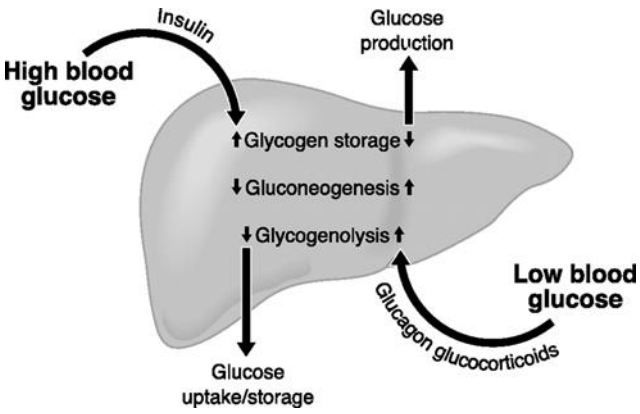
- PKA in turn activates phosphorylase kinase (PPK) which then phosphorylates glycogen phosphorylase b (PYG b) (inactive) to active phosphorylase a (PYG a).
- Phosphorylase a is responsible for glycogenolysis, to release Glucose 1-phosphate from glycogen, which is then converted to glucose by enzymatic reactions and release it into the bloodstream.
- Glycogen, the storage form of glucose in the liver, when become depleted, glucagon then encourages the liver and kidney to synthesise additional glucose by gluconeogenesis.
- Glucagon turns off glycolysis in the liver, causing glycolytic intermediates to be shuttled to gluconeogenesis.

Effect of Insulin Hormone

- Insulin is a non steroid hormone containing 51 amino acids, polypeptide A and B, linked together by disulphide bridges.
- When levels of blood sugar rise, insulin is released from β-cells of the islets of Langerhans in the Pancreas, causes the liver to convert more glucose into glycogen by glycogenesis to prevent hyperglycemia.



- The Insulin receptor (two α and two β chains linked by disulphide bonds) which is embedded in the plasma membrane, is a tyrosine kinase. It transfers phosphate groups from ATP to tyrosine residue on intracellular target proteins. Binding of insulin to the α- subunits of the receptor causes the β-subunits to phosphorylate themselves and activate the catalytic activity of the receptor and so phosphorylation occurs.
- At the cell surface, GLUT 4 transporter permits the facilitated diffusion of circulating glucose down its concentration gradient into muscle and fat cells.
- Insulin stimulated glucose uptake into these cells is mediated by the transporter GLUT 4.
- When insulin concentrations are low, GLUT 4 glucose transporters are present in cytoplasmic vesicles, where they are useless for transporting glucose. Binding of insulin to receptors on such cells leads rapidly to fusion of those vesicles with the plasma membrane and insertion of the glucose transporters thereby giving the cell an ability to efficiently take up glucose.
- The glucose that enters the β-cell is phosphorylated to glucose-6-phosphate by glucokinase/hexokinase which then enters glycolytic pathway and then to TCA cycle.



Therefore, Glucagon and insulin have antagonistic effects, with glucagon promoting glucose production and release into the bloodstream, whereas insulin signals the cell to insert GLUT 4 transporters into the membrane, promoting the transport of glucose into the cells from the bloodstream and inhibiting glucose production.

References :

1. Voet D, Voet JG (2011), Biochemistry (4th ed.), New York : Wiley
2. www.vivo.colostate.edu/h books / Path Phys/endocrine/Pancreas/insulin_Phys.html
3. www.google.com
