Biochemistry
2nd stage
Dr.Lamees Majid Al-Janabi

TRIGLYCERIDES

ILO:K2,S11,A0.

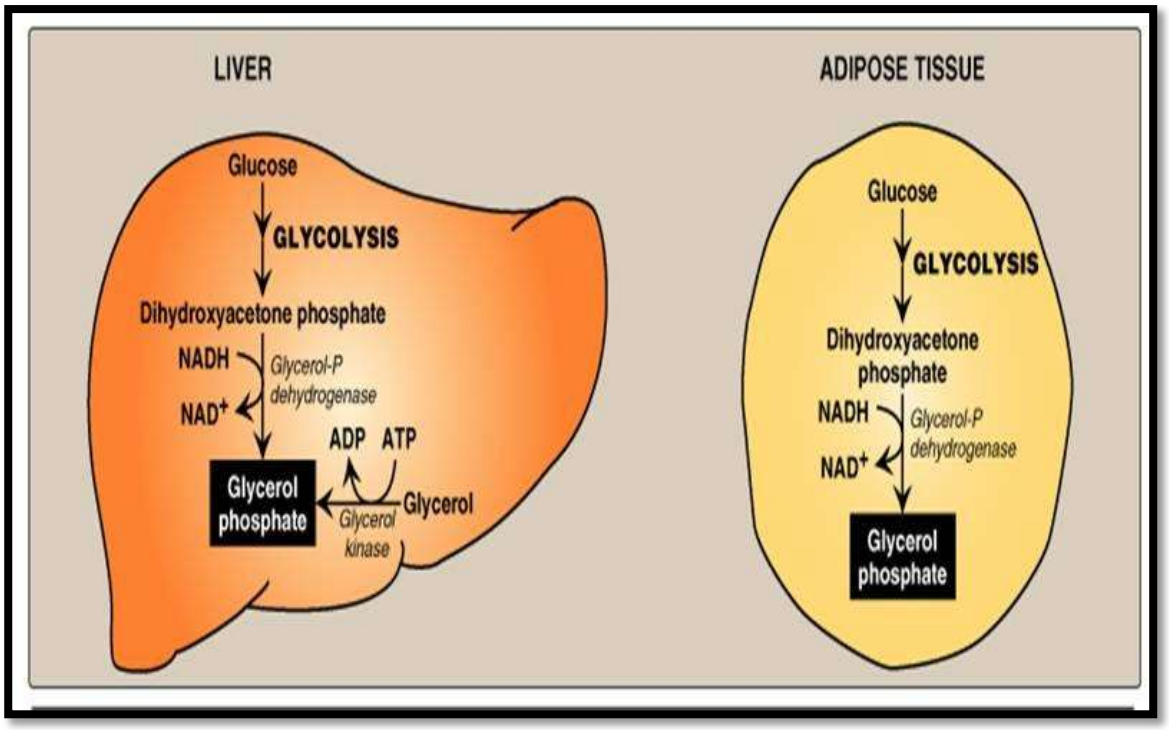
Objectives:

The students are learned to understand the Triglycerides metabolism including the following points:
-Synthesis of Triglycerides
- Source of glycerol -3-Phosphate
- Hormonal Regulation of Triglycerides Degradation in Adipose tissue

SYNTHESIS OF TRIGLYCERIDES

fatty acids stored as components of triacylglycerol. Monoacylglycerol, diacylglycerol, &triacylclycerol formerly called Glycerides. e.g. Triglyceride consist of one, two, or three molecules of fatty acid.

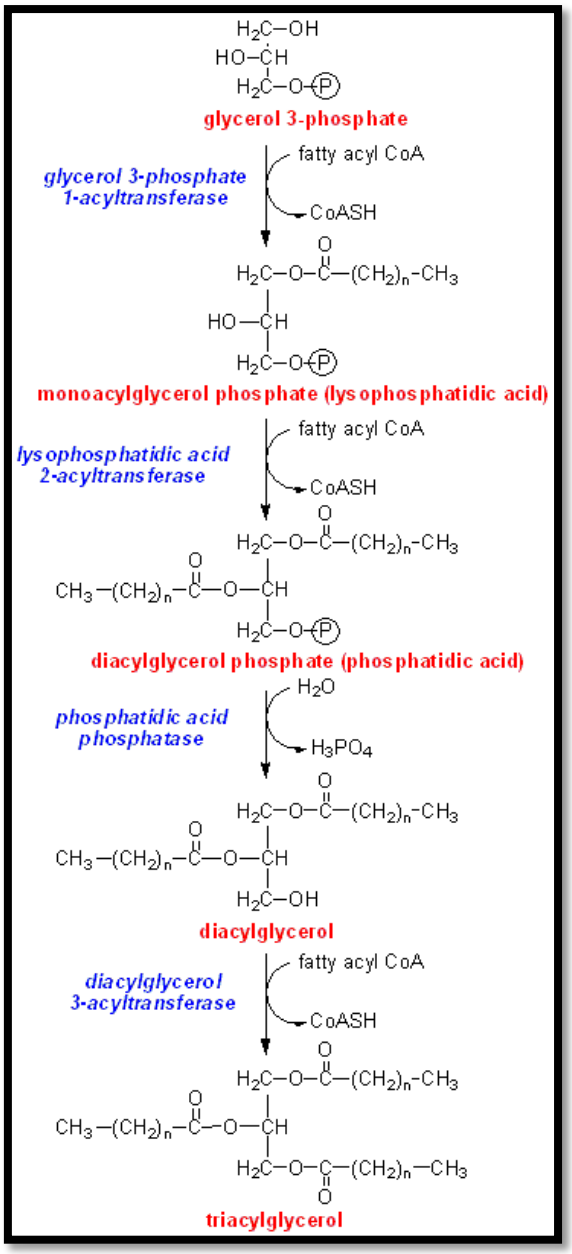
-Synthesis:- Liver and adipose tissue are the major sites of triacylglycerol (TAG) synthesis. The TAG synthesis in adipose tissue is for storage of energy whereas in liver it is mainly secreted as VLDL and is transported to peripheral tissues. The TAG is synthesised by esterification of fatty acyl CoA with either glycerol-3-phosphate or dihydroxy acetone phosphate (DHAP)



Pathways for production of glycerol phosphate in liver and adipose tissue

Note:- a- Adipocyte can take up glucose only in the presence of the hormone insulin. Thus, when plasma glucose—and, therefore, plasma insulin—levels are low, adipocytes have only a limited ability to synthesize glycerol phosphate, and cannot produce TAG.]

b- A fatty acid must be converted to its activated form(attach to co enzyme A) before it can participate in triacylglycerol synthesis.



Synthesis of triacylglycerol

Typically the fatty acid on carbon no.1 is saturated and on carbon no.2 is typically unsaturated and the fatty acid on carbon no.3 could be the either .So the type of the fatty acid on carbon no.3 usually determine the melting point of TG.

METABOLISM OF ADIPOSE TISSUE

The adipose tissue serves as a storage site for excess calories ingested. The triglycerides stored in the adipose tissue are not inert. They undergo a daily turnover with new triacylglycerol molecules being synthesized and a definite fraction being broken down.

Adipose Tissue in Well-fed Condition

i. Under well-fed conditions, active lipogenesis occurs in the adipose tissue.

ii. The dietary triglycerides transported by chylomicrons and the endogenously synthesized triglycerides from liver brought by VLDL are both taken up by adipose tissue and esterified and stored as TAG.

iii. In well-fed condition, glucose and insulin levels are increased. The stimulant effect of insulin on the uptake of glucose by adipose tissue, on

iv. the glycolysis and on the utilisation of glucose by HMP pathway also enhances lipogenesis.

v. Insulin also causes inhibition of **hormone sensitive lipase**, and so lipolysis is decreased.

Adipose Tissue in Fasting Condition

i. TAG from the adipose tissue is mobilised under the effect of the hormones, **glucagon and epinephrine**.

ii. The intracellular hormone sensitive lipase is enhanced ,which acts on TAG and liberates fatty acids.

iii. Under conditions of starvation, a high glucagon, ACTH, glucocorticoids and thyroxine have lipolytic effect. The released free fatty acids (FFA) are taken up by peripheral tissues as a fuel.

Well-fed state	During fasting
Lipogenesis increased	Lipogenesis inhibited
Lipolysis inhibited	Lipolysis increased
Lipoprotein lipase active	**Glucagon activates**
Insulin inhibits HS-lipase	**HS-lipase FFA in blood increased**

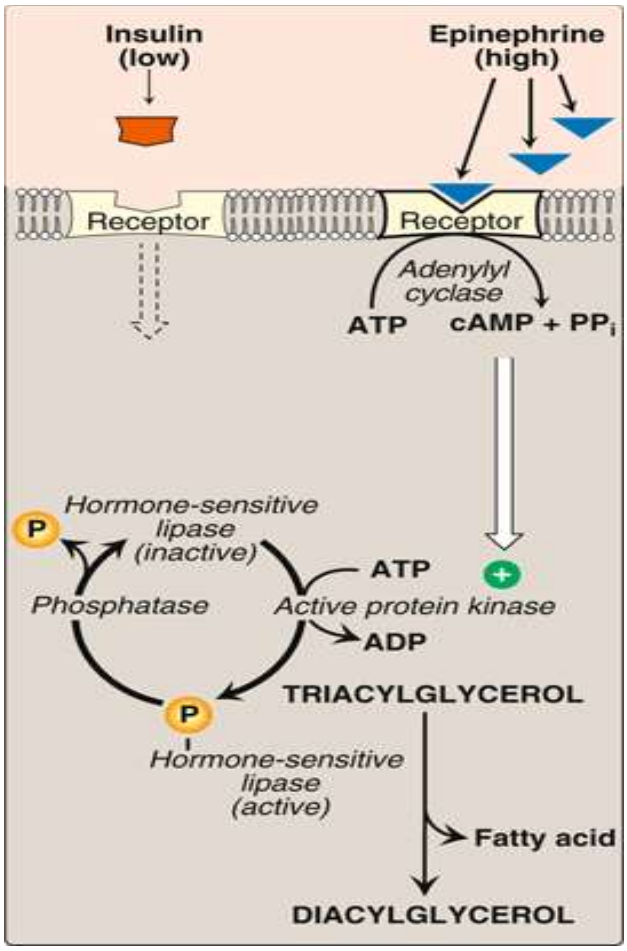
Adipose Tissue and Diabetes Mellitus

i. Lipolysis is enhanced and high FFA level in plasma is noticed in diabetes mellitus.
ii. The insulin **receptors** on the cell surface of adipocytes **are decreased**, leading to **insulin insensitivity** in diabetes.
iii. In type 2 diabetes mellitus, there is insulin resistance and Hepatic gluconeogenesis occurs uninhibited leading to hyperglycemia.
iv. Increased mobilization of fatty acids from adipose tissue and the persistently high free fatty acid levels in the presence of hyperinsulinemia stimulate synthesis of triacyl glycerol.
v. The overproduction of TAG leads to increased release of VLDL from liver causing hypertriglyceridemia.
vi. The excess deposition of TAG in adipose tissue accounts for the obesity prevalent in type 2 diabetes patients.

Adipose Tissue and Obesity

i. The fat content of the adipose tissue can increase to unlimited amounts, depending on the amount of **excess calories** taken in. This leads to obesity.
ii. Plasma insulin level is high. But the **insulin receptors are decreased**; and there is peripheral resistance against insulin action.
iii. When fat droplets are overloaded, the nucleus of adipose tissue cell is degraded, cell is destroyed, and TAG becomes extracellular. Such TAG cannot be metabolically reutilised and forms the dead bulk in obese individuals.

Hormonal regulation of triacylglycerol degradation in the adipocyte



- ***Fate of glycerol:*** The glycerol released during TAG degradation cannot be metabolized by adipocytes because they apparently lack glycerol kinase. Rather, glycerol is transported through the blood to the liver, where it can be phosphorylated. The resulting glycerol phosphate can be used to form TAG in the liver, or can be converted to DHAP by reversal of the glycerol phosphate dehydrogenase reaction. DHAP can participate in glycolysis or gluconeogenesis.

- ***Fate of fatty acids:*** The free (unesterified) fatty acids move through the cell membrane of the adipocyte, and immediately bind to albumin in the plasma. They are transported to the tissues, where the fatty acids enter cells, get activated to their CoA derivatives, and are oxidized for energy.