Overview and Integration of Cellular Metabolism

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Lecture 20: Digestion and absorption of Lipid

Hello everyone, here we are with the classes of Overview and Integration of Cellular Media Metabolism. Today we are going to start lipid metabolism. In next few classes we will discuss different types of lipid, lipid their synthesis, their breakdown and their metabolic effect in our body. In today's class we will basically discuss about the digestion and absorption of lipid. The concepts covered in this class will be the dietary composition of lipid, then digestions of lipid at different levels of GI tract, then different enzymes which are required for this lipid digestion and finally, how these lipids are absorbed through GI tract. So, here at the dietary fat composition I am going to discuss, but before that you should remember that in Indian diet the average normal content of lipid is mostly 40 to 150 grams of them 95 percent are actually triglycerides.

The other lipids which are in the rest 5 percent are cholesterol, cholesterol esters, phospholipids and unsterified fatty acids. So, you can see the major dietary lipid is actually triglyceride. Now the very digestion of lipid is actually starting from mouth. So, here is the important enzyme that is lingual lipase, this is the important enzyme which is catabolizing the lipid products.

Now remember one important thing lipase group of enzymes are basically digesting triacyl glycerol mostly. So, this lingual lipase is actually secreted from Ebener's gland which is situated on the dorsal surface of the tongue. The active enzyme is actually working in low pH mostly pH 2 to 7.5, but then the optimum range is actually 4 to 4.

5. So, basically it works in acidic pH and you all know that the stomach is actually the content of stomach is acidic. So, lingual lipase can even be active in stomach as well. Now the ideal substrate for lingual lipase is short chain triglycerides. Basically short chain triglycerides are mostly present in milk fat. So, these the milk lipid can be easily digested by lingual lipase.

Now the digested short chain fatty acids which is actually generated from short chain

triglyceride they can be directly absorbed from stomach well as well as enter through the portal vein. So, before going to further discussion of the lipases let us see just a look into the triglyceride degradation how triglyceride is degraded by different lipases. Actually there are 3 fatty acid rather 3 ester bonds where glycerol is actually attached to 3 fatty acid here you can see 3 fatty acids are attached here. Now lipase when acts on this triglycerides they break the ester bonds one by one how? See you can see the first ester bond is actually this is the first ester bond actually broken here to generate fatty acid along with a diglyceride. Then again lipase works on another ester bond here actually here.

So, it again gives rise to another fatty acids to generate monoglyceride. Finally this monoglyceride is broken down then the ultimate product of triglyceride breakdown is actually 3 fatty acids along with one molecule of glycerol. So, you can see there are 3 ester bonds and these 3 ester bonds are not always broken down by all the lipases. So, basically the lipases in our digestive tract different lipases are there and they are specific to specific ester bonds. So, in case of lingual lipase lingual lipase is mostly is actually acting on SN 3 ester bond this ester bond.

Now, going to stomach in stomach there is gastric lipase gastric lipase is secreted from the cheap cells of gastric mucosa. Then in stomach around 30 percent of the digested triacylglycerol dietary triacylglycerol are digested. Then this you know the stomach content is actually acidic. So, gastric lipase is environmentally active in stomach. So, they are acid stable and the optimum working pH is 5.

4. The secretion of gastric lipase is stimulated by gastrin hormone and its action requires calcium. So, basically gastric lipases are most effective in breaking down short chain and medium chain triglycerides giving rise to short chain and medium chain fatty acids. And they are present in milk, egg yolk and fats like ghee which contain short chain fatty acids they are the suitable substrate for gastric lipase. Next there is one important statement like fats are having high satiety value why? Now, one very important effect of fat in gastric empting is that it delays gastric empting. Now, what happens when the content the dietary content which contains fat when it reaches intestine there is release of enterogastrone and this enterogastrone inhibits gastric motility influenced by the dietary fat.

And what happens because of delaying the gastric empting the food particle remains for more time inside the stomach which induces stomach contraction or stomach churning. Now because of this metabolic churning effect there is release of certain peptides which induces the gut peptide signaling to induce satiety. Now, what are those gut peptides? Those are cholecystocyanin, glucagon like peptide 1, 2 as well as auxintomodulins these

are the gut peptides which induces satiety. So, the crux is that fat while delaying the gastric empting it induces the release of certain gut peptides which actually causes satiety. Then the significance of lingual gas and gastric lipases that I have already told that these are they are basically specific for SN 3 ester bonds and they are very effective in digesting milk lipids milk.

Now if a baby is suffering from some congenital disorders like cystic fibrosis or pancreatic disorder where the pancreatic lipid digesting enzymes are deficient they can also easily digest those babies can also easily digest milk. So, they can degrade those short chain and medium chain fatty acids and can survive. So, these gastric and lingual lipases are important in this type of pancreatic disorder metabolic disorders pancreatic insufficiencies. Next is digestion in small intestine. Now in small intestine the digestive enzyme is pancreatic lipase the most important one along with that bile salt is another bio molecule which is important in helping the digestion of lipid.

Now in pancreatic juice apart from pancreatic lipase there are other enzymes as well like colipase which acts in conjunction with the lipase then phospholipase A 2 important for breaking down phospholipids and cholesterol esterase which is important for breaking down cholesterol esters. Now secretion of pancreatic juice is stimulated by the passage of gastric acidic gastric content in the duodenum as well as there are few other hormones like secreting cholocystokinin and pancreasimin. Now bile salt plays an important role in emulsification of fat. Now what is emulsification? Now emulsification is one very important phenomena which is required for digestion of lipids. Now you all know that lipid is actually a hydrophobic molecule, but the enzymes the digestive enzymes they are water soluble and they need to work on fat globules which is hydrophobic.

So, what is required they we need emulsification where fat can lipids can have one water lipid interface in such a way that the enzyme can act. How by increasing the surface area. Now how that surface area can be increased if a large globule of fat can be broken down to multiple smaller droplets the surface area definitely will increase where enzymes can act. Now these phenomena is enhanced or helped by bile salts. So, bile salt here is acting as MLC fires.

Now again the rate of triglyceride digestion is definitely dependent on the surface area and that surface area is not only enhanced by bile salt it is also enhanced by the churning peristaltic movement these are the shearing movements in the stomach as well as the intestine which helps in breaking down of the lipid bigger lipid droplets to the smaller ones. Now bile salts these are the cholesterol derivatives actually which is synthesized in the liver, but stored in gallbladder. Now why they are salts these are basically the conjugation of conjugated product of storin or glycine to the bile acid and they are

amphipathic in nature. Now how they functions these bile salts there you can see that here the bigger fat globule is with the help of bile salts are broken down to the smaller ones while increasing the surface area of the fat droplets. Now what happens even if these fat globules are broken down to the smaller droplets they have the tendency to coalesce with each other and that coalescing tendency is once again prevented by bile salts.

So, bile salts not only breaks down the fat droplets they it actually inhibits their coalition. Again bile salt also helps in the function of pancreatic lipase. Now as I mentioned previously there is another molecule colipase. Colipase is basically a small protein a peptide. Now this colipase what it does it actually anchors the lipase with the triglyceride particles.

So, that it can act properly or attach properly with the triglyceride surface the lipase can attach over the triglyceride surface. So, basically colipase remember colipase is actually acting as a cofactor of pancreatic lipase. Now, triacyl triacyl glycerol degradation by pancreatic lipase is basically occurring in the primary ester linkage. So, the primary ester linkages are the SN 1 and SN 3. So, digestion of triglyceride proceeds by removal of terminal fatty acids these are the terminal fatty acids which finally, gives rise to alpha beta diglycerides.

Then once again this diglyceride is broken down to release another fatty acid which is beta monoglyceride. So, finally, what we are having fatty acid attached to glycerol by secondary ester bond that is monoglyceride where pancreatic lipase cannot act. So, what will be the effect that there is a residual secondary ester bond. Now what we need we need to shift this secondary ester bond to or rather conversion of the secondary ester bond to the primary one and that is done by the enzyme isomerase. So, you can see with the help of pancreatic lipase in presence of colipase as well as calcium there is formation of beta monoglyceride with release of 2 fatty acids which were actually linked by the primary ester bond.

Now with the help of the enzyme isomerase where you can see there is shifting of the ester bond and formation of the primary one. Again pancreatic lipase can act over it to produce glycerol and the one single fatty acid which were attached to it. So, this is the end product of triglyceride breakdown by pancreatic lipase that there is around 78 percent of the breakdown product is actually beta monoacylglycerol. Again also there is alpha monoacylglycerol as well as the least one is free fatty acid and glycerol the complete breakdown product. Next is significance of pancreatic lipase definitely pancreatic lipase is present in high concentration in pancreas so much so that even only in very severe condition of pancreatic deficiencies like cystic fibrosis there is the

deficiencies felt actually in the form of malabsorption of fats.

Then another drug is there which is known as ORLISTAT. ORLISTAT is one anti obesity drug, but it does it inhibits gastric and pancreatic lipases. So, basically it hinders the digestion of lipid and finally, induces the weight loss. Next digestion of cholesterol ester which is done by the enzyme cholesterol ester is remember the dietary cholesterol is basically the non esterified from major cholesterol is actually non esterified whereas, the only 10 to 15 percent of the dietary cholesterol is actually in esterified form. Now the action of cholesterol ester is also enhanced by bile salt.

Then phospholipid degradation with the help of the enzyme phospholipase A 2 remember phospholipase A 2 actually breaks down the secondary ester bond that is SN 2 which finally, gives rise to the product which can be digested by lysophospholipase. So, the fatty acid attached in the position one can be broken down by phospho lysophospholipase which finally, gives rise to glycerol phosphoryl base and that can be excreted through phases as well as can be degraded further or can be absorbed as well. So, this is the phospholipid breakdown. So, these are all how triglycerides cholesterol cholesterol esters or phospholipids are broken down inside gut. Now how these broken down products are absorbed? Remember the shorter ones can be directly absorbed.

Shorter ones means the where the chain length is less than 14 carvings like glycerol short and medium chain fatty acids. They can be directly absorbed from intestinal lumen can enter portal vein and can be circulated in the lymphatics. Whereas, the longer ones like long chain fatty acids free cholesterol cholesterol esters beta acyl glycerols phospholipids lysol acetines these these lipid derivatives they cannot directly be absorbed through intestine. So, what they need to do? They form mixed micelles with bile salts. Now what are what is this mixed micelle? Mixed micelle basically a complex of lipid and bile salts which are actually soluble in water.

Now in the mixed micelle definitely if you want to be soluble in water the periphery must be hydrophilic. So, in the periphery of this mixed micelle there are products like bile salts end products of phospholipids and cholesterol. So, these are the amphipathic lipid moieties. Whereas, in the centre of the mixed micelle there are more hydrophobic forms of lipids like 2 monoacylglycerols free fatty acids and as well as fat soluble vitamins. So, inside the mixed micelle there is the hydroph more hydrophobic form of lipid whereas, in the periphery there are amphipathic part the hydrophilic part of the amphipathic lipids are located in the periphery as well as the bile salts.

Now these mixed mice through these mixed micelles actually the lipids are absorbed inside the through the intestine. Now what happens this mixed micelle are attached to

the enterocyte membrane you can see here that this is our mixed micelle which is attached over the enterocyte membranes through which the lipid particles slowly can cross the mucosal surface through endocytosis and get internalized. Whereas, bile salts bile salt portion of the mixed micelle is not absorbed rather it is it cannot cross the intestinal mucosal membrane. So, it is retained in the lumen and finally, get recycled recycled through enterohepatic circulation it again is through the ileum basically through the ileum it is absorbed through enterohepatic circulation and again resecreted in the digestive tract for the further actions. So, this is how through mixed micelle lipids are absorbed in the circulation.

Now inside the enterocyte so, basically what happens in mixed micelle through mixed micelle those lipids enters the enterocytes of the intestinal epithelium from gut lumen. Now inside the enterocytes the there is re synthesis of the complex form of lipid basically those products which were digested which the derivative of digestion are again forming the complex lipid inside the enterocytes. So, you can see that there is a cycle or pathway which is monoacylglycerol. Now what happens that alpha monoacylglycerol where one fatty acid is basically attached to the glycerol that is hydrolyzed to generate glycerol and one molecules of fatty acids that fatty acid here is attached to 2 monoacylglycerol you can see this fatty acids can be attached to 2 monoacylglycerol with the help of the enzyme acyltransferase to form reform triacylglycerol. So, once again triacylglycerol is formed from the digested product like 2 monoacylglycerol or 1 monoacylglycerol with the help of fatty acid.

Now basically lysophospholipids are recycled to form phospholipids. So, once again phospholipids is reformed similarly cholesterol esters are also reformed by esterification of cholesterol means fatty acid is once again attached to cholesterol with the help of the enzyme acyl coenzyme a cholesterol acyltransferase. So, basically whatever is digested in the intestine or the inside GIT is again reformed after absorption inside the enterocyte. So, what we are getting once again there is triacylglycerol, once again there is phospholipids and once again there is cholesterol esters along with few directly digested product which were actually directly absorbed the shorter ones. Then of course, here the long chain fatty acids are also there and they are also used up to for esterification of triglycerides phospholipids and cholesterol esters.

So, these are the short chain and medium chain fatty acids those are directly entering the portal circulation they are carried in circulation by serum albumin. So, remember serum albumin is the trans transport protein for transport of short chain and medium chain fatty acid in the circulation. So, what happens in lipid malabsorption whenever there is lipid malabsorption remember along with the lipid along with lipid there is vitamin deficiency vitamins those are fat soluble and these malabsorption can be from pancreatic

insufficiencies like cystic fibrosis I mentioned. Apart from that there are different other chronic diseases of pancreas like pancreatitis there can be surgical removal of pancreas in case of malignancies or other disease then shortened bowel celiac disease, sprue or Crohn's disease these are all the malabsorption syndrome. Where actually in these cases of pancreatic insufficiencies there are deficiencies of enzymes, but again bile salt deficiency can also lead to malabsorption and bile salt deficiency can can be derived from bile duct obstruction due to gall stone, tumors in the head of pancreas or different enlarged lymph nodes.

So, these are the causes of lipid malabsorption which is also known as steatoria. Then the re synthesized product of lipid which were re synthesized in enterocytes remember once again they are not hydrophilic. So, they cannot circulate in the aqueous medium directly what they again need is solubilization. Solubilization in the form of chylomicron. So, basically those triacylglycerol along with cholesterol, cholesterol esters fat soluble vitamin they are packaged in chylomicron and chylomicron is a conjugated lipid containing different proteins.

Now this chylomicron once formed inside the enterocyte is actually released from enterocytes via exocytosis from its basolateral surface, then it is absorbed through lactials. What are the lactials? Lactials are actually the lymphatic capillaries which are present exclusively inside the intestinal villi. So, basically these chylomicrons are transported through lymphatic circulation. It enters the intestinal villi through lactials then it enters the circulation. So, this is how the lipids are absorbed through chylomicron.

So, one very important product of lipid important form of lipid which is inside our which is circulating inside our body is actually chylomicron which is a conjugated lipid containing different lipid as well as different dietary lipid as well as proteins. Now you can see from the intestinal tract this chylomicron can be absorbed and circulated through thoracic dirt duct and coming to venous circulation reaching the systemic artery peripheral capillaries where they are finally, digested and broken down. So, at the end of this session we can see there are different type of lipases present important for digestion of lipid. So, one is lingual lipase which is acid stable active in mouth as well as in stomach. It breaks down triacylglycerol with short or medium chain present in milk finally, giving rise to free fatty acid and diacylglycerol.

Then comes pancreatic lipase pancreatic lipase are secreted from intestine small intestine it acts in conjunction with the colipase as well as in presence of bile salts digests triacylglycerol. Then intestinal lipase as well, but remember intestinal lipase has nothing much left to digest actually most of the functions are done by gastric and pancreatic lipase. Then phospholipase A 2 is important for breaking down the dietary

phospholipids which breaks the secondary ester bonds giving rise to unsaturated fatty acid and lysol acetin. Then lipoprotein lipase and hormone sensitive lipase we will read in the in our next few sessions where these lipases are actually present after which actually these enzymes act after absorption inside the circulation during catabolism of the lipoproteins. So, in this sessions the key points to be which have been all discussed are how lipids are digested in different levels of GI tract like mouth, stomach and intestine with the help of different enzymes like different lipases as well as other lipid metabolizing enzyme like phospholipase and cholesterol esterase.

Then the role of bile acid how they are how bile bile salts how those bile salts are emulsifying emulsifying the lipids and helping in their absorption and finally, post absorption re synthesis of lipids which finally, giving rise to chylomicron the transport form of lipid and the transport form of dietary lipid in our circulation. So, these are my references. Thank you all in the next session of lipid digestion.