

Lipids: Classification, functions and role in human health

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ABSTRACT

Lipids are the naturally occurring hydrophobic biomolecules which consists of oils, fats, waxes, fatty acids, some vitamins, sterols, steroids and phospholipids. They can be classified on the basis of their composition, chain length, saponification or degree of unsaturation. Lipids are the concentrated source of energy and produce twice the energy produced by carbohydrates and proteins. Lipids are also involved in many of the biological functions. The saturated fatty acids are considered unhealthy while the unsaturated fatty acids rich diet is recommended by the Indian Council of Medical Research. Among the unsaturated fatty acids linoleic acid and linolenic acid are two essential fatty acids as they cannot be produced by our body. The major food sources of essential fatty acids are nuts, seeds, legumes and fish. Nowadays, the diet rich in fats and low in carbohydrates (Keto diets) have been used to control several diet related diseases.

Key words: Lipids; oils; diseases; health

Introduction

The term 'Lipid' is used for naturally occurring heterogeneous group of biomolecules which are soluble in non-polar organic solvents. They may be broadly defined as hydrophobic or amphiphilic small molecules. This group consists of fats, oils, waxes, fatty acids, monoglycerides, diglycerides, triglycerides, fat soluble vitamins, sterols, steroids and phospholipids. Lipids perform many biological functions in the body as they are important component of cell membrane which acts as mechanical barrier to the external environment of the cell. They are also the dense source of energy and provide 9 Kcal/g of fat consumed. They also play an important role in signalling. In mammals living in cold climates, subcutaneous fat retards loss of body heat. Lipids along with the proteins make lipoproteins which are important constituent of the cell membrane and also aids in the transportation of

lipids. Fat soluble vitamins are also lipid in nature and are also source of essential fatty acids (EFA).

Humans get their most of the food from food sources which may be originated from animal or plant sources. The fat obtained from the animals (except the aquatic animals) is mostly the saturated one, while the long chain fatty acids (LAFs) present in plant oils possess varying degree of unsaturation. The hydrolysis and synthesis of lipids in the human body can be achieved by various biosynthetic pathways. However, some of the fatty acids (FAs) cannot be synthesised by our body which makes such FAs essential in the food. Omega-3 and omega-6 are the essential fatty acids. Beside these, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), conjugated linoleic acid (CLA), phytosterols and many medium and short chain fatty acids (SCFAs) are known to have functional properties (Alabdulkarim et al., 2012). The short chain fatty acids like acetate, propionate and butyrate play an important role in the maintenance of intestinal homeostasis (Venegas et al., 2019).

Classification of lipids

On the basis of their composition

On the basis of their composition the lipids are classified as simple lipids, compound lipids, and derived lipids.

Simple lipids

The esters of fatty acids with various alcohols are known as simple lipids. They are further classified as fats and waxes. Fats are mainly triglycerides and are found in adipose tissue. These various sources of fat are based on animals like lard, butter, fish and oils from plant sources like olive or corn. In the triglycerides a glycerol molecule is attached to three fatty acids. The fatty acids may be same or different. Waxes are the esters of fatty acids which contain monohydric alcohol of higher molecular weight other than glycerol. Waxes have been found in the wax of bees, oil obtained from the head of sperm whale, carnauba oil and lanolin etc.

Compound lipids

Compound lipids are the esters of fatty acids which contain an additional group in addition to an alcohol and a fatty acid. The various type of compound lipids are as follows:

Phospholipids

Phospholipids are also known as phosphatides and are found chiefly in the animal tissues. They consist of two fatty acids, a molecule of glycerol and one alcohol modified

phosphate group. Phospholipids possess both hydrophilic (phosphate group) and hydrophobic (uncharged fatty acids) properties.

Glycolipids

Glycolipids are also known as glycosphingolipids and they contain a fatty acid, sphingosine, and carbohydrate in their structure.

Lecithin

Lecithin contains a phosphatide linked to choline. It is also known as phosphatidyl choline or serine. It is found mainly in organ meats, yolk of the egg and the brain. It aids in the metabolism and transportation of the fats. It is also used as an emulsifier in the food industry.

Cephalin

It contains a phosphatide linkage to serine or ethanolamine. This occurs predominantly in nervous tissue and helps in the clotting of blood.

Plasmalogen

Plasmalogens play an important role in the structural membranes especially in the stability of cholesterol rich membranes which are involved in cellular signaling. These belong to the glycerophospholipids having a vinyl-ether and an ester bond at position sn-1 and sn-2. It is found in brain, heart, and muscle.

Lipositol

It is also known as phosphatidyl inositol where phosphatide is linked to inositol. It is rapidly synthesized and degraded in the brain. Kidneys, heart, brain and plant tissues are the major sources of lipositol. It functions in the cell transport processes.

Sphingomyelin

It is a sphingosine-containing phosphatide which yields fatty acids, choline, phosphoric acid, and sphingosine on hydrolysis. However, no glycerol is produced on the hydrolysis. The major sources are brain, nervous tissue and red blood cells. It is also a source of phosphoric acid in the body.

Cerebrosides

Cerebrosides consist of ceramide i.e. a sphingosine and fatty acid and a mono sugar bound to the C1 of sphingosine by a β -glycosidic bond. Most commonly found carbohydrates in these are galactose while the fatty acids are 24 carbon lignoceric, ceribonic or hydroxylignoceric acid. The lignoceric acid containing cerebrosides are known as kerafin, while those containing ceribonic acid are called phrenosin. White matter of the

brain and nerve myelin sheaths is the sources of cerebrosides. Small quantities are also present within the cell membranes of other tissues.

Ganglioside

Ganglioside is composed of a glycosphingolipid. It contains a ceramide or oligosaccharide which is linked to a hexose sugar, n-acetylneuraminic acid, fatty acids and sphingosine. This is present in brain, nerve tissue and spleen etc.

Sulfolipid

It is a sulphur containing glycolipid in which the sulphur is present in ester linkage with galactose. This is present in brain, liver, testicle and plant chloroplast.

Proteolipids

In these the proteins are covalently bound to lipid moieties like fatty acids, cholesterol, isoprenoids and glycosylphosphatidylinositols. They are present in brain and nerve tissue.

Precursor and derived lipids

These lipids are derived from simple or conjugated lipids by hydrolysis. This class includes fatty acids, glycerol, fatty aldehydes, ketone bodies, steroids, hydrocarbons, lipid soluble vitamins, and hormones.

Terpenes, terpenoids and steroids

Terpenes are simple hydrocarbons which consist of five carbon isoprene units which are attached to each other in different ways. These are the largest class of secondary metabolites and found in resin acids, essential oils, rubber and plant originated pigments like carotenoids and lycopene's. The modified form of terpenes with different functional groups is known as terpenoids. Depending on the carbon units' terpenoids may be classified as monoterpenes, diterpenes, triterpenes, sesterpenes and sesquiterpenes. A list of sterols, their sources and role in human body has been provided in the Table 1.

Classification on the basis of chain length and unsaturation

Fatty acids (FAs) are the small units of lipids. These are a straight hydrocarbon chain of even carbon atoms. This chain has hydrogen atom (H) at one end and carboxyl group (-COOH) at other end. FAs are not found in nature in their free form and generally join in a group of three with an alcohol to form triglyceride. Fatty acids can be classified on the basis of chain length, degree of unsaturation and the amount of essential acids present. The fatty acids having less than 8 carbon atoms in chain are known as short chain fatty acids, 8-12 carbon atoms as medium chain fatty acids and 14 and above carbon atoms as long chain fatty

acids. The fatty acids with single bonds are known as saturated while those with the double bonds are known as unsaturated. There are two essential fatty acid i.e. linoleic acid (ω -6) and linolenic acid (ω -3). Nuts like walnut; seeds like flaxseed, rapeseed; legumes like soyabean are the rich source of Alpha-linolenic acid. Aquatic animals particularly the fish is rich in the longer-chain omega-3 fatty acids like alpha linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Table 2 depicts some of the unsaturated fatty acids found in the food along with their sources.

Dietary recommendations

Near about 25-30% of total calories should come from the fats. The unsaturated fats are recommended above the saturated fats. The various unsaturated fats like monounsaturated, desaturated and polyunsaturated are considered as healthy fats. The amount of saturated fats should not exceed 10% of total calories intake (ICMR, 2010). Linoleic acid and linolenic acid are two essential fatty acids which cannot be synthesised in the body. In addition to essential fatty acids other unsaturated fatty acids like EPA and DHA plays an important role in anticoagulation, cardiovascular function, coronary events and peripheral artery disease. The World Health Organization (WHO) has concluded that saturated fats negatively affect cholesterol profiles, predisposing individuals to heart disease, and recommends avoiding saturated fats in order to reduce the risk of a cardiovascular disease.

Classification on the basis of saponification

On the basis of saponification the lipids are classified as saponifiable and non-saponifiable lipids. The saponifiable lipids can be broken down into smaller molecules by hydrolysis in the presence of acid, alkali or enzymes. This group consists of triacylglycerides, glycerophospholipids, and the sphingolipids. Non-saponifiable lipids cannot be hydrolysed by the acids, alkalis and enzymes and this group includes steroids, prostaglandins, and terpenes.

Beneficial effects of lipids in body

Component of membranes

Glycerophospholipids are the main components of biological membranes like cellular plasma membrane and the intracellular membranes of organelles. Structurally, glycerophospholipids contain a glycerol core that is linked to two fatty acids and one phosphate by ester linkage. This lipid molecule has amphipathic properties as it possess both hydrophobic and hydrophilic regions. The glycerophospholipid membrane physically

separates the inside of the cell from the exterior environment. In addition to phospholipids; glycolipids, sphingolipids and cholesterol are also found in biological membranes (Dowhan and Bogdanov, 2002).

Cell signaling and brain development

Lipid can help in signalling by activating the G-protein and nuclear receptors. The lipids like diacylglycerol (DAG) and phosphatidylinositol phosphates (PIPs) are responsible for the activation of protein kinase mediated by calcium. Prostaglandins prevent inflammation and enhance immunity. The steroid hormones like estrogen, testosterone and cortisol play an important role in reproduction, metabolism and blood pressure. Human brain contains a high concentration of lipids. These lipids play an important role in the central nervous system and cell signalling (Adibhatla and Hatcher, 2007). Cholesterol, phospholipids, cerebroside, sulfatides, and gangliosides are the major lipids present in the brain (Carlson, 2009). The pattern of fatty acid phospholipids changes during the fetal development stage. In the last trimester of pregnancy and the early two years of a child the accumulation of DHA has been reported. Human milk is a good source of DHA and helps in its accumulation during the early stages of life. The low DHA accumulation during development has been reported to cause slower maturation and slower processing of brain. In addition to DHA, influences of cholesterol and gangliosides in brain development have been reported in some studies conducted on the animals. Long chain essential fatty acids, especially the PUFAs, along with choline (Ziesel, 2009) perform important function in postnatal nutrition during the phase of rapid brain growth.

Store house of energy

Lipids, particularly the triacylglycerols are the major store house of energy in animals (USDA, 2002). On the complete oxidation fats provide near about 9 kcal/g, which is two times higher in comparison to 4 kcal/g provided by carbohydrates and proteins. During starving it provides energy and saves the glycogen reserves for the activity of brain. Polar bears during hibernation and the birds which migrate to the long distances by flying for hours without eating use stored energy of triacylglycerols to fuel their flights.

Cutaneous function of lipids

The permeability barrier is important for the terrestrial life of the cells. Stratum corneum (SC) is the outermost layer in the mammalian skin and exhibits the main skin barrier which controls the water penetration. A protection from dehydration and external dangers is

provided to the cells by this layer. The SC layer has ceramides (50%), cholesterol (25%) and FFAs (15%) in its composition. In the studies conducted on humans to compare the major SC lipids in the humans, ceramide 1 and to a lesser extent ceramide 3 has been reported to affect the pathogenesis of atopic dermatitis. The role of the essential fatty acids in the permeability and normal structure of the SC was also found (Feingold, 2007). In case of the deficiency of essential fatty acids, linoleate present in the acylceramides are replaced with oleate which results in abnormalities in cutaneous permeability barrier function.

Nutrition and health

Food is the main source of lipids in our diet. The major lipids that we get from our food are triacylglycerols, cholesterol and phospholipids. These lipids help in the absorption of the fat soluble vitamins i.e. A, D, E and K. The omega-3 fatty acids have been reported to play an important role in the physical and medical development of infants, prevent the cardiovascular diseases and prevention of cancer. The saturated fats are considered unhealthy and Indian council of medical research (ICMR) has recommended reducing the intake of the saturated fats and trans fats. Leukotrienes lipoxins are potent regulators of many disease processes.

Other functions

Lipids are also essential for the absorption of fat soluble vitamins. Acyl-carnitines aids in the transport and metabolism of fatty acids in and out of mitochondria. The transportation of the oligosaccharides across the membranes is facilitated by the polyprenols and their phosphorylated derivatives. In the extracellular polysaccharide biosynthesis like peptidoglycan polymerization in bacteria and N-glycosylation in eukaryotic protein, polyprenol phosphate and disphosphate sugars play an important role. The inner mitochondrial membrane contains cardiolipins a subclass of glycerophospholipid in abundance. The cardiolipins activates the enzymes involved in oxidative phosphorylation.

Association of lipids with diseases

The lipid intake is associated with several health conditions like increased level of cholesterol in the blood, high blood pressure, cardiovascular diseases (CVD), coronary heart diseases (CHD), obesity, atherosclerosis and cancer. The association of some of the diseases with the lipid intake has been discussed in this section.

Lipids and obesity

Obesity is a medical condition which results from the accumulation of excess fat in the body. More scientifically when the body mass index (BMI) of a person increases beyond 30 Kg/m^2 , he/she is known as obese. The accumulation of the excess fat causes several adverse health effects. This disease is caused by the consumption of excess of calories without any physical activity. The energy from fat is absorbed more efficiently in intestine as compared to the carbohydrates and proteins. The fat also has low thermogenic effect as compared to proteins and carbohydrates, hence, results in low energy expenditure (Astrup, 2005). The relation of dietary fat intake and obesity is controversial, however, according to a study conducted by Dansinger et al., (2005) a low fat and carbohydrate diet for 1 year may result in weight management. The metabolic consequences of obesity are highly dependent on fat distribution. The increase in the accumulation of the abdominal fat accumulation leads to the insulin resistance. This can occur in both men and women and this type of obesity is known as android obesity. The other form of obesity i.e. visceral obesity is associated with hyperinsulinemia, hypertriglyceridemia, glucose intolerance, hypertension, and common forms of cancer. Infertility is also more common in overweight women.

Lipids and diabetes

Lipid abnormalities in human body result in development of diabetes mellitus in some cases and are found to be a major concern. This variability of lipid concentration in majority gives rise to Type 2 diabetes in both males and females (Ozder et al. 2014). Most common symptoms include high levels of triglycerides and low levels of high density lipoproteins (HDL). However, low density lipoproteins (LDL) concentration does not varies much in type 2 patients. The level of triglycerides in type-2 diabetic patients is less than 2.3 mmol/L (200 mg/dl) (Gerog et al. 2000). Lipid abnormalities also triggered dyslipidemia as hypercholesterolemia, hypertriglyceridemia, elevated LDL and decreased HDL. A mass of interrelated plasma lipid and lipoprotein abnormalities contribute to the development of risk for atherosclerosis and chronic heart diseases in the majority of type 2 diabetes patients (Krauss 2004).

Lipids and cancer

It has been reported in studies that abnormal levels of lipids leads to development of carcinogenic activities and cancer metastasis. The higher levels of TC, TG and HDL concentrations can lead to development of prostate cancer, breast cancer, ovarian cancer, gastric cancer, and colorectal cancer (Branco et al 2014). Quercetin a polyphenolic flavonoid

compound, having anti-lipid oxidative activity has been used for cancer treatment. It effectively decreases the expression of fatty acid synthase, which inhibits the growth of nasopharyngeal carcinoma cells of human gastric cancer cells and of human leukemia T-cells. Moreover, quercetin has significant effect on the plasma non-enzymatic antioxidant capacity and reduces lipid peroxidation, which prevents from oxidative damage elicited by doxorubicin and docetaxel during the course of treatment of breast cancer. Quercetin also uplifts the lipid peroxides which in turn reduces the tumor size. It has also been indicated that quercetin treatment inhibits the lipid peroxidation and helps in maintaining the H₂O₂ level, resulting in the prevention of development of prostate cancer. (Long et al 2004).

Role of lipids in multiple sclerosis

Multiple sclerosis (MS) is a disease of central nervous system which is very common in young adults. It causes the chronic autoimmune demyelination of the central nervous system. The upregulation of the cytokines like TNF- α , IL-1 β , IL-2, LT α , LT β , and IFN γ in the cerebrospinal fluid (CSF) of the brain tissue has been reported in the studies conducted on animals. In MS the myelin forming cells of CNS (oligodendrocytes) are the main target cells. The life cycle of the cells like the brain cells is regulated by the ceramide and sphingosine-1 phosphate (Jana and Pahan, 2010) Glycosphingolipid can promote or suppress the immune responses by activating the natural killer T-cells (Halmer et al., 2014). Sphingomyelin a phosphosphingolipid has been found to be beneficial in preventing the vulnerability of brain to the oxidative stress. The reactive oxygen species activates the macrophages or microglia which is responsible for the damage of oligodendrocyte and myelin. Plasma lipids also decline in MS (Montfoort et al., 1966).

Role of lipids in lipidosis

Lipid storage disorder or lipidosis is a genetic disorders of fat metabolism by the accumulation of distinctive types of lipids in the cells and tissues in the brain, PNS, liver, spleen and bone marrow in abnormal amounts. Children born with lipidosis, does not contain the specific genetic codes and certain enzymes, which can complete digestion and utilization of fat. Majorly they are inherited by two ways, autosomal recessive and X-linked recessive inheritance. Autosomal recessive occurs when both the parents carry and pass a copy of the faulty gene, but neither parent is affected by the disorder. In X-linked recessive inheritance, mother carries the affected gene on the X-chromosome.

Role of serum cholesterol in atherosclerosis and coronary heart disease

Atherosclerosis is an inflammatory disorder of hyperlipidemia and lipid oxidation which results in the thickening of the intimal layer of arteries and accumulation of fat. Low-density lipoproteins (LDLs) are one of the most important factors to initiate atherosclerosis. It enters the artery wall from plasma and thus accumulates and modifies them to stimulate endothelial cells to express monocyte chemotactic protein-1 (MCP-1). The monocytes from the blood are attracted by the protein into the artery wall (Setorki, 2014). The differentiation of monocytes into macrophages is promoted by the modified LDLs which promotes the formation of lipid-filled foam cells. The onset and progression of atherosclerosis and coronary heart diseases begins with the entry of LDLs into the artery wall (Barter, 2005). Eicosapentaenoic acid from fish oil has shown a reduction in the triglycerides and cholesterol by 30% at the doses of 3 g/day (Lewis, 2008).

Lipids and fatty liver

The accumulation of free cholesterol in the liver takes place when the synthesis of the hepatic triglyceride is more than its catabolic rate (Hartley et al., 2019). The accumulation of cholesterol in the liver activates the intracellular signalling pathway in the Kupffer cells (KCs), Stellate cells (HSCs) and hepatocytes which leads to liver injury (Wang et al., 2019). The activation of these cells further promotes the inflammation and fibrogenesis. The increase in the cholesterol level of mitochondria impairs the mitochondrial GSH transport and disrupts the fluidity of the membrane. As a result there is an increase in the reactive oxygen species which triggers the response of unfolded protein in the endoplasmic reticulum (ER) causing the consequent ER stress and apoptosis. As a result a viscous circle is created which contributes to the maintenance of steatosis and promotes the death of hepatocytes and damage to the liver. The treatment of non-alcoholic fatty liver disease (NAFLD) can be achieved by controlling hepatic fat accumulation (Marchesini et al. 2016) by changing the lifestyle (Wang et al., 2019). Vitamin E has been found effective in the treatment of nonalcoholic steatohepatitis (NASH) (Harrison et al., 2019).

Ketogenic diet and its health benefits

Ketogenic diet is now a days proving out to be a very popular treatment for several diseases such as epilepsy, obesity, high cholesterol. Ketogenic diet acts as first line of defence for the enlisted diseases. It also has some adverse effects such as gastro-intestinal

diseases, nausea and vomiting, lethargy, hypoglycemia, kidney stones, elevated blood ketones, hypoglycemia, bone mineral loss, renal damage, weight loss etc. (Allen et al 2014). These diets are considered to be of high fat concentration, low carbohydrate and average protein concentrations, favouring mitochondrial respiration for metabolic process of energy transformation (Branco et al. 2014) For the treatment of respiratory epilepsy in children it was found out to be very much effective by increasing the levels of serum total cholesterol, LDL, and triglycerides, but in case has also shown some side effects as development of hyper-cholesterolemia and hyper-triglyceridemia. (Zamani et al 2016). In the study carried out regarding the skeletal muscle and fat mass, it showed that lean body mass has increased ($4.3 \pm 1.7\text{kg}$), muscle mass has increased to a level of ($0.4 \pm 0.5 \text{ kg}$) and the fat mass has decreased to ($-2.2 \pm 1.2 \text{ kg}$) (Rauch et al 2014).

Conclusion

In the light of the literature discussed it can be concluded that the lipids play an important role in the human diet. They are involved in many biological functions. It is not the fat that is bad for our health but its good and bad effects depends upon the source of the lipid. The fats derived from animals are mostly saturated while the lipids derived from the plant sources are unsaturated fatty. The essential fatty acids which are mandatory to be taken in diet are also unsaturated i.e. linolenic acid and linoleic acid. The dietary guidelines by the ICMAR also recommend limiting the consumption of saturated fatty acids only to 8-10% of total calories intake. The application of high fat and low carbohydrates (e.g.- ketogenic diets) diet has been also recommended by some researchers in the prevention of cancer. However, further studies need to be carried out in this field.

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Table 1: Sterols/steroids, food sources and their role in human body

Sterol	Source	Role in human body
Cholesterol	Animal tissues, dairy products, egg yolk	A constituent of bile acids Precursor of Vitamin D
Ergosterol	Plants, yeast, and fungi	Converted to Vitamin D ₂ on irradiation
7-dehydrocholesterol	Animal tissues underneath skin	Converted to D ₃ on irradiation
Androgens and estrogens	Ovaries, testes	Sex hormone
Adrenals corticosteroids	Adrenal cortex and blood	

Table 2: Nomenclature of fatty acids

Name of fatty acid	Carbon atoms and number of double bonds	Position of unsaturation	Formula	Food sources
Palmitoleic acid	16:1	C9	$\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$	Whale oil
Oleic acid	18:1	C9	$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$	Olive oil
Linoleic	18:2	C9, C12	$\text{CH}_3(\text{CH}_2)_4\text{CH}=\text{CH}$	Safflower and

acid			$\text{CH}_2\text{CH}(\text{CH}_2)_7\text{COOH}$	soyabean oil
Linolenic acid	18:3	C9, C12, C15	$\text{CH}_3(\text{CH}_2)(\text{CH}=\text{CHCH}_2)_3(\text{CH}_2)_6\text{COOH}$	Linseed oil, fish oil
Arachidonic acid	20:4	C5, C8, C11, C14	$\text{CH}_3(\text{CH}_2)_4(\text{CH}=\text{CHCH}_2)_4(\text{CH}_2)_2\text{COOH}$	Liver
Eicosapentaenoic acid	20:5	C5, C8, C11, C14, C17	$\text{CH}_3\text{CH}_2(\text{CH}=\text{CHCH}_2)_5(\text{CH}_2)_2\text{COOH}$	Salmon, sardine, algae
Docosahexaenoic acid	22:6	C4, C7, C10, C13, C16, C19	$\text{CH}_3(\text{CH}_2)_4(\text{CH}=\text{CHCH}_2)_4(\text{CH}_2)_2\text{COOH}$	Algae, fatty fish (salmon, mackerel, tuna)