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Nature and Effects of Cholesterol; Its Origin, Metabolism and Characterization

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ABSTRACT: *Cholesterol ((3β)-cholest-5-en-3-ol) is basically a fatty component present in blood, plasma and tissues. It belongs to the class of lipids namely steroids and is formed from squalene via lanosterol. It is present as a combination of cholesterol and cholesteryl esters in almost all types of foodstuffs. There is the direct relation between the risk of cardiovascular sicknesses and the total cholesterol amount in human blood. The bad- and good-cholesterol are types of lipoproteins. Good-cholesterol basically eliminates cholesterol from bloodstream while bad-cholesterol releases cholesterol into the blood and various part of body. Cholesterol amount can be reduced by physical activity or by use of proper diet. Cholesterol can be characterized by the SIM-selected ion monitoring, HPLC, UHPLC, GLC, GC-MS, LC-MS.*

Key words: *Cholesterol; Hazard; Diet; Exercise; Analysis*

INTRODUCTION

Cholesterol is present in the form of fats or lipids in animal tissues (also including human) and insoluble in blood. It is essential for better human health as it participates to break-down the oil contents present in our meals (Essaka, 2007). But on other hand excess of cholesterol also affects the human health and causes cardiovascular diseases. Cholesterol is basically a type of "sterol" and fall in the class of "lipids" commonly known as "steroids", containing identical four-ring system termed as perhydro-cyclopentano-phenanthrene (Miettinen et al., 1990). It consists of twenty seven carbon containing molecule with a hydroxyl group and an aliphatic chain (i.e. minimum 8 carbons chain) at position C_3 and C_{17} respectively (as given in Fig. 1).

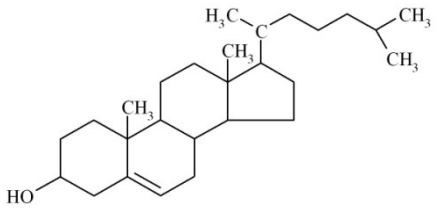

Fig. 1: Structure of cholesterol (Nes, 2011)

Lipids perform a significant role in the composition of biological membranes. About half of the body cholesterol is dispersed in the lipid bilayer of cell membrane (Fig. 2). Cholesterol is distributed as a precursor of adrenal hormones and involved in the digestion of oil and fat contents which exist in our routine food. Actually, cholesterol is important for body which is added to body not only from foodstuffs but also produced in the liver and some other tissues.

Keeping in view the adverse effects of higher concentration of cholesterol in human body, current studies were performed to overview the nature and effects of cholesterol. Attempts were also made to discuss its origin, metabolism and characterization by various analytical techniques.

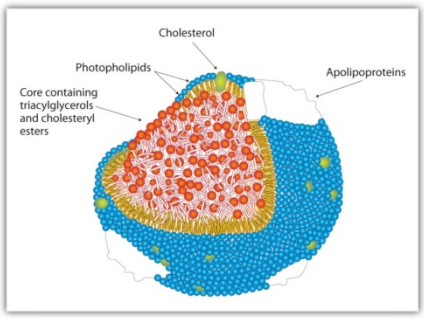

Fig. 2: Schematic diagram of cell membrane
(https://www.pinterest.com/pin/717550153100824845/)

Methodology

Studies were conducted to review the origin, nature, characterization and effects of cholesterol. The literature has been consulted regarding the transportation (Albuquerque et al., 2016; Essaka, 2007; Miettinen et al., 1990), nature (Albuquerque et al., 2016; Cook, 2015; Essaka, 2007; Kramer et al., 2006; Miettinen et al., 1990; Nelson et al., 2008), metabolism (Cook, 2015; Itakura and Riggs, 1993; Montgomery, 1996), factors affecting accumulation (Cornfield, 1962; Kajiwara et al., 2016), effects (Einhorn, 2009; Essaka, 2007; Goad and Akihisa, 2012; Kramer et al., 2006; Montgomery, 1996) and characterization (Ahmida et al., 2006; Albuquerque et al., 2016; Careri et al., 2001; Chevy et al., 2005; Dyer et al., 1995; Essaka, 2007; Hamid and Omar, 2003; Hidaka et al., 1990; Kasama et al., 1987; Keller and Jahreis, 2004; Kuriyama et al., 1991; Lin et al., 2010; Miettinen, 1982; Miettinen et al., 1990; Palmgrén et al., 2005; Phillips et al., 1999).

DISCUSSION

Transportation of Cholesterol

Cholesterol is produced in various tissues, intestinal walls and liver by different cells of the body (Kramer et al., 2006; Nelson et al., 2008) and is present as a mixture of cholesterol and cholesteryl esters in almost all types of food products, including eggs, milk, butter, cheese, cream, fish and meats (Albuquerque et al., 2016; Miettinen et al., 1990). Cholesterol is absent in non-animal sources (e.g., fruits, vegetables etc). The transformation of cholesterol is done by "lipoproteins", that are basically a combined form of lipids and proteins. Lipoprotein exists in various kinds but bad-cholesterol and good-cholesterol are most familiar lipoproteins (Essaka, 2007). In solution, cholesterol is not present in free form.

LDL-Bad Cholesterol/LDL & CVD

Low-density lipoproteins (LDL) basically act as carriers of cholesterol (known

as "bad cholesterol") in the blood and to various part of body. LDL is also found in arteries of brain and heart and results in blockage of the arteries. For a healthy person upper limit of LDL cholesterol level is 160 mg/dL and for heart patient its value is 100 mg/dL (Essaka, 2007). The immune system identifies the change in cholesterol level which causes any damage. Any accumulation of cholesterol causes coagulation (*i.e.* clots) by interaction of cholesterol with proteins. Low density cholesterol causes Atherosclerosis-disease which involves the stiffening of blood vessels.

HDL-Good Cholestrol

The high-density lipoprotein (HDL) is basically opposite to LDL in its behavior, and cardioprotective. It is also said to be "good-cholesterol", as good-cholesterol collects the contents of bad-cholesterol from blood-vessels, tissues and sends it back to the liver. HDL eject-out the surplus amount of cholesterol and slows down its development; it thus decreases the chance of heart attack. Therefore high value of good-cholesterol favors the good health while it is dangerous if its concentration is lesser than forty milligram/dL and fifty milligram/dL in male and female, respectively (Albuquerque et al., 2016; Essaka, 2007; Kramer et al., 2006; Miettinen et al., 1990; Nelson et al., 2008).

Biological-fabrication of Cholesterol

In 1940s it was firstly elaborated by Konrad Bloch that acetates are the source of all C-atoms of cholesterol. His prediction urges the scientists to inspect the cholesterol fabrication complexities (Cook, 2015). The fabrication of cholesterol occurs in four steps that are initiated from acetate group (i.e. of two carbon atoms) of the Acetyl-coenzyme A; in first step acetate produces mevalonate, which then in second stage is converted into 2 activated isoprenes. In third step, six components of activated isoprenes are combined to form squalene, which eventually forms the nucleus of the four-ringed steroid in the 4^{th} step (Nelson et al., 2008).

Metabolism of Cholesterol

In our body, a large amount of cholesterol is produced in liver. But on other hand, most of the tissues (i.e. gut, skin or nervous tissues) also participate in its production. Normally in a healthy person, cholesterol is produced ~800 mg per day and that amount can be increased by using foodstuff (Cook, 2015). So in order to avoid from health diseases caused by excessive cholesterol levels in body, one must have to control his/her diet. Cholesterol also has its own importance in production of animal's tissues for membrane synthesis. Furthermore, the cholesterol acts as a precursor (through its metabolism) of 5 categories of hormones related to steroids which are glucocorticoids, androgens, mineralocorticoids, estrogens and progestagens (Cook, 2015).

The disintegration of cholesterol is a source of bile salts, which are polar in nature and are generated in liver, accumulate in gallbladder, and finally liberate into small intestine. They dissolve regime lipids, and therefore increase their hydrolysis (by lipases) and thus absorption (Itakura and Riggs, 1993). The liver turns 80% of cholesterol into different types of bile acids, which then combine with taurine or glycine and produce bile-salts (e.g., glycocholate is produced from combination of cholate and glycine) (Cook, 2015). In liver exceeding amount of cholesterol can be overcome by the transformation of cholesterol-into-bile acids, as its high concentration can harm the tissues. In a healthy person, extra cholesterol is

released as sterols or bile acids (Montgomery, 1996).

Factors affecting the Cholesterol

There are several factors that can increase the chance of bad cholesterol i.e.,

- ***Diet.*** By intake of fatty food the chances of high cholesterol level increases. These foodstuffs also involve dairy products and meat, which can raise the risk of cholesterol.
- ***Weight.*** If a person become chubby then the risk of high cholesterol increases.
- ***Physical Activity.*** With the help of exercise our body increases the concentration of good-cholesterol which is good for our health.
- ***Smoking.*** Smoke from an any source (e.g., cigarette, vehicles, chimneys etc) has bad effects on our body by damaging our respiratory system and blood vessels. It makes pores in our vessels and increases the chance of accumulation of fatty deposits. And it also decreases our good-cholesterol level.
- ***Effect of Age.*** With the increase of age the chances of high cholesterol also increases. Because with age liver becomes weak to excrete bad-cholesterol.
- ***Diabetes or High blood sugar.*** By the increase of sugar level in blood the walls of arteries become damage due to which good-cholesterol level deceased, finally bad-cholesterol level is increased. (Cornfield, 1962; Kajiwara et al., 2016)

Effect of Cholesterol-World Survey

Cholesterol is good for health to some extent (as mentioned in 1.3), but higher concentration of bad-cholesterol can cause the different cardiovascular diseases, blockage of arteries, brain stroke and heart attack. Cholesterol can be transported from parents to children. Good health depends on daily routine intake and exercise. There is no other source of indication of high cholesterol except blood tests (Essaka, 2007). Furthermore, in 2016 American Heart Association's (AHA) reported that one patient out of every three die with the Heart Disease and Stroke in the U.S. in 2013. CVD disease is not only the major killer in the U.S. but also in worldwide (Essaka, 2007; Montgomery, 1996).

The worldwide survey showed that:

- According to 2013th report ~31% died with CVD disease, out of which 80% were belonging to backward countries.
- In 2010 almost 16.9 million lives worldwide had a first stroke.

Heart diseases are mostly caused by high-cholesterol levels in the blood, high blood pressure, fatness, diabetes, and smoking. The National Health Institutes reported that the risk of heart diseases is generally increased among men having ages from 30 to 49 years whose cholesterol levels was found above 260 mg/100 mL of serum. The blood-cholesterol level changes greatly with age, diet, and sex. Cholesterol level in blood for adults is about 170 mg per 100 mL, whereas men at age of 55 may have $\geq$ 250 mg/100 mL due to decrease in rate of cholesterol decay with age. But in female's blood, cholesterol level is lower than males (Goad and Akihisa, 2012; Kramer et al., 2006). Fig. 3 displays graphically the death-rate due to heart-diseases (United States: 1900–2009) (Einhorn, 2009).

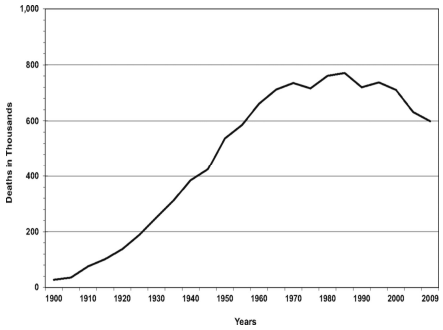

Fig. 3: Graph showing the death-rate due to heart-diseases (United States: 1900–2009) (Einhorn, 2009)

Characterization of Cholesterol

The simplest and affordable method for the determination of cholesterol in blood serum depends on the reaction in which esterase and oxidase of cholesterol act as a catalyst (Hamid and Omar, 2003). In biological samples, sterol can be determined by different methods such as HPLC (Hidaka et al., 1990; Kasama et al., 1987; Kuriyama et al., 1991), GLC (Miettinen, 1982; Miettinen et al., 1990; Phillips et al., 1999), GC-MS (Chevy et al., 2005; Dyer et al., 1995; Keller and Jahreis, 2004; Lin et al., 2010) and LC-MS (Careri et al., 2001; Palmgrén et al., 2005).

HPLC is not efficient to give good separation as compared to GLC because of poor separation result in 3β-sterol. Additionally, both HPLC with Ultra Violet detector and GC with Flame Ionization detector are incapable for determining the clarity of peak (Ahmida et al., 2006).

Albuquerque, T.G. et al 2014 have validated two chromatographic methods (HPLC and UHPLC) to attain the best results for the quantitative analysis of cholesterol in food product. Those methods were applicable for cholesterol quantification in various food products (i.e. dairy products, egg, and chicken). HPLC and UHPLC both are accurate, sensitive and less time consuming methods. For HPLC, the reported results was LOD = 3 microgram per mL but LOQ = 11 microgram per mL; on other hand for UHPLC, LOD = 0.7 microgram per mL but LOQ = 2.4 microgram per mL. UHPLC technique became able to decrease the analysis time to 4 minute by decreasing the use of the organic solvents (i.e. 8 times lower); it is eco-friendly and useful for cholesterol determination, as compared to conventional HPLC methods (Albuquerque et al., 2016).

Christian (2007) presented an HPLC procedure for determining the amount of cholesterol within foodstuff. The sample was loaded by using C-18 column as stationary phase while methanol:2-propanol (70:30) was used as mobile phase at wavelength 212nm. For the various analyzed samples, the linearity and reproducibility with relative standard deviation fall in the range of 5.0 - 100.0 µg/mL and 4.22%, 2.71%, 4.8%, and 3.7%, respectively. The mean of results for the butter sample was 106.5% (Essaka, 2007).

Ahmida et al. (2006) originated a procedure for the cholesterol determination by using capillary GC-MS with more than one SIM-selected ion monitoring. In this method free sterol and its derivatives were separated on the basis of alkaline hydrolysis of sterol esters. All the results fell within the 76-101%. And RSD-relative standard deviation of all components was not more than 8%, and the plasma levels were found to be 4.73 $\pm$ 2.57 (cholestanol), 2.37 $\pm$ 1.04 (desmosterol), 6.23 $\pm$ 3.14 (lathosterol), 3.67 $\pm$ 1.95 (campesterol) and 5.92 $\pm$ 3.62 (beta-sitosterol) µmol/l (Ahmida et al., 2006).

CONCLUSION

Cholesterol is important for health due to distinctive characters like lipid and a steroid but the exceeding amount of cholesterol in body is responsible for different diseases. The above discussion describes the correlation between coronary heart diseases and high blood cholesterol levels. The problem arises in the presence of excessive cholesterol levels in the blood-serum, particularly in form of bad-cholesterol, because it causes high blood-pressure, coronary-artery disease and stroke, when atherosclerotic plaques is produced within arteries and blocks blood vessels. High concentration of blood-cholesterol doesn't show any symptoms, therefore blood test is required. So it is necessary to study the methods for determination of cholesterol amount within blood and foods. However, UHPLC is most reliable, fastest and accurate technique for the determination of cholesterol.

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