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## **LDL Cholesterol**

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### Abstract

LDL cholesterol or low-density lipoprotein is considered as the nemesis of health as it can lead to various heart diseases. The structural composition, biosynthesis, functions, manipulation, and interaction of LDL cholesterol is discussed to emphasize its importance of presence in our body and at the same time importance to keep it at minimum range. Structural composition gave us the idea of its cholesterol and lipoprotein composition. Biosynthesis of cholesterol describes step by step breaks down of cholesterol into a simpler compound. The Function of cholesterol defines its importance and its absence can cause various disease. The Medicine which manipulates the levels of cholesterol are also discussed and its interaction with various drugs.

## LDL Cholesterol

LDL cholesterol is the abbreviation of low-density lipoprotein cholesterol commonly known as bad cholesterol because when it exceeds its normal range then it has an adverse effect on health. Cholesterol is a form of fat which is present in every cell of our body. There are two types of cholesterol, high-density lipoprotein (HDL) also termed as good cholesterol and LDL cholesterol. Our body need both types of cholesterol as they have their own pros and cons which is highly debatable among scientist since LDL has less protein part and more cholesterol part which can clog arteries hence it has more cons and advised to a patient to keep a close eye on your LDL levels

### Location

Cholesterol is found in our bloodstream, HDL takes cholesterol to the liver which flushes out excess cholesterol from our bloodstream and hence works as a cleanser, while LDL is the cholesterol which can obstruct our arteries and can lead to stroke or heart diseases. Outside source of cholesterol is the food we eat. “Your liver, other organs, and other cells in your body produce about 75 percent of the cholesterol in your blood. The other 25 percent of the cholesterol in your body is affected by the foods you eat. As you take in more cholesterol, your liver compensates by reducing its own production of cholesterol and removing excess cholesterol.” [Watson,n.d.]

### Structure

There is a structural difference in LDL and Hence also a difference in properties “main structural difference between LDL and HDL is their compositions. Approximately 50 percent of the weight of an LDL particle is cholesterol and only 25 percent is protein. High-density lipoprotein particles, on the other hand, consist of 20 percent cholesterol by weight and 50

percent protein. Since protein is denser than fat, HDL particles are more dense than LDL particles, hence the names "high-density" and "low-density" lipoproteins." [Kamps,n.d.].

### Importance

Cholesterol is not all bad, in fact it is essential for human body. It is a blob of fat which cannot dissolve in the bloodstream, so it is transported to the designated organ with the help of transporters known as a lipoprotein. The certain amount of cholesterol is needed for the human body to produce hormones (testosterone, estrogen, and progesterone) and boost our metabolism.

There are different foods which are a good source of cholesterol and by consuming them in the certain quantity, exercise (30 minutes of brisk walking), cut down smoking/alcohol, and by keeping eye on blood sugar and weight you can always have <sup>6</sup> safe blood cholesterol levels.

"Health authorities recommend that cholesterol levels should be no higher than 5.5 mmol per liter if there are no other risk factors present. If there are other cardiovascular risk factors such as smoking and high blood pressure or pre-existing cardiovascular (heart) disease, then the aim for the LDL levels would be less than 2 mmol/l." [Wallis,n.d.]

### Biosynthesis

<sup>15</sup> Cholesterol is an extremely important biological <sup>10</sup> molecule and it is a precursor for the synthesis of steroid hormone, bile acid, and vitamin D. Cholesterol is stored in the cell in the form of esters and it is transported via circulation in lipoprotein particles. Our body tightly regulates synthesis and utilization of cholesterol in order to avoid its over-accumulation which can lead to coronary heart diseases.

### **1** Pathway of cholesterol biosynthesis

“Cholesterol is biosynthesized in various tissues of the human body. Cytostome and mitochondria of the cells of these tissues contain the enzymes required to carry out the synthesis of cholesterol. The intestine and liver synthesize the most cholesterol out of all the organs.

**1** It is estimated that synthesis takes place in four stages

#### **1** 1.formation of mevalonate (6C) by the condensation of three acetate (2C) molecules.

The chain of reaction starts with the condensation of 2 acetate molecules to form acetoacetyl-CoA in the presence of the enzyme thiolase. This acetoacetyl-CoA then reacts with one more molecule of acetate catalyzed by HMG-CoA synthase to give the six-carbon compound  $\beta$ -hydroxy- $\beta$ -methylglutaryl CoA (HMG-CoA).

Now, this six-carbon compound undergoes reduction by HMG-CoA reductase to form mevalonate. This is a rate-limiting step and the electrons are donated by 2 molecules of NADPH. The cholesterol lowering drugs called “statins” such as Atorvastatin inhibit HMG-CoA reductase to lower the body’s production of cholesterol.

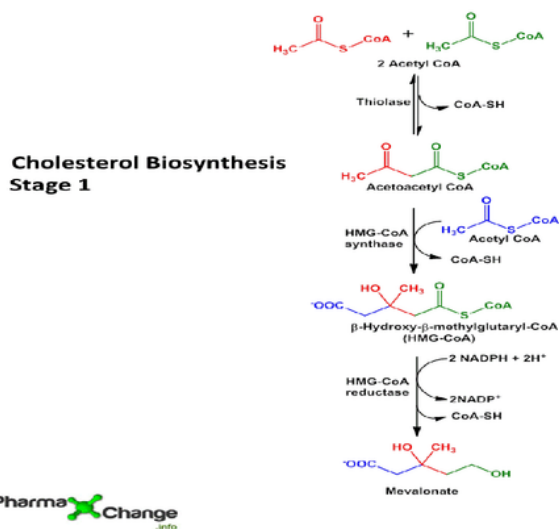


Figure 1[Mehta.2013]

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## 2. formation of activated isoprene (5C) units ( $\Delta^3$ -Isopentenyl pyrophosphate and dimethylallyl pyrophosphate) from mevalonate.

Kinases catalyze the addition of phosphate groups to mevalonate to form 3-phospho-5-pyrophosphomevalonate. 3-phospho-5-pyrophosphomevalonate by releasing carbon dioxide forms the first activated isoprene unit  $\Delta^3$ - isopentenyl pyrophosphate. The phosphate groups are donated by 3 molecules of ATP. The second activated isoprene unit dimethylallyl pyrophosphate is obtained by isomerization of  $\Delta^3$ -isopentenyl pyrophosphate.

### Cholesterol Biosynthesis Stage 2

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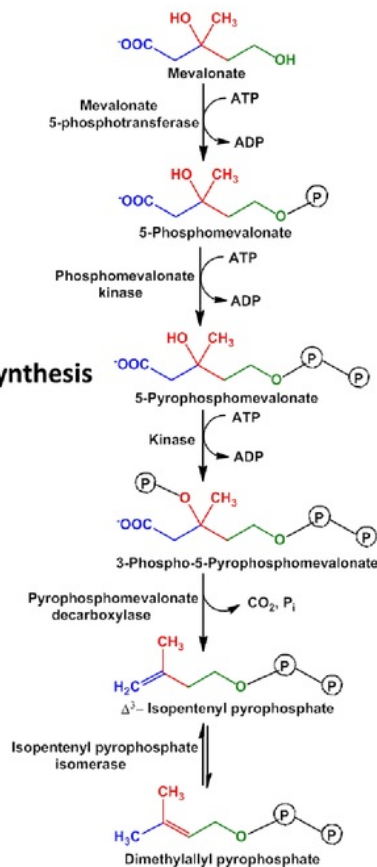


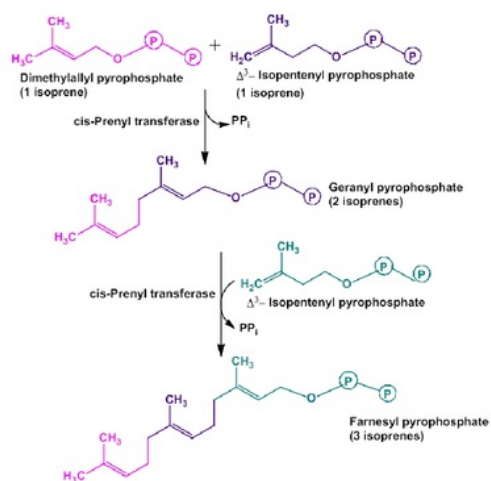
Figure 2[Mehta,2013]

**1**  
3.formation of squalene (30C) (6-isoprenes) by polymerization of activated isoprene units.

The previously formed isoprene units undergo a head-to-tail condensation to form geranyl pyrophosphate by displacing one pyrophosphate group. This 10-carbon compound then reacts with one more molecule of isopentenyl pyrophosphate to yield a 15-carbon compound called as farnesyl phosphate. Squalene is formed with the condensation of 2 farnesyl molecules in a head-to-head manner by the displacement of both the pyrophosphate groups.



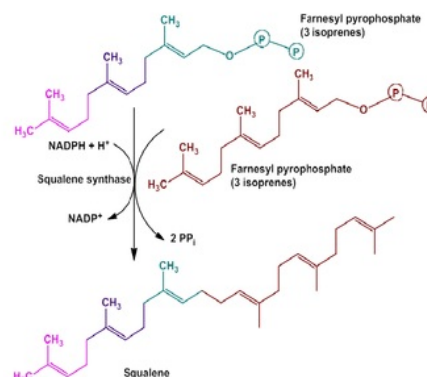
### Cholesterol Biosynthesis Stage 3 - A



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Figure 3[Mehta,2013]

### Cholesterol Biosynthesis Stage 3 - B



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Figure 4[Mehta.2013]

**1**  
4.formation of cholesterol by cyclization of squalene (to form the sterol nucleus) and several other reactions.

An oxygen atom is added to the end of the squalene chain by squalene monooxygenase to form squalene 2,3 epoxide. The other oxygen atom is reduced by NADPH to water. The oxygen atom attached forms an epoxide ring, which along with the double bonds in the structure of squalene 2,3 epoxide is unique to carry out cyclization of the linear structure of squalene. Cyclization by cyclase to form lanosterol. This lanosterol on undergoing further a series of reactions (~ 20) involving removal and addition of certain methyl groups forms cholesterol as highlighted in the figure. 7-dehydrocholesterol, a precursor to vitamin D3, is the penultimate product formed before the formation of cholesterol.” [Mehta,2013]

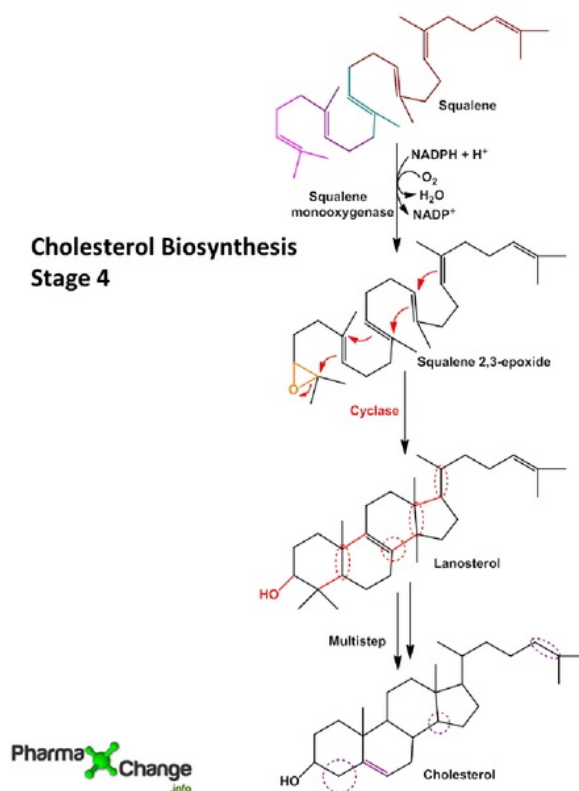


Figure 5[Mehta,2013]

### Functions

Cholesterol aid our body on many levels but there are three main functions of cholesterol.

1. Synthesis of steroid hormone
2. Digestion
3. Building cell membrane

### 1.Synthesis of steroid hormone

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“One of the most important jobs of cholesterol is to aide in the production of hormones.

Cholesterol is stored in the adrenal glands, ovaries and the testes and is converted to steroid

hormones. These steroid hormones perform other vital duties to help the body function properly.

without steroid hormones we will have malfunctions with weight, sex, digestion, bone health and mental status.” [Andrei.2017]

### 2.Digestion

Cholesterol help in the process of digestion as it helps liver to form bile, then bile enters in stomach through bile duct to mix with food and break down in order to help digestion, If fat goes undigested then it will enter in blood stream and start to clog arteries which will lead to stroke and other heart disease.

### 3.Building cell membrane

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“Cholesterol along with polar lipids make up the structure of each and every cell in our bodies.

Cholesterol is there to basically provide a protective barrier. When the amount of cholesterol

increases or decreases, the cells are affected. This change can affect our ability to metabolize and

produce energy. This can ultimately affect other aspects of our bodies' function such as food

intake and digestion.” [Andrei,2017]

### Manipulation

Various drugs are used in order to manipulate the level of cholesterol in blood if lifestyle changes do not lower the levels, the class of drug which is widely used to lower cholesterol levels is known as statins. Statins(also known as HMG CoA reductase inhibitors) are best at lowering LDL cholesterol levels and increasing HDL cholesterol levels. Following people should consult doctor about the risk of high cholesterol and taking statins therapy.

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1. <sup>3</sup> “Adults 40-75 years of age with LDL (bad) cholesterol of 70-189 mg/dL and a 7.5 percent or higher risk for having a heart attack or stroke within 10 years.
2. People with a history of a cardiovascular event (heart attack, stroke, stable or unstable angina, peripheral artery disease, transient ischemic attack, or coronary or another arterial revascularization).
3. People 21 and older who have a very high level of LDL (bad) cholesterol (190 mg/dL or higher).
4. People with diabetes and an LDL (bad) cholesterol level of 70-189 mg/dL who are 40 to 75 years old.” [Cholesterol Medicine, 2017]

### Interaction

Interaction of cholesterol in the body depends upon its synthesis and absorption and that can be affected by various factors such as, age, diet, sedentary lifestyle, medicines etc.

- <sup>2</sup> “Some statins – such as lovastatin, simvastatin and atorvastatin – are more likely to interact with other medications, including some antibiotics and antifungal medications, amiodarone and calcium channel blockers (for example, diltiazem and verapamil). The drug interaction may result in adverse effects that can range from mild muscle aches to a severe breakdown of the muscles (this is called rhabdomyolysis).”
- <sup>2</sup> Gemfibrozil, one of the fibrates that is used for lowering cholesterol, has a strong potential of altering the metabolism of other medications. When combined with certain medications for diabetes such as sulfonylureas, repaglinide, pioglitazone and rosiglitazone, it can make them more powerful in lowering blood glucose.

- When gemfibrozil is combined with selected ARB's (losartan or irbesartan), it can heighten the blood pressure lowering effect. This is also the case with warfarin, and its effect on blood thinning." [Leung.n.d.]

### **Conclusion**

LDL cholesterol considered as a bad cholesterol has its own benefit and it is as important in human body as HDL cholesterol, but it should be kept in controlled range. Its importance is highlighted on various places in this essay as well as light is shown over its hazardous effects in detailed discussion

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