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# Effect of Vitamin D3 on Lipids Metabolism and Adipose Tissue Biology

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**ABSTRACT:**

There are many different kinds of cells that make up adipose tissue, and it plays a vital part in the regulation of inflammation and the maintenance of energy balance, both locally and throughout the body. It is one of the most important organs that is not skeletal in nature and serves as the principal storage location for vitamin D. Vitamin D also has an effect on this organ. It is vital to take into consideration the specific cell type, the stage of differentiation, and the length of time that the therapy is delivered in order to determine how vitamin D can affect multiple aspects of adipose tissue function and development. This is because vitamin D can help determine how vitamin D can influence these aspects. In spite of this, vitamin D has the ability to either slow down or speed up the differentiation process of adipocytes, which are cells that are responsible for the synthesis of fat. This is dependent on the specific cell type. Vitamin D is not only responsible for this, but it also plays a role in the regulation of the energy metabolism that occurs in adipose tissue. The oxidation of fatty acids, the expression of uncoupling proteins, insulin resistance, and the synthesis of adipokines are all altered as a result of this process. Furthermore, inflammation of adipose tissue is a substantial contribution to the metabolic abnormalities that are often associated with obesity. This is because adipose tissue is a major source of fat. There is evidence that vitamin D has the potential to influence the inflammatory response of immune cells, as well as the systemic response and adipocytes that are present in adipose tissue. Vitamin D also has the ability to influence the inflammatory response of immune cells. Additionally, vitamin D has the capacity to prevent the development of cancer in some people.

**KEYWORDS:** Adipose tissue, Vitamin D3, Synthesis, Inflammation ,Metabolism disorder

## INTRODUCTION

### 1-1 What is the adipose tissue?

There are many different kinds of cells that can be found in adipose tissue, which is a type of connective tissue. These cells include adipocytes, immune cells such as macrophages, fibroblasts, smooth muscle cells, and endothelial cells. There is a form of connective tissue known as adipose tissue (Luo &Liu,2016).

The management of inflammation, both locally and throughout the body, is one of the significant roles of adipose tissue, which is made up of a wide variety of cell types. Adipose tissue is responsible for the preservation of energy balance. The non-skeletal organ is considered to be one of the most important organs that is influenced by vitamin D. This is because it is the primary storage location for vitamin D, which puts it in a position of importance. Vitamin D can have a range of effects on the function and development of adipose tissue. One of these effects is the suppression or stimulation of adipocytes, which are fat cells. The exact cell type, stage of differentiation, and duration of therapy all play a role in determining how vitamin D can alter these effects. Vitamin D has the ability to influence these processes in a variety of different ways, and this potential exists because vitamin D is present. Another essential function of vitamin D is that it regulates the energy metabolism in adipose tissue. Vitamin D is responsible for this control, which is another key function of vitamin D. It accomplishes this result via influencing the expression of uncoupling proteins, fatty acid oxidation, insulin resistance, and the generation of adipokines, all of which are in turn affected by it. Adipose tissue inflammation is yet another component that plays a significant part in the metabolic abnormalities that are typically associated with obesity. These abnormalities are characterized by a lack of metabolic efficiency. Vitamin D is able to efficiently manage the inflammatory response of immune cells, in addition to the systemic reaction and adipocytes that are found within adipose tissue. Vitamin D is also able to regulate the systemic response. In addition to this, vitamin D has the capacity to control the inflammatory response that immune cells exhibit (Chan &Sung, 2021). Vitamin D's ability to target the vitamin D receptor (VDR) gene and the enzymes that are responsible for the metabolism of vitamin D in immune cells and adipocytes is the underlying explanation for the significant influence that vitamin D has on the biology of adipose tissue. Vitamin D is associated with a number of health benefits, including a reduction in the risk of various diseases. In order to accomplish its function, vitamin D is directed toward the enzymes that are accountable for the metabolism of vitamin D. Adipose tissue appears to be the primary target for vitamin D consumption outside of the skeletal system, as indicated by the research that has been presented here. (Chan &Sung, 2021).

The relevance of adipose tissue in the body is investigated in this paper, with a special focus on its role in the functioning of vitamin D metabolism. The purpose of this study is to investigate the impact that vitamin D has on energy metabolism and inflammation inside adipose tissue, as well as the role that vitamin D plays in the proliferation and differentiation of adipocytes. Furthermore, the review emphasizes the physiological roles of vitamin D, highlighting the significance of vitamin D in the biology of adipose tissue throughout the process.

**1-2 Storage and metabolism of (vitamin D )in adipose tissue**

When the skin is subjected to ultraviolet (UV)-B radiation, it has the capability of producing vitamin D, which is a fat-soluble vitamin, from 7-dehydrocholesterol on its own. This process can take place in the skin. It is possible to acquire vitamin D by the consumption of food, or it can be produced by the skin itself. Vitamin D, along with other dietary lipids, is absorbed in the upper small intestine through a process known as passive diffusion when it is consumed as part of a diet. This helps to ensure that vitamin D is absorbed properly. (Abbas, 2017).

Consuming vitamin D results in the formation of chylomicrons, which are then discharged into the lymphatic system after being mixed with the vitamin. The body is the location where both of these processes take place. When it comes to the process of chylomicron lipid absorption, the adipose tissue and the skeletal muscle are the ones accountable for it. A further duty that these tissues carry out is the absorption of a portion of vitamin D, which is another responsibility that they are responsible for. Even while research is presently being carried out to determine the particular mechanism by which vitamin D is deposited in adipose tissue, the process by which vitamin D is stored in adipose tissue is not yet completely understood. This is despite the fact that study is currently. After preliminary research, it was discovered that adipose tissue contains a considerable quantity of vitamin D storage space. This was one of the conclusions of the research. These findings were ultimately obtained as a consequence of the analysis of the radioactivity of radiolabeled vitamin D3 in adipose tissue, which was conducted in an indirect manner. ( Landrier *et al*., 2012).

In spite of the fact that it has also been discovered in the tissues of the liver and muscles, it has been demonstrated that the bulk of vitamin D is stored in adipose tissue as **cholecalciferol**, which is one form of vitamin D3. Despite the fact that there are a number of challenges involved in determining the amounts of vitamin D in tissues from a variety of species, this happens. As per the hypothesis that was presented by the authors, the reduction of 13% in total body fat that occurred after 12 weeks of calorie restriction did not have a significant impact on the amounts of 25-hydroxyvitamin D (25[OH]D) that were discovered in human subcutaneous fat and blood. This was the conclusion that was reached. In light of this, they suggested that the authors make use of a strategy that does not include reducing their weight in order to raise their vitamin D requirements. For instance, they suggested that the authors either increase the amount of vitamin D that is absorbed via the diet or increase the amount of vitamin D that is created from the skin and absorbed through the body. (Didriksen *et al*.,2015).

Insufficiency in vitamin D is associated with unhealthy weight growth, and there is a significant component that contributes to the explanation of this connection. The buildup of vitamin D in adipose tissue is the component that is being discussed here. As a result of the findings of the study, it was determined that individuals who were obese had blood 25[OH]D concentrations that ranged from 20 to 30 ng/mL, which indicated that their vitamin D levels were deemed to be inadequate. The 25-hydroxyvitamin D concentrations in the blood of obese individuals were found to be lower than 20 ng/mL, which suggested that these individuals had insufficient quantities of vitamin D. In addition, it was observed that these individuals had decreased levels of vitamin D. Furthermore, there was a negative connection between serum 25(OH)D levels and both body mass index and body fat mass. This was the case for both of these variables. When it came to both of these variables, this was the situation. When it came to both of these variables, this was the situation. This was the predicament we found ourselves in when it came to both of these variables. It was shown that individuals who were obese had a prevalence of vitamin D deficiency that was 35% greater than those who were of a normal weight, and those who were overweight had a prevalence that was 24% higher than those who were of a normal weight. (Drincic *et al*.,2012).

The storage of a considerable quantity of vitamin D is the responsibility of adipose tissue, which performs an important purpose in the organization of the body. Additionally, the substance known as 1,25(OH)2D, which is the active form of vitamin D, is involved in the differentiation of fat cells as well as immune responses. This substance is also involved in the process of regulating the immune system. Specifically, this is due to the fact that there is a correlation between the two. This circumstance has come about as a result of the fact that vitamin D is the form of vitamin D that is still active. Both the liver and the kidney are the key organs that are involved in the metabolic process that is responsible for the transformation of vitamin D into 25(OH)D and then into 1,25(OH)2D. This mechanism is responsible for the transformation of vitamin D. The transformation of vitamin D is the name given to this stage of the process. This particular metabolic process is initiated by the liver, which is the organ in question. The enzymes 25-hydroxylase and 1-hydroxylase have been found to be present in pre-adipocytes, subcutaneous adipose tissue (SAT), and visceral adipose tissue (VAT) in rats and people alike. This was identified through research conducted in the United States. This demonstrates that these enzymes are performing their functions in these tissues at the appropriate degree. Both rats and people were used in this experiment, and the results were gathered from both different sources. On rats, this experiment was carried out. The diagram that can be found in (Fig. 1) provides an illustration of the mechanism that is responsible for the absorption and activation of vitamin D that is obtained from food. (Ding *et al*.,2012).

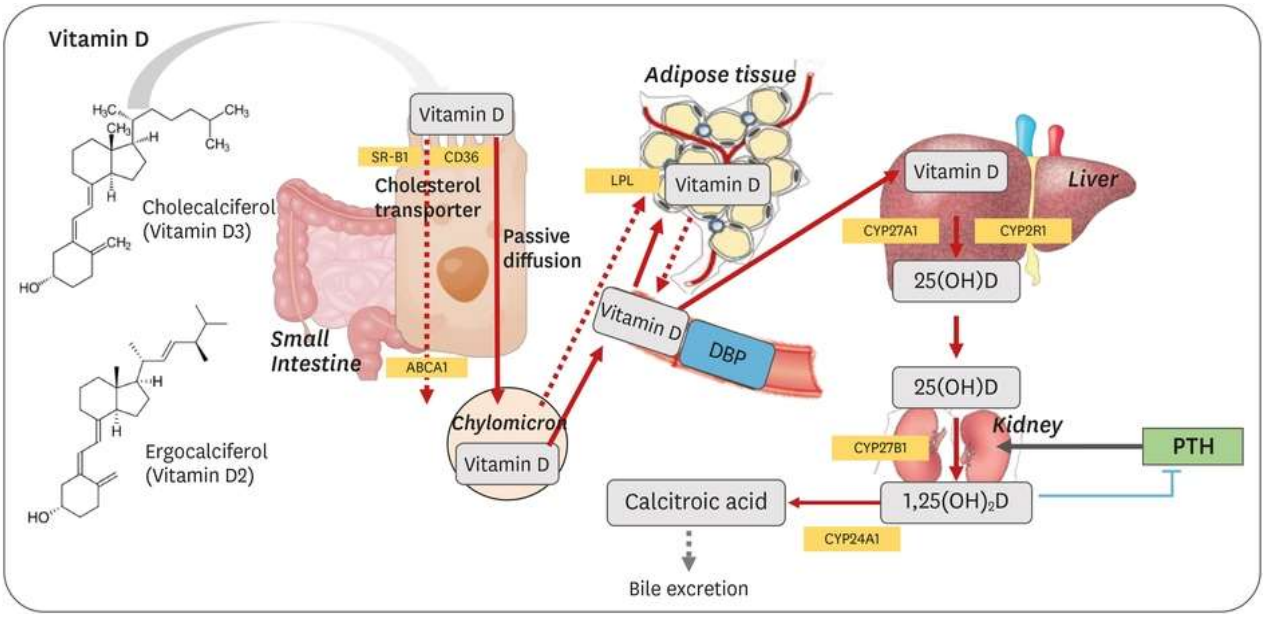


**Fig. 1 : Process of activating dietary vitamin D absorption ( Ding *et al*.,2012).**

### 1-2-1 Adipocytes differentiation by vitamin D

The process of adipogenesis is a strictly controlled procedure that is divided into two stages. Activation of transcription factors is the initial step in the process, and it is responsible for controlling the expression of markers that are unique to adipocytes. The expression of genes that are involved in the synthesis of fatty acids is increased during the second step, which ultimately leads to an increase in the production of fatty acids. This is something that happens during the process. The culmination of this process is an increase in the creation of fatty acids which is the final outcome.

After undergoing commitment to the adipocyte lineage, fibroblast-like cells, more precisely mesenchymal stem cells, develop into pre-adipocytes. This process begins at the beginning of the process. Pre-adipocytes go through a process of differentiation and mature into adipocytes during the subsequent stage. This occurs when the pre-adipocytes stop growing, begin to store lipids, and become responsive to insulin. Due to the fact that it has a strong binding to the nucleus VDR, the biologically active form of vitamin D, which is known as 1,25(OH)2D, has been discovered to have a major influence on the process of adipocyte differentiation. This has been the subject of a great deal of examination in the past. (Ghaben & Schere, 2019).

### 1-3 Regulation of energy homeostasis by Vitamin D

Triglycerides (TG) are a kind of fuel that can be stored in white adipose tissue, which serves as a storage place for excess energy. Lipogenesis is the process by which fatty acids are created within adipose tissue. They are made up of fatty acids that arise from circulating triglycerides in chylomicrons and very-low-density lipoprotein (VLDL), in addition to fatty acids that are generated by lipogenesis. These triglycerides are a type of triglyceride. The lipid subtype known as triglycerides can be seen in adipose tissue from time to time. During times when there is a high demand for energy, the principal location where fatty acids are synthesized is in the white adipose tissue. These fatty acids can be utilized as fuel by other organs. The gluconeogenic process also benefits from the production of glycerol by this substance. It is important to note that adipose tissue makes a considerable contribution to the process of energy homeostasis maintenance and plays a vital function in this process. By participating in a process that is referred to as thermogenesis, brown adipose tissue, also known as BAT, contributes to the generation of heat. Cold exposure causes BAT to increase its absorption of fat and to trigger the creation of uncoupling protein 1 (UCP1) within the tissue. This occurs when the tissue is exposed to cold. Additionally, this leads to the production of heat as a consequence. (Choe *et al*.,2016).

There are a number of hormones and adipokines that are accountable for the regulation of energy metabolism by adipose tissue. The activity of adipokines is responsible for the regulation of this process. When it comes to the process of glucose being transported into adipose tissue, insulin is a hormone that plays a significantly important function. An other hormone that plays a vital role in the regulation of energy balance is called leptin. Leptin is mostly produced in adipose tissue. By interacting with the brain, leptin is able to reduce the quantity of food that is ingested, increase the amount of energy that is wasted through sympathetic nerve activity, and stimulate thermogenesis by boosting the expression of UCP1 in brown adipose tissue (BAT). All of these effects are brought about by the connection that leptin has with the brain (Adiyaman *et al*.,2020 ).

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Through its production of adipocytokines, as well as its capacity to store and release energy, adipose tissue exerts a substantial influence on the metabolic processes that occur throughout the body. When a person is obese, their adipose tissue becomes dysfunctional. This dysfunctional adipose tissue is characterized by larger adipocytes, increased inflammation, lower oxygen levels (hypoxia), and impaired development of new blood vessels (angiogenesis) (Izabela *et al.*,2022). In addition to being located beneath the skin, adipose tissue is a form of loose connective tissue that surrounds organs and other structures. In addition to protecting internal organs from damage, providing thermal insulation, and regulating body temperature, adipose tissue helps to control the supply of energy and serves as a storage location for fat. It also plays an important function in regulating body temperature. This structure is composed of a wide variety of cells, each of which makes up a separate type. The following types of cells are included in this category: fully developed fat cells (adipocytes), precursor cells for fat cells (preadipocytes), multipotent cells that can differentiate into multiple cell types (mesenchymal stromal/stem cells or MSCs), cells that line blood vessels (vascular endothelial cells), cells that are responsible for muscle contraction (smooth muscle cells and pericytes), nerve cells (neurons), and certain immune cells. The function of an endocrine organ is carried out by adipose tissue by the secretion of a number of adipocytokines. These adipocytokines include hormones, cytokines that promote and inhibit inflammation, acute-phase proteins, and growth factors. These adipocytokines have an influence on other cells and organs in addition to the effect that they have on themselves. (Ambele *et al*.,2020).

Adipose tissue can be broken down into two distinct categories: brown adipose tissue (BAT) and white adipose tissue (WAT). Both of these types of adipose tissue go by the acronym "adipose tissue." The form of adipose tissue that is most frequently discovered is called white adipose tissue, which is also widely referred to as WAT. It is made up of adipocytes that have sizable lipid droplets that are contained within a single chamber. When it comes to the storage of energy within the body, WAT is primarily responsible. White adipose tissue (WAT) is responsible for the creation of adipokines, which include adiponectin and leptin, one of the factors that contributes to the maintenance of energy balance. Brown adipose tissue (BAT) adipocytes, on the other hand, are differentiated from other types of adipocytes by the large number of mitochondria and intracellular lipid droplets. In contrast to brown adipose tissue (BAT), which has a greater quantity of mitochondrial uncoupling protein 1 (UCP1), white adipose tissue (WAT) has lower levels of this specific protein. UCP1 is a molecule that plays a role in the process of thermogenesis, which generates heat. This is performed by uncoupling the respiratory chain, which is the means by which it achieves the lowering of the proton gradient from its previous state. In addition to this, it plays a role in the production of cyclic adenosine monophosphate (cAMP), which is a molecule that increases the capacity of mitochondria to produce free radicals. (Zhang *et al*.,2021).

### 1-3-1 Vitamin D metabolism, mechanism of action, and Tissue distribution

Vitamin D is a secosteroid, which means that it has the ability to dissolve in fat. Generally speaking, it is derived from the diet, more especially from fatty fish, mushrooms, and pharmaceutical supplements; alternatively, it can be produced by the skin on the inside of the body. When 7-dehydrocholesterol is exposed to ultraviolet (UVB) light in the skin, it goes through a process that results in the formation of prebiotic vitamin D. An extremely brief period of time is required for the transformation of pre-vitamin D into vitamin D (cholecalciferol; calciol), which is accomplished through a process that is dependent on heat. Through a procedure that is referred to as passive diffusion, the upper portion of the small intestine is the organ that is accountable for the absorption of vitamin D from the meal, in addition to other lipids that are derived from the diet. (Abbas,2017).

The exposure of sterol precursors to ultraviolet radiation results in the production of a number of vitamin D analogs, including D2, D3, D4, and D5. These vitamin D analogs can be found in a variety of foods. Along with the possibility of being utilized in the treatment of hyperparathyroidism, it is predicted that all vitamin D analogs will have some anti-osteoporotic and calcium regulating properties [30]. This is in addition to the fact that they have the potential to be utilized in it. Vitamin D3 is the most prevalent form of vitamin D that can be found in food, which is taken by the great majority of people. This is in addition to the fact that vitamin D is produced in the skin through a process that is known as synthesis. Despite the fact that both vitamin D3 and vitamin D2 have vitamin D activity, research conducted on humans has demonstrated that vitamin D3 is more effective than vitamin D2. More specifically, this is because D2 has a lower affinity for VDBP and hydroxylases. This is the reason why this is the case. The cycle of vitamin D absorption, distribution, metabolism, and elimination is depicted in Figure 2, which is a visual representation of the cycle. The vitamin D receptor, also known as the VDR, is the receptor that vitamin D attaches to in order to produce a biological impact. This is accomplished via binding to the vitamin D receptor. This receptor is present in human pre-adipocytes in addition to adipocytes that have already been formed. (Ding *et al*.,2012).

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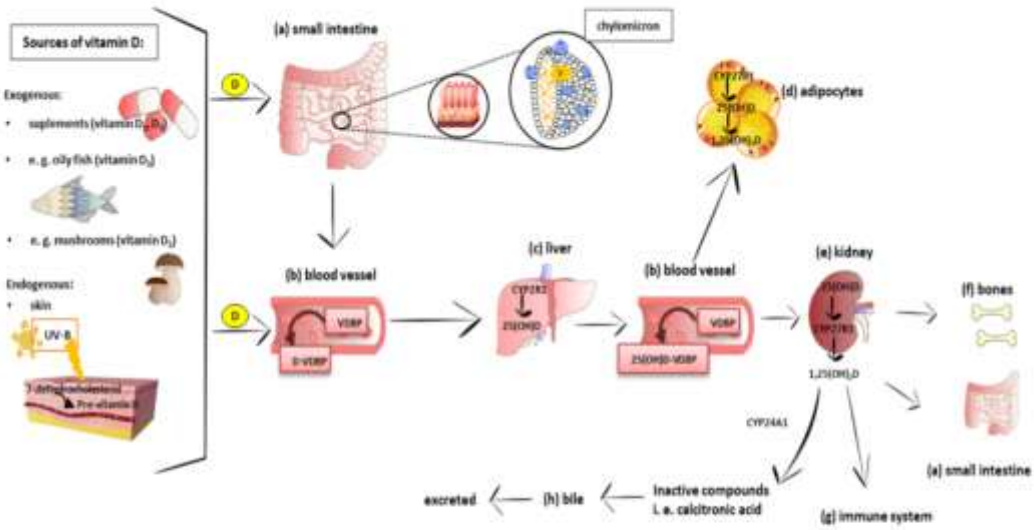


**Fig 2: Vitamin D absorption, distribution, metabolism, and clearance diagram (Ding *et al.*,2012)**

### 1-4 Modulation of inflammation by Vitamin D in adipose tissue

A multi-level response that an organism has in order to protect itself from potentially harmful stimuli and to initiate the healing process is called inflammation. In spite of the fact that inflammation is treated in the majority of cases in a short amount of time, acute inflammation can become chronic if the initial trigger is not eliminated or if the trigger continues to be present. Adipose tissue, which is thought of as an endocrine organ, is responsible for the secretion of around 260 distinct adipokines. Mechanisms that contribute to the creation of adipose tissue that results in obesity include hyperplasia, which refers to an increase in the number of adipocytes, and hypertrophy, which refers to an increase in the size of adipocytes. Both of these mechanisms are present in obese individuals. Both of these mechanisms are responsible for the development of obesity. Obese persons experience the death of enlarged fat cells (hypertrophic adipocytes) and a lack of oxygen in the affected area (local hypoxia), leading to inflammation. Subsequently, there is an elevation in the release of monocyte chemoattractant protein. (Young-Min Park,2014).

Visceral obesity, a part of the metabolic syndrome, is marked by inflammation throughout the body and in specific organs, known as metaflammation. This phenomenon can be characterized as a persistent, non-infectious, and mild form of inflammation. It is not caused by infection, injury, tumor, or autoimmunity. Instead, it is caused by inflammation of the fatty tissue surrounding the internal organs (visceral adipose tissue), known as adipose inflammation or adipoflammation. This inflammation occurs due to an increase in the size and number of fat cells (adipocyte hypertrophy and hyperplasia) and an increased presence of monocytes and macrophages infiltrating the tissue (Schaffler A. 2022).

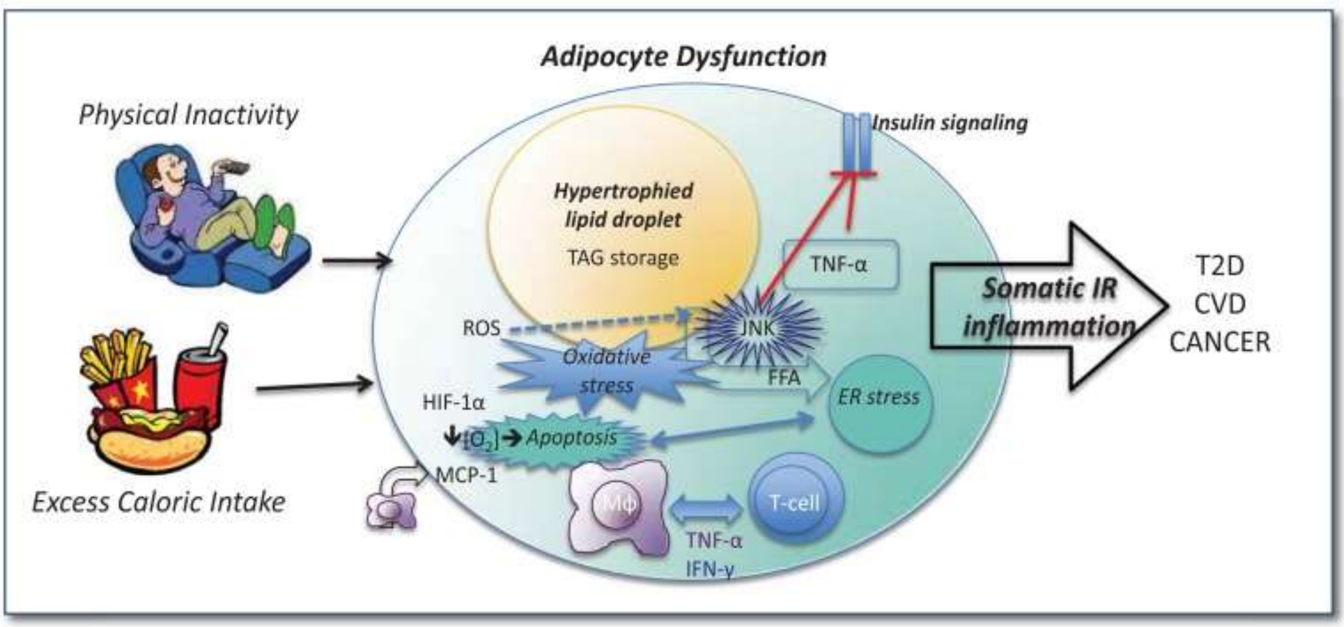


**Fig 3: Lack of exercise and overeating promote adipocyte malfunction (Young-Min Park,2014).**

**1-4 Effect of vitamin D on adipose tissue and its clinical significance.**

According to the findings that have been compiled from the various bodies of study that have been conducted, the location of the production, storage, and breakdown of the active form of vitamin D is found in the adipose tissue of the body. For the purpose of putting together this content, references to these many bodies of study have been consulted. Because adipocytes include both VDR and 1,25D-MARRS, it is possible for vitamin D to produce both a genomic and a non-genomic response in adipose tissue. This is because adipocytes contain both of these signals. The reason for this is that both of these chemicals are present in the environment. The fact that adipocytes include both of these receptors is the reason why this particular scenario exists. Some of the processes that are affected by vitamin D include adipogenesis, apoptosis, oxidative stress, inflammation, the release of adipocytokines, lipid metabolism, and thermogenesis. Vitamin D also has a role in both of these processes. In addition, vitamin D is involved in the process of adipocyte formation to some degree. The aforementioned are but a handful of the numerous processes that vitamin D has the potential to influence. On the other hand, vitamin D is also involved in a wide range of other systems and processes. When it comes to the formation of adipocytes, vitamin D is not only involved in the process, but it also plays a role in the production of adipocytes with its support. For the purpose of determining whether or not vitamin D supplements are effective for individuals who have varied degrees of severity of metabolic disorders and obesity, it is required to do additional clinical research. This is due to the fact that complete comprehension of the advantages of vitamin D supplementation has not yet been achieved. It is necessary to have this specific information, which is one of the reasons why this is the case. In order to achieve the desired level of control, it is necessary to have a wide range of metabolic processes and signaling channels. These include adipogenesis, apoptosis, oxidative stress, inflammation, the release of adipocytokines, lipid metabolism, and thermogenesis. In the control of various processes and pathways, vitamin D is an essential component that plays a crucial function. These processes are all essential for the body's ability to function at its optimal level and maintain homeostasis (fig. 4) (Xiang *et al*.,2020).

Modifications in the quantity and size of fat cells, also known as adipocytes, have an effect on the environment surrounding fat tissues that have grown in size. This results in alterations in the secretion of adipokines, which are hormones that are secreted by fat cells; these changes also lead to the death of fat cells, decreased oxygen levels (hypoxia), and altered transport of fatty acids. In addition, the adipose tissue contains a wide variety of cells, including immune cells, which are involved in adaptive activities. These processes include the elimination of dead fat cells, the production of new fat cells, and the formation of new blood vessels (angiogenesis). When fat people remodel their adipose tissue, these mechanisms are disturbed, which leads to the development of obesity. In addition, an excessive consumption of nutrients can set off uncontrolled inflammatory reactions, which can lead to persistent low-grade inflammation as well as metabolic diseases such as insulin resistance. ( Park *et al.,*2018).

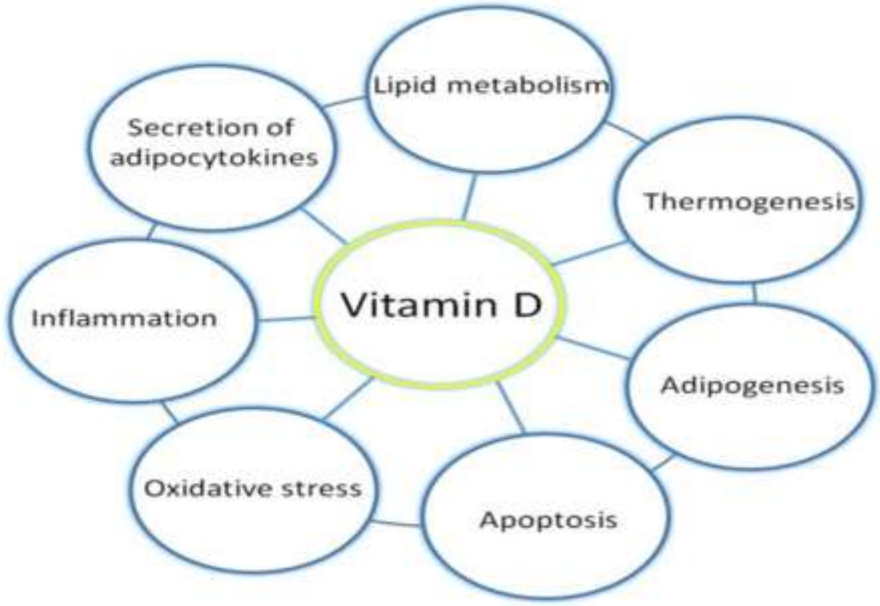


**Fig 4: The function of vitamin D in adipose tissue (Xiang et al.,2020).**

**1-5 Role of vitamin D3 as anti-fibrotic agent in liver fibrosis**

Through the action of the vitamin D receptor (VDR) and particular signal transduction pathways, it has been discovered that vitamin D has an antifibrotic effect on liver fibrosis. This effect is exerted on hepatic stellate cells (HSC). Because of this, the expression of genes that promote fibrogenesis is inhibited. Patients diagnosed with liver fibrosis are usually reported to have a significant incidence of vitamin D deficiency, according to the findings of certain studies. In light of this, it appears that monitoring vitamin D levels can function as a biochemical marker for tracking the progression of hepatic fibrosis. (Udomsinprasert & Jittikoon,2019).

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During the neonatal period, hyperbilirubinemia is a disorder that is rather common, and it has the potential to cause harm to the brain. In light of this, it is of the utmost importance to prevent, diagnose, and treat hyperbilirubinemia. Vitamin D has the potential to affect bilirubin levels, and the association between neonatal hyperbilirubinemia and vitamin D levels is being investigated. The condition known as neonatal jaundice, which is often referred to as hyperbilirubinemia, is characterized by the release of unbound bilirubin into the circulation, where it forms a complex with albumin and bilirubin. The complex is carried to the liver, where it interacts with glucuronidase in the cells of the liver to form mono-bilirubin and di-glucuronic acid. These compounds are then discharged into the bile and the intestinal system (Huang *et al.*,2021).

By decreasing the synthesis of collagen in stromal hepatic stellate cells (HSCs), vitamin D has been shown to have the ability to play a role in the regulation of the fibrotic process for a number of reasons. The idea that the involvement of vitamin D-mediated VDR may be implicated in the prevention of hepatic fibrogenesis is supported by an increasing body of evidence, which is a rising amount of evidence. Given that they provide credence to the idea, these findings are notable. Inhibiting the formation of fibrotic cells in the liver, also known as hepatic stellate cells (HSCs), is one of the functions that vitamin D is able to do as a result of its interaction with the vitamin D receptor (VDR). This lends credence to the idea that VDR-mediated liver fibrosis might have some practical implications. (Ding *et al*.,2013), .

### 1-6 Vitamin D biology

### 1-6-1 Vitamin D biosynthesis

Vitamin D2 and vitamin D3 are the two forms of vitamin D that are available for purchase, and they are both bioequivalent to one another. Both forms can be received through dietary sources such as fatty fish, eggs, and foods that have been fortified with the chemical. Other methods of obtaining the substance include supplementation. On the other hand, vitamin D2 and vitamin D3 come from different kinds of nutrients and sources. Vitamin D2, also known as ergocalciferol, is primarily produced as a result of the action of ultraviolet B (UVB) on ergosterol. Ergocalciferol is another name for vitamin D2. During this process, fungus and plants are both capable of becoming involved. Vitamin D3, on the other hand, is the most significant natural source of vitamin D that one may obtain within the body if they want to do so. In the skin, the creation of this chemical is stimulated by the ultraviolet B radiation that is absorbed by the skin. This radiation comes from the sun. During this process, the metabolite 7-dehydrocholesterol (DHC), which is formed from cholesterol, is converted into pre-vitamin D3 at the lower epidermis. This transformative process takes place. Specifically, this is the location where the transition takes places. Thermal-dependent isomerization is the process that is used to convert pre-vitamin D3 into vitamin D3, which is also referred to as cholecalciferol. This process is carried out in order to get vitamin D3. (Bikle , 2021).

Telipophilic cholecalciferol is biologically inactive and must undergo two hydroxylations in a row before it may become active. Both the liver and the kidney are responsible for these hydroxylations, which are the processes by which cholecalciferol is transformed into an intermediate metabolite and subsequently into its final active form. Cholecalciferol is largely bound to vitamin D binding protein (DBP) or albumin in the bloodstream before it is delivered to the liver. This occurs before the cholecalciferol is found in the liver. The process of 25-hydroxylation takes place in the liver, which ultimately leads to the formation of 25-hydroxyvitamin D, also known as calcidiol or 25(OH)D3. When measuring the amounts of vitamin D in the body, this particular type of vitamin D is typically utilized. When 25(OH)D3 reaches the kidney, it is subjected to further hydroxylation, mostly in the proximal tubule, by the enzyme 25(OH)D-1α-hydroxylase. This process ultimately results in the formation of the biologically active form of vitamin D, which is calcitriol, which is represented by the formula 1α,25(OH)2D3 (Song & Rockey,2013).

### 1-6-2 Plant sources of vitamin D

Only a limited number of food sources, such as fish, milk, eggs, microalgae, and mushrooms, naturally contain Vitamin D. Unfortunately, the general population is unable to obtain an adequate amount of this vitamin because of a lack of awareness and the use of nutritionally-depleted food sources. Therefore, it is imperative to educate the general people about the importance of Vitamin D. Promoting knowledge about Vitamin-D rich foods and implementing fortification measures can be a potential endeavor to enhance understanding of this bone-strengthening vitamin, hence reducing the prevalence of severe health conditions linked to Vitamin D deficiency ( Umar Khan *et al*. 2022).

Mushrooms are by far the most potent source of vitamin D2 that can be gotten from any food that does not originate from animals. This is because mushrooms have a high concentration of vitamin D2. The utilization of pulsed irradiation, which is a method that has been established, is a method that has the capability of rapidly increasing the quantity of vitamin D2 that is present in mushrooms. According to the assertions made by scientists, the use of these substances has been linked to a multitude of health advantages, including anti-oxidant, anti-tumor, anti-microbial, anti-inflammatory, anti-tyrosinase, immunomodulation, anti-atherogenic, and hypoglycemic qualities. As a result of the nutritional and therapeutic benefits that they offer, a number of people have contemplated ingesting them, and it has been observed that their consumption reflects the benefits that they offer. (Taofiq *et al*., 2017).

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There are a variety of applications for mushrooms, including their use as food, dietary supplements, ingredients in cosmetics, and as matrices for the production of various pharmacologically active compounds. They grow a fruiting body that is rich in sterols, whether they are preserved in their natural state or through processing. Ergosterol is the primary type of vitamin D that may be found in mushrooms. Ergosterol has the potential to be converted into vitamin D2 when it is exposed to ultraviolet radiation. Different species of mushrooms contain varying quantities of vitamin D, and even within the same species, the amount of vitamin D may vary from mushroom to mushroom. There is also a wide range of vitamin D content across the many species of mushrooms. The fact that mushrooms belonging to the genera Agaricus, Lentiula, and Pleurotus that have been exposed to ultraviolet radiation have been shown to contain considerable levels of vitamin D is a particularly amazing discovery. These mushrooms were shown to possess vitamin D in significant quantities. (Nölle *et al*., 2017).

Antioxidants are substances that assist in protecting the body from the damage that is caused by free radicals, which are molecules that are damaging to the body. There are a number of specific antioxidants, such as flavanones, hesperidin, and naringin, which are nutrients that have been discovered to have positive impacts on health. According to the findings of a study, persons who were deficient in vitamin D had considerably greater levels of serum 25(OH)D2 when they took orange juice that was supplemented with 1000 IU of vitamin D3. This was in comparison to individuals who consumed a placebo or orange juice that did not include vitamin D (Balachandar *et al*., 2021). Fortifying bread with vitamin D is an approach that has been advocated as a means of boosting the daily intake of this nutrient and avoiding and/or treating health problems that are related with vitamin D insufficiency. This was done in order to increase the amount of vitamin D that is consumed. Supplementation and dietary fortification are the most frequent strategies of improving insufficient daily exposure to vitamin D. This strategy is an additional method that can be utilized to improve vitamin D levels. This strategy is intended to increase the amount of vitamin D that is typically absorbed on a daily basis in order to achieve the desired objectives. (Souza,2021).

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