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Covid 19 And Human Immune Function: The Chemistry Of Vitamin – D

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Abstract

The epidemic COVID-19 is the utmost dreadful disaster of current human life that led to public health's global health as a major health care issue. Patients of COVID-19 have the signs, for instance, fever, dry cough, dyspnoea, sore throat, nasal congestion, besides glassy lung opacities. The infection of COVID-19 has two immune protective and damaging phases, and physicians attempt to improve the patient immune reactions. Vitamin D has various ways of action to reduce infection risk and death and has beneficial effects on viral infections. Supplementation of vitamin D during infection conditions of COVID 19 is still controversial. Scientific investigations are required to define improved cut-offs for vitamin D levels and, finally, which quantity will be the better as supplementations. Most of the works showed the people who are deficient in Vitamin D are more prone to infection. Broad familiarity with Vitamin D will make it supportive and protective for health. The present study focused on the worth of Vitamin D for the immune role, its presence in optimal amounts, and its effectiveness in COVID 19. Sun exposure synthesizes vitamin D in the human body, which ultimately enhances immunity, and protects from many viral infections, including COVID-19.

Keywords: Pandemic, Human–health, Mechanism, Viruses, and Bacteria.

1. Introduction

The world is amid the pandemic of COVID-19. WHO currently working with more than 50 different organizations and institutions of the world are working to follow the epidemic, occasionally counseling overall concerning issues like public health safety and vaccine of COVID-19. Vaccines are vital to saving lives, and they increase the natural defense system to spot the viruses and bacteria to fight off [1]. The third wave is now advancing with the new variants of the virus across the world. The infection rate in Europe is now at its highest level since the beginning of 2021[2]. According to the WHO global reports on health statistics, health awareness regarding the current virus, covering 133 countries and around 87% globally. Millions of people are affected and died worldwide by the coronavirus, and still, numbers of cases are increasing in many countries, but at the same time, encouraging news is coming. May control Its spread, despite the new variants are in transmission, and people have to keep some measures to prevent infections and save public lives. Even though the vaccination starts, it's essential to continue the precautions to keep ourselves safe. Pertinent, reliable, and actionable data is crucial for governments and health organizations to make decisions and create awareness among the people to protect health. The pandemic needs advanced health information systems worldwide to keep track of COVID-19 as primary health significances [3-6]. Before one year in February 2020, the World Health Organization (WHO) termed the pandemic COVID-19. The principal sign of COVID-19 is the temperature in 85% of its cases; also, in the beginning, 45% of patients include febrile, dyspnea, dry cough, sore throat, nasal and lung congestion. Injury to the lung tissue causes severe respiratory distress syndrome

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(ARDS). Some additional symptoms, for example, bone and muscle aches, chills, also headaches, are also observed. Signs of vomiting 5% and diarrhea 3.7% in cases of minors are reported. The treatment of COVID – 19, a viral disease, yet to be established; at the same time, antiviral drugs continue under trial. Only a few official vaccines have been approved, and the maximum is under the experimental stage [7][8].

1.1. Human Immune Function and Mechanism

Human beings have a natural resistant system to combat diseases and play a significant role in preserving health. In the body, the white blood cells played a fundamental role in defence mechanism, which is available all over the body via arteries. In protecting against offensive microorganisms, the body allows the lymphatic system to exchange cells and fluids in the blood and lymphatic vessels and help transport lymph. Each lymph node has appropriate compartments ubiquitously, making it accomplished to combat antigens. The immune cells conglomerate, activate, and encounter antigens are existing in the spleen's nodules and the lymph nodes [9-11]. Till now for COVID-19, appropriate medicine is not available, and even vaccination started at a slow pace.

Consequently, the body's natural defence function is the best mechanism to support and defend against offensive microorganisms or diseases. This resistance or immunity system, everyone has inborn, has three kinds of it (a) passive immunity, (b) adaptive immunity, and (c) innate or natural immunity. The adaptive immune reaction is activated in the body when an organism is exposed to the environment and pathogens. The passive immune response is activated when the resistant products have penetrated the body, natural immunity as of the maternal side. Can artificially achieve it from medicine like antibodies given to medication or avert diseases [12]. The natural resistance mechanism protects from various infections and pathogens [13]. When the body experiences an attack of microorganisms or viruses, the immune system becomes activated and ejects the attacking pathogens. Once the immune function is ineffectual to functioning suitably, the infection can have attacks badly. This condition is similarly happed in the case of COVID-19 also [14].

When the immune cells are susceptible to disease-causing pathogens, they attempt to overcome the attacking pathogen and interacting with the central and peripheral lymphoid organs through the blood to affect the injury spots to overcome the invaders. Blood, a carrier for naïve and antigen, moves in the whole body. As the immune cells become exposed to the area of injury, it acts as a mode of interface for the immune system, penetrating the blood, immune cells. Once the immune cells are vulnerable to disease-causing pathogens, they try to kill the invading pathogen and complete their assignment by interacting with the central and peripheral lymphoid organs through the blood to impact the wound places. Blood moves into the whole body and carries the naïve and antigen. For the study of human defence functions, different molecular and cell profiling efforts are possible. The modernization and advancements in science and technology have also caused population health and diseases. Because of the inherent heterogeneity in human studies, samples must be examined in a short while [15].

Then infection with pathogenic microbes, the immune system responds to mediate antibody production against the pathogen. The T cells helped the B cells distinguish over plasma cells and memory cells; plasma cells generate antibodies precise to a viral antigen. The neutralizing nature of antibodies is effective in obstructing the virus from penetrating healthy host cells. Hence restrict the disease and developed a strong immune function to protect from the further viral attack. Antibodies in circulation and memory cells avert the reoccurrence of the disease. Cell-mediated immunity reaction noticed within the infected cells mounted by circulating T-lymphocytes. Broadly, an adaptive immune response is observed through helper T cells, and also, T cells play a significant role during the removal of the viral-infected host cells [16]. The comprehensive collected data based on SARS-CoV and MERS-CoV research can make available to observe a piece of additional evidence about SARS-CoV-2 outflows and how the host’s immune response against the SARS-CoV-2 is still limited. As the comparable succession calculation shows, 80% of the SARS-CoV RNA series and 50% of the RNA series of MERS-CoV support the RNA of SARS-CoV-2 [17], also these SARS-CoV-2 illustrate in different genomic. The difference between SARS-CoV and the new related coronaviruses, its S protein is 20–30 longer chain amino acids. Thus, SARS-CoV-2 is expected to have commensurate with resistant elusion methods. Still, the other explanation of its working mechanisms to host interaction is unexplained [18,19].

Various researchers have different ideas to manage the COVID-19 patients, and its infections have the immune defence-based protective phase and the other inflammation-driven damaging phase. Initially,

clinicians are trying to boost the patient immune function, and in parallel, to repress the inflammatory immune response. For example, as the coughing started due to COVID-19 infection, Vitamin D3 should serve immediately; and upon the start of breath complexity, hyaluronidase has to serve intratracheally. Simultaneously, 4-MU may have applied to contain HAS2. Vulnerability of pieces of information of different types has to be given by HLA to control and manage the disease.

1.2. Chemistry of Vitamin D

A fat-soluble vitamin is found only in animal sources, and the body synthesizes it on exposure to sunlight. Vitamin D, or calciferol, is the common name for collecting steroid-like substances, with vitamin D2, ergocalciferol (Figure-1), and vitamin D3, cholecalciferol (Figure-2). The vitamins D2 and D3 structures vary in the side chain; D2 has a double bond (C22-23) and a methyl group attached to C24.

Askew et al. (20) were the first ones who established the structure and isolated the vitamin D2 (ergocalciferol) from plant sterols (ergosterol) formed by exposure to U.V rays. Windaus et al. (21) set the systems and mechanism of formation by which 7-dehydrocholesterol (7-DHC) in the skin transformed to vitamin D3 (cholecalciferol). The vitamins D_2 and D_3 differ in the side chain, where D_2 has a double bond ($C_{22\text{-}23}$) and with a methyl group attached to C_{24}. Both Vitamin D_3 and D_2 are commonly called Vitamin D. The Chemical Structure of Vitamin D2 (Ergocalciferol), Vitamin D3 (Cholecalciferol), Calcidiol, and Calcitriol can be seen in the given figures 1-4.

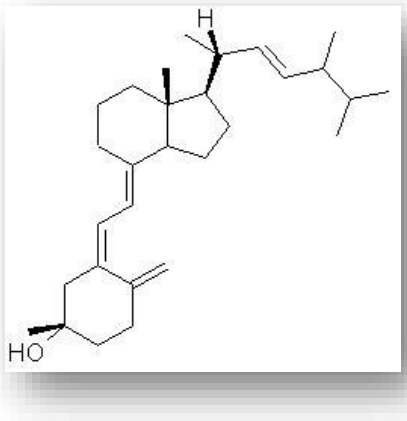

Figure 1. The Chemical Structure of Vitamin D2 (Ergocalciferol).

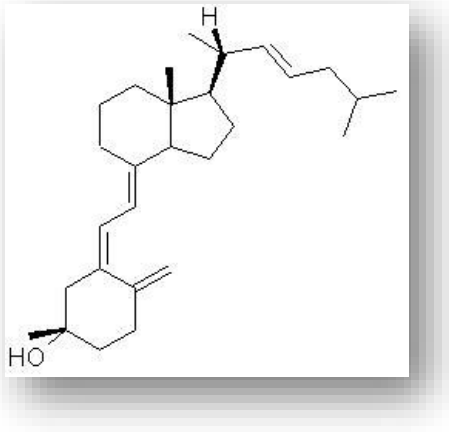

Figure 2. The Chemical Structure of Vitamin D3 (Cholecalciferol).

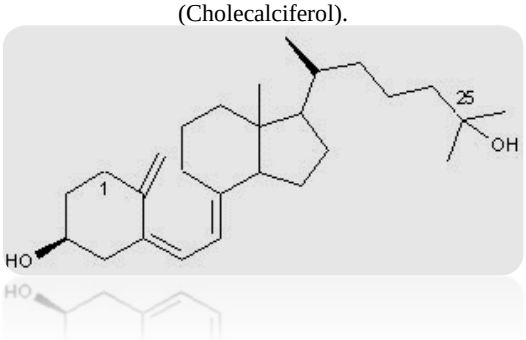

Figure 3. The Chemical Structure of Calcidiol.

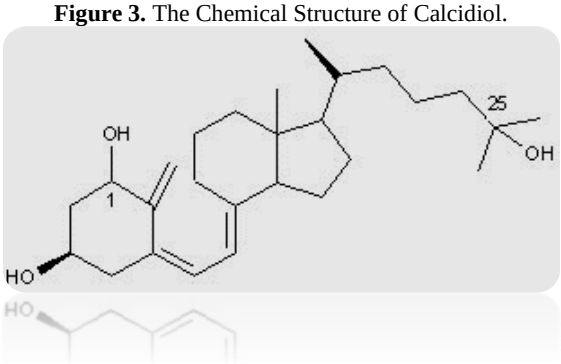

Figure 4. The Chemical Structure of Calcitriol.

1.3. Ultraviolet B (UVB) rays are the best natural source of vitamin D

The human body required a fixed amount of vitamin D; the sun rays are the best natural source. According to the council of Vitamin D reports published on 10th of March, 2021: for the synthesis of vitamin D by the sun rays' people should spend -15 minutes for an individual having light skin and a few hours for an individual having dark skin.

Once the sun's ultraviolet B (UVB) rays come in contact with the skin, a chemical reaction occurs, actions inside the tissues initiate to synthesize vitamin D. Not essential to become burn to get vitamin D from the sun. The body system will synthesize the required vitamin D, fulfil the requirements for a day.

Features that affect the synthesis of vitamin D from the sun, for instance:

♠ The more the amount of skin exposed, the more vitamin D the body will synthesize.

♠ The body synthesize more vitamin D in the sun-exposure during the middle of the day.

♠ Light-colored skin produces vitamin D more rapidly than darker-colored skin.

♠ Regular, modest exposure to the sun rays is beneficial, but extended exposure can be unsafe.

The factors that reduce exposure to UVB light and consequently decrease vitamin D synthesis in the inside skin:

♠ The use of sunscreen; reduces vitamin D synthesis by more than 90%.

♠ Wearing a dress that covers the skin.

♠ Spending partial time in the sun.

♠ Dark skin.

♠ There is a reduction in 7-dehydrocholesterol levels in older ages, and people are expected to spend more time inside the home.

♠ People are living above the equator in northern latitudes where the exposure to UVB light is not intense.

Vitamin D in the skin synthesis due to the sunlight (UVB) exposure is maximum when sunlight exposure does not burn the skin [22-25].

1.4. Mechanism of Vitamin D_3 synthesis under the exposure of U. V. radiation

Once the sun's ultraviolet B (UVB) rays come in contact with the open skin, actions inside the tissues initiate synthesizing vitamin D; steroid termed 7-dehydrocholesterol is decomposed in the UVB light of the sun's rays, also called "tanning" rays. Simultaneously, UVB rays' radiation produces 7-dehydrocholesterol, known as pre-D3, a structural rearrangement due to sun energy [26-28]. Formation of pre-D3 in the presence of U.V irradiation is maximum at the range between 290-310 wavelength, and hence pre-D3 to changes lumisterol and tachysterol. The yield of synthesis of pre-D3 level depends on the concentration of epidermal pigment and UVB rays exposure intensity.

However, pre-D3 concentration became maximum when the biologically inactive lumisterol remains to store with prolong U V exposure. Also, like pre-D3, Tachysterol is formed but does not change with prolonged U V exposure. The synthesis of lumisterol under U.V rays' exposure is reversible and possibly reconverted to pre-D3 once the pre-D3 concentration decreases. At 273 K (0.0 ˚C), D3 is not produced; however, at 310 K (37 ˚C), pre-D3 is gradually changed into D3. Consequently, partial exposure to U.V rays may lead to an extensive synthesis of D3 in the naked skin due to the sluggish change of pre-D3 to D3, the conversion of lumisterol pre-D3 at low temperature, and for a long-time exposure of sunlight may not yield excess amounts of D3. The synthesis of D3 due to light exposure, including suprasterols I and II and 5,6 trans vitamin D3[29]. The intensity of U V radiation is similarly significant for practical D3 synthesis, with higher summer and lower winter levels. The maximum level of D3 production happens during midday and in the summer [30,31]. The synthesis of Vitamin D by the sun exposure is summarised and can be seen in the **Figure 5.**

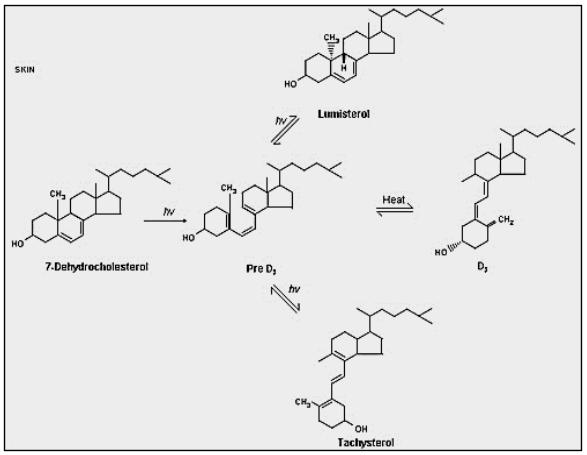

Figure 5. The synthesis of Vitamin D.

1.5. Metabolisms of Vitamin D

The thermal action of UVB radiation is synthesized vitamin D3 in the body when it comes to contact with 7-dehydrocholesterol in the skin. Correspondingly, when consumed orally, it is transformed in the liver to 25(OH)D and kidneys to the hormonal metabolite 1,25(OH)2D (calcitriol). Calcitriol reaches the nuclear receptor of vitamin D. A bond formed with DNA allows direct contact with the regulatory sequences (near target genes) to activate the complexes chromatin genetically and epigenetically, ultimately altering the transcriptional yield. Calcitriol regulates serum calcium absorption via its response with parathyroid hormone (PTH), thus modifying the body's various significant functions[32,33].

1.6. Vitamin D and immune response of the host

Vitamin D reduces the threat of microbial infection or diseases. It is involved mainly in actions, which are

divided into three parts: physical obstacles, natural cellular immunity, and adaptive immune function [34]. Innate cellular immune function is actively supported by vitamin D, partially by the induction of antimicrobial peptides and partly by the human cathelicidin LL-37, and by 1.25-dihydroxy vitamin D. The defensins, generally high in the amino acid cysteine (Cys), play a significant role in protecting against attacking microorganisms [35-38].

It is crucial to assert the effects of cathelicidins that show an extensive antimicrobial effect, like bacteria Gram-positive and Gram-negative, enveloped and non-enveloped viruses, as well as fungi [39]. It also stimulates the chemotaxis of neutrophils, monocytes, macrophages, and T lymphocytes into the infection site. It introduces a different pro-inflammatory cytokine and reduces respiratory congestion by inducing apoptosis and autophagy of infected epithelial cells[40,41]; similarly, 1,25(OH)2D–vitamin D receptor complex increasing the transcription of cathelicidin[42]. COVID-19 plays the immune system's innate actions due to viral and bacterial infections, producing pro-inflammatory and anti-inflammatory cytokines [43].

Vitamin D reduced the building of pro-inflammatory T helper (Th)1 cytokine, (TNF-α and IFN-γ), and rises the expression of anti-inflammatory cytokines by macrophages [44,45]. It helps in the cytokine production by Th2 lymphocytes, increasing the indirect suppression of Th1 cells by complementing mediated by many cell types [46]. Additionally, it favors the T regulatory (Treg) cells' induction, thus suppressing inflammatory processes[47,48].

In the Serum, vitamin D concentrations reduction in old age because of not as much time spent in the sun by older people, which decreases the levels of 7-dehydrocholesterol in the skin [49,50]. The concentrations of vitamin D decrease in the Serum may be due to antiepileptics, antineoplastics, antibiotics, anti-inflammatory agents, antihypertensives, antiretrovirals, endocrine drugs, and may also due to the use of some herbal medicines which activated the pregnane-X receptor [51]. The antioxidation like glutathione reductase and the glutamate-cysteine ligase modifier subunit are enhancing by supplementing Vitamin D. Thus, glutathione also has antimicrobial activities, increased the production spares the use of vitamin C [52-54]. For much more understanding of the Immune Modulator of Vitamin-D has been explained in the following flow chart (**Figure 6**.).

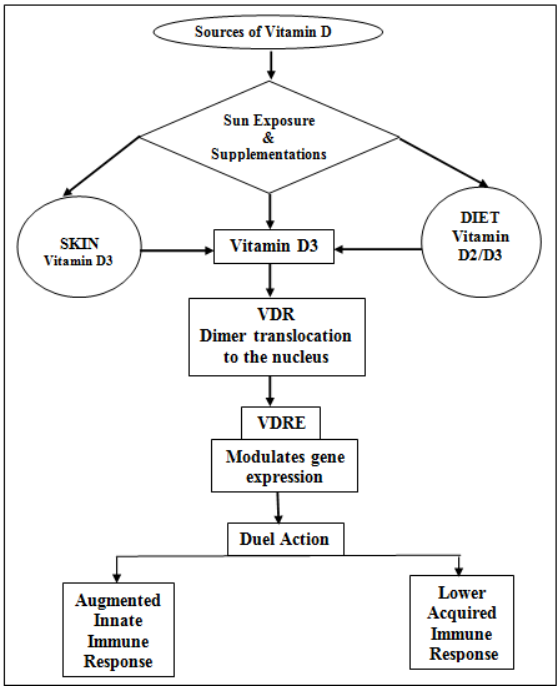

Figure 6. A flow chart of Vitamin-D as an Immune Modulator.

1.7. COVID-19 and Vitamin D

Vitamin D supplement in winter appears to decrease the menace of rising flu. The benefit of vitamin D supplements is also reported in human immune deficiency virus- 1 (HIV) infection. The action of vitamin D in patients with COVID-19 disease has a positive role in decreasing the menace of COVID-19; in winter, the serum vitamin D levels became bottom, the outbreak arisen. Its deficiency pays to severe respiratory distress syndrome. The fatality rates increase with age and multiple chronic diseases. In both cases, the concentration of vitamin D deficiencies is reported[55-57]. Although vitamin D supplements may increase host immune action against COVID-19, they affect all-important body systems. Vitamin D supplements in high-dose are suggested for people who have a deficiency, mainly for the elderly, obese, those with dark skin, and those living at higher latitudes. The vitamin D supplement that increases the serum levels above 50 ng/ml (125 nmol/l) may have advantages in decreasing the occurrence and severity of several viral diseases, including COVID-19 [58,59].

1.8. Vitamin D intake recommendations

The optimum amount of vitamin D (1000–4000 IU, or 25–100 micrograms) is needed to keep the body healthy. It helps to make strong bones and may help to prevent diseases. Its deficiency may cause muscle

weakness, pain, fatigue, and depression. As said by the Institute of Medicine (IOM) recommendation,4000 IU is the safe upper limit. If the consumption of vitamin D is more than 10,000 IU daily is toxic. How much is vitamin D needed every day to be healthy? The Institute of Medicine advised the regular consumption of vitamin D is as following [60]:

Table 1. Suggested daily consumption of vitamin D (According to the Institute of Medicine).

S. No.	Age group	Suggested Daily Consumption of Vitamin D
1	1-70 Years	600 IU
2	Age 71 and older	800 IU

In the U.S. A, the suggested everyday consumption of vitamin D is as follow:

In November 2010, the Institute of Medicine expert committee updated the Daily Consumption of Vitamin D's recommendation and established a new dietary reference intake

1.9. Important Food sources with Vitamin – D

A large number of foods have Vitamin – D. Vitamin – D3 found in bulk, largely in the flesh of fatty fish and fish liver oils. Egg yolks, cheese, and in the beef liver, it is found in lesser quantity. Some mushrooms have vitamin D2 in lesser amounts; moreover, some commercial mushrooms are rich in D2. Hence, the leading sources of Vitamin – D that have to be part of daily dietery intake like, Cod liver oil, Salmon, Swordfish, Tuna fish, Orange juice , dairy, and plant milk (soy milk, and cereals), Beef liver, Fortified cereals, Fatty fish, mackerel, Cheese, Egg yolks, etc. Fish is a better choice to get vitamin D. Three ounces of cooked salmon has about 570 international units (I U) [61].

Sources of vitamin D-rich foods that should be part of nutritional intake can be seen in Table 4

Table 2. Recommended daily consumption of vitamin D (In the U. S. A).

S. No.	Age group	Recommended Daily Consumption of Vitamin D (International units) or in µg (microgram)
1	Children and teenagers	600 (I U) or 15 µg
2	Adults to 70 years	600 IU or 15 µg
3	Adults aged 71 years and older	800 IU or 20 µg
4	During pregnancy and breast feeding	600 IU or 15 µg

Table 3. Updated recommendation of Daily Intake of Vitamin D (The Institute of Medicine expert committee).

S. No.	Age group	Recommended adequate Daily Intake of Vitamin D (international units) IU/Day	Recommended maximum safe upper Limit of Intake (international units) IU/Day
1	Infant's age 0 to 6 months	400 IU	1,000IU
2	Infant's age 6 to 12 months	400 IU	1500 IU
3	Age 1-3 years	600 IU	2500 IU
4	Age 4-8 years	600 IU	3000 IU
5	Age 9-70	600 IU	4000 IU
6	Age 71 years and above	800 IU	4000 IU

Table 4. A Selected Food Sources with vitamin D.

S. No.	Food	Quantity	Micro gram(µg)/each normal serving	International Units (I U)
1	Cooked Socked Salmon	3 ounces	Fourteen µg	570 IU
2	Drained Canned Tuna	3 ounces	Six µg	240 IU
3	Drained Canned Sardines	3 ounces	Four µg	165 IU
4	1% fortified milk	1 cup	Three µg	120 IU
5	low-fat vanilla yogurt	6 ounces	Two µg	80 IU
6	fortified orange juice	three-quarters of a cup	Two µg	75 IU
7	fortified breast cereal	One serving	One µg	40 IU
8	Boiled egg	One large	One µg	45IU

For adults, it is advisable to intake no more than 4000IU of vitamin D daily from food and supplements.

2. Remarks and Discussions

Today, the world suffers from the third wave and the new variants of the virus of COVID-19 since 2021. Around 87% of the world population is affected, and millions died. Even though the vaccination is started in many countries, the WHO recommends following the essential precautions to keep ourselves safe. The guidelines to counter the pandemic to make people safe.

♠ Frequently and carefully clean hands with a sanitizer or clean hands with soap and water.

♠ Avoid touching the nose, eyes, and mouth.

♠ Always cover mouth and nose on coughing or sneezing.

♠ Clean and disinfect the surfaces such as door handles, faucets, and phone screens frequently.

♠ The people who have low immunity should restrict themselves from public activities.

To safeguard and preserve the healthy immune system all year round, Vitamin D has a multidimensional effect on the immune function and has a significant role in the human body. Many researchers reported that vitamin D supplements may increase host immune reaction to counter COVID-19; it positively affects all-important body systems. Vitamin D is an essential component that the human body synthesizes under sunlight exposure. When the sun UVB rays hit the human skin, a chemical reaction occurs and synthesized the vitamin D. Hence, short exposure to U. V radiations caused a constant synthesis of D_3 in the bare skin due to the slow thermal conversion of pre-D_3 to D_3 and the conversion of lumisterol to pre-D_3. The U.V radiation alters the immune system, making it more immunotolerant. Thus, people should take Sunbaths occasionally because sun exposure synthesizes vitamin D in the body, which ultimately enhances immunity and protects from many viral infections, including COVID-19. We can obtain it from our diet or supplements also. Moderate and unrestricted sun exposure eats vitamin D-rich foods naturally. Using its supplement should ensure vitamin D. People should be aware and intake Vitamin D-rich foods. People must be aware of their health matters; their lifestyle and dietary patterns can change fate.

3. Conclusions and Outcomes

Currently, the world is suffering from the worst human disasters, the pandemic COVID-19. Millions of people are affected and died. Although the vaccination against the COVID-19 is started in many countries, the WHO recommends continuing to follow preventive measures to keep ourselves safe. People should take nutritious foods, make a healthy lifestyle, and keep the immune system healthy are the most important ways to overcome the pandemic. Vitamin D is an important component synthesized inside in the body in the sunlight's exposure, plays a substantial part in improving the defense function, and has multiple features of the immune function's roles. The reported data in the literature concerning vitamin D supplement effects is debatable regarding the COVID-19 patients. The human immune system and the pathology of COVID-19 have a complex multifunctional correlation. But vitamin D has various immunomodulating and positive effects in several viral diseases, as well as COVID-19. The lifestyle and dietary hobbits of people are important factors that can make humans safe. The optimum limit intakes of vitamin D for people were observed effective. The optimum amount of vitamin D (1000–4000 IU, or 25–100 micrograms) is needed to keep the body healthy. For adults, it is advisable to intake no more than 4000IU of vitamin D daily from supplements and food. Thus, body exposure to Sun rays synthesizes vitamin D, which ultimately enhances immunity, and protects from many viral infections, including COVID-19.

4. Conflicts of interest

The author declares that there is no conflict-of-interest Formatting of funding sources

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Abbreviations

World Health Organization - WHO
Corona**vi**rus **D**isease of 2019 - COVID-19
Ultraviolet - U.V
Ultraviolet A, has a longer wavelength - UVA
. Ultraviolet B, has a shorter wavelength - UVB
International Units - IU

Acute Respiratory Distress Syndrome - ARDS
Severe acute respiratory syndrome coronavirus 2 - SARS-CoV-2
Middle East respiratory syndrome - MERS
Middle East respiratory syndrome-related coronavirus - MERS-CoV
Human Leukocyte Antigen - HLA
Hyaluronan synthase 2 - HAS2
4-Methylumbelliferone - 4-MU
7-dehydrocholesterol - 7-DHC
Microgram - µg

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