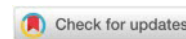


VITAMIN D3 OIL AND WATER SOLUTION, PREPARATION AND USE IN CASE OF DEFICIENCY

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Abstract: Vitamins are natural and essential nutrients, which have different biochemical functions and play a major role in growth and development, help in the digestion and utilization of mineral salts and carbohydrates in the body, healing of wounds, stimulate and give strength to the digestive and nervous system, maintenance of healthy bones and tissues, for proper functioning of the immune system and other biological functions. Vitamins generally cannot be synthesized in quantities sufficient to meet the body's needs and therefore must be obtained from the diet or from some synthetic source. Because of this, vitamins are called essential nutrients. Both plants and animals are important natural sources for vitamins. All vitamins can be synthesized or produced commercially and are available for human consumption as pharmaceutical preparations. Vitamins also differ from other biological compound, because relatively small amounts are required to complete their functions. If a vitamin is absent from the diet or is not properly absorbed by the body, it can develop a specific disease due to deficiency.

Keywords: vitamin D3, aqueous solution, oil solution, deficiency.

Field: Pharmaceutical technology

1. INTRODUCTION

Vitamins are regulators of reactions in metabolism, unlike other macronutrients (eg, fats, carbohydrates, and proteins), which are compounds used in reactions regulated by vitamins. Because of this, if a vitamin deficiency occurs, one or more specific metabolic reactions in the cell are blocked and can lead to a disturbance of the metabolic balance in the cell and the whole organism.

Vitamin D is a fat-soluble vitamin that helps the body absorb and retain calcium and phosphorus, which are very important for building bones. Laboratory studies have also shown that vitamin D reduces the growth of cancer cells, can help control infections and reduce inflammation. Many organs and tissues in the body have receptors for vitamin D, suggesting that this vitamin has a large role beyond bone health, while scientists are actively investigating its other functions. Very few foods naturally contain vitamin D, although some are fortified with this vitamin. There are a few that naturally have vitamin D. These are fatty fish such as salmon, tuna and mackerel, beef liver, cheese, mushrooms, egg yolks. Vitamin D can also be obtained from fortified foods. The most commonly added vitamin D is found in milk, breakfast cereals, orange juice, dairy products such as yogurt, and soy beverages.

For most people, the best way to get vitamin D is through a supplement because research shows that you don't get enough from your diet.

1.1 FORMS OF VITAMIN D3

Vitamin D supplements are available in two forms:

- Vitamin D2 (ergocalciferol)
- Vitamin D3 (cholecalciferol).

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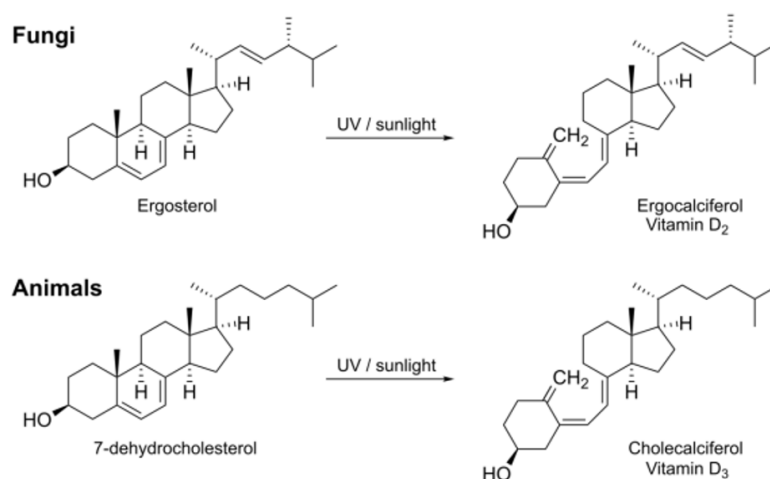


Figure 1. Photochemistry of vitamin D biosynthesis in animals and fungi.

Both are natural forms that are produced in the presence of the sun's ultraviolet-B (UVB) rays, which is why it is also called the "sunshine vitamin", but D2 is produced in plants and fungi, and D3 in animals and humans. The production of vitamin D in the skin is the primary natural source of vitamin D, but many people are deficient because where they live, sunlight is limited in the winter or because they have limited exposure to the sun because they spend most of their time inside. Also, those people who have darker skin tend to have lower levels of vitamin D in their blood because the pigment (melanin) acts as a shadow, reducing vitamin D production.

1.2 RECOMMENDED QUANTITIES

The recommended dietary allowance for vitamin D provides the daily amount needed to maintain healthy bones and normal calcium metabolism in healthy people, assuming minimal sun exposure.

The recommended dietary allowance for adults 19 years of age and older is 600 IU (15 mcg) per day for men and women, and for adults over 70 years of age it is 800 IU (20 mcg) per day. The recommended dietary allowance for adults 19 years of age and older is 600 IU (15 mcg) per day for men and women, and for adults over 70 years of age it is 800 IU (20 mcg) per day.

The term "tolerable upper intake level" is also described in the literature. It is about the maximum daily intake that is unlikely to cause harmful effects on health. The Tolerable Upper Level for vitamin D for adults and children ages 9+ is 4000 IU (100 mcg).

Many people do not meet the minimum daily requirements for vitamin D. The average intake of vitamin D from food and supplements among women aged 51 to 71 years was 308 IU per day, but only 140 IU from food alone (including fortified products). Worldwide, about 1 billion people have inadequate levels of vitamin D in their blood, and deficiencies can be found in all ethnicities and age groups. For example in the United States, about 20% of white adults and 75% of black adults have blood levels below 50 nmol/L. In industrialized countries, doctors are seeing a resurgence of rickets, the bone-weakening disease that was largely eradicated by vitamin D fortification.

1.3 VITAMIN D DEFICIENCY OR VITAMIN D HYPOVITAMINOSIS

It is a disorder caused by a vitamin deficiency that can result either from suboptimal intake of the vitamin or from conditions that prevent the use or absorption of the vitamin in the body.

Vitamin D deficiency can occur for various reasons:

- insufficient intake of vitamin D through diet,
- not enough vitamin D is absorbed from food (malabsorption problem),
- insufficient exposure to sunlight,

- the liver or kidneys do not convert vitamin D into its active form in the body, when using drugs that reduce the body's ability to convert or absorb vitamin D.

Some people are at greater risk of vitamin D deficiency, for example infants because breast milk is a poor source of vitamin D, then older people because their skin does not produce vitamin D when exposed to the sun as efficiently as younger people, and their kidneys are also less able to convert vitamin D into its active form. Also people with dark skin, which has less ability to produce vitamin D from the sun. Then, people with disorders like Crohn's disease or celiac disease that don't handle fat properly, because vitamin D needs fat to be absorbed. Individuals with increased body weight, because their body fat binds to vitamin D and prevents it from entering the blood, as well as people with osteoporosis, with chronic kidney or liver disease.

Vitamin D deficiency can lead to loss of bone density, leading to osteoporosis and fractures. A severe lack of vitamin D can also lead to other diseases, for example in children it can cause rickets, a disease that causes the bones to become soft and bend.

In adults, severe vitamin D deficiency leads to osteomalacia, which weakens the bones, causing bone pain and muscle weakness. The relationship of vitamin D to several other conditions such as diabetes, high blood pressure, cancer and autoimmune diseases such as multiple sclerosis is also being studied. But experts say more research needs to be done to determine and understand the effect of vitamin D on these conditions.

Due to the great need of vitamin D in infants in the first months of life it is not by chance that for the purpose of this specialist paper we chose the preparation of an aqueous and oily solution of vitamin D3 that is used for prophylactic and therapeutic purposes.

2. MATERIALS AND METHODS

The aqueous solution of vitamin D3 was prepared according to the composition given by Vitamins, BASF, Germany. The preparation of the solution itself is performed in the dark because vitamin D is sensitive to light. First, a certain amount of vitamin D3, tocopherol and cremophor RH40 is measured in a tared glass container. They are heated in a water bath at a temperature of 65°C. In another tared glass container, the amount of distilled water is measured and it is heated in a water bath to 65°C. After reaching the required temperature, water is added to the vitamin solution and mixed completely. After cooling, the pH of the solution is determined and phosphate buffer is added to pH 7. The amount of the solution is filled in pre-sterilized bottles, the air is replaced with an inert gas, the bottles are closed and packed in the outer paper packaging.

The preparation of the oil solution is in the same way as the water solution, it is carried out in the dark, the prescribed amounts of the given substances are measured in a tared glass container and heated in a water bath at a temperature of 40°C. After cooling, the solution is added to the indicated amount with neutral olive oil. Filling is done in the same way as the aqueous solution.

The signature of the preparations is carried out with a signature on which is written the name of the medicine, the amount of the active component expressed in I.E./ml, the antioxidant used and the date of manufacture.

During the production of the aqueous and oily solution of vitamin D3 in the form of drops for oral use as a galenic preparation, materials and technological procedures are used that ensure their stability.

3. DISCUSSION

The solutions are made according to the general regulations for oral drops, which include certain auxiliary agents such as solubilizer (Cremophor RH40), antioxidant (DL- α -Tocopherol), buffer (phosphate) and are dosed in an inert medium (nitrogen) for greater stability of D3.

For the selection of the formulation in the aqueous solution, we decided on the following composition: Vitamin D3 1,000,000 I.E./g, Cremophor RH40, DL- α -Tocopherol, Phosphate buffer (pH-7), Aqua destilata; while the oil solution has the following composition: Vitamin D3 1,000,000 I.E./g, DL- α -Tocopherol, Olive oleum neutralisatum.

The aqueous solutions produced are clear, odorless and bitter tasting, and the oil solutions

produced are also clear, yellow oily liquids with a pleasant mild odor and taste.

The stability of the aqueous and oil solutions was determined by monitoring the required parameters and the content of D3, during 3 months kept at two different temperatures: 4°C and 25°C.

The obtained results show that during 3 months there are no changes in the clarity and microbiological purity in water and oil solution.

The pH value of the aqueous solution in the solutions kept at two different temperatures is within normal limits because it does not exceed the pH value given in the general regulations for the neutral pH area (6.5-7.5).

The acid number in the oil solutions stored at two different temperatures is also within normal limits because the acid number of Olive oleum is neutral. after Ph.Eur. is max 0.2.

The content of the water and oil solution is within the prescribed permissible limits.

In vivo studies of aqueous and oily solutions of vitamin D3 show satisfactory results. In the group of patients who were prescribed aqueous solutions of vitamin D3 for the purpose of protection and treatment from rickets, satisfactory results were obtained and no adverse events were observed.

Likewise, in the group of patients who were prescribed vitamin D3 oil solutions for the purpose of protection and treatment of rickets, satisfactory results were obtained and no adverse events were observed.

4. CONCLUSION

The number of people with vitamin D deficiency is constantly increasing and it is common in all age groups. The importance of this vitamin in overall health and the prevention of chronic diseases is the target of much research. In this paper, two preparations of vitamin D3 4000 I.E./ml were formulated and analyzed as an aqueous and as an oil solution. From the results obtained during the examination, we can conclude that we received two preparations of vitamin D3, professionally prepared, which meet the basic pharmacopoeial requirements and which can be used for the prophylaxis of rickets and for the treatment of rachitic changes.

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