شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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جامعة عين شمس

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قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

HANAA ALY

INTRODUCTION

Irritable Bowel Syndrome (IBS) can be divided into three subtypes according to bowel habits –IBS with diarrhea (IBS-D), IBS with constipation (IBS-C), and IBS with mixed bowel habits (IBS-M). Incidence of IBS has been increasing over last two decades ***(Sprake, Grant and Corfe, 2012).***

IBS pathogenesis is poorly recognized and many theories have been proposed to explain its pathogenesis. ***(Oświęcimska, et al, 2017).*** Low-grade mucosal inflammation, bacterial overgrowth, immune activation, visceral hypersensitivity, and disturbed gastrointestinal motility are possible mechanisms of pathogenesis ***(Carding, et al., 2015).***

Studies have suggested a relationship between vitamin D and IBS. Vitamin D has a potential role as immune modulator, anti-inflammatory, and anti-microbial agent that can explain its role in IBS ***(Coussens, Martineau and Wilkinson, 2014).***

Furthermore, vitamin D receptors (VDR) are expressed in the gut affecting gut function, motility, and IBS symptoms ***(Kong J, et al., 2008)***. Moreover, depression, which initiates or aggravates IBS symptoms, is more common in vitamin D deficiency.

Low vitamin D level was recorded in IBS patients in many studies ***(Nwosu, Maranda and Candela., 2017).***

This deficiency can be attributed to many factors as altered digestive pattern or intolerance to dairy and fatty food. Supplementation of vitamin D in adult IBS patients significantly improves their symptoms and quality of life ***(Abbasnezhad, et al., 2016).***

AIM OF THE WORK

The Aim of the study was to assess the effect of food rich in vitamin D and supplementation in patients with irritable bowel syndrome in medical students in Faculty of Medicine Ain Shams University.

VITAMIN D

Introduction

Vitamin D was first characterized like a vitamin in the 20th century and now it is recognized as a prohormone. Two major forms of vitamin D are vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). Vitamin D3 is synthesized in the skin of humans and is consumed in the diet through the intake of animal-based foods, mainly fish oils, whereas vitamin D2 is derived from plant sources, is not largely human-made, and added to foods. Vitamins D2 and D3 forms vary only in their side chain structure. The differences do not affect metabolism (i.e., activation), and both forms have the prohormone function ***(Gil et al., 2018)***.

1α, 25-Dihydroxyvitamin D3 (1,25D3, calcitriol, **(Figure 1)** is the most active metabolite of vitamin D (vit D, cholecalciferol). This *seco*-steroid hormone has many biological roles ***(Norman, 2012).***

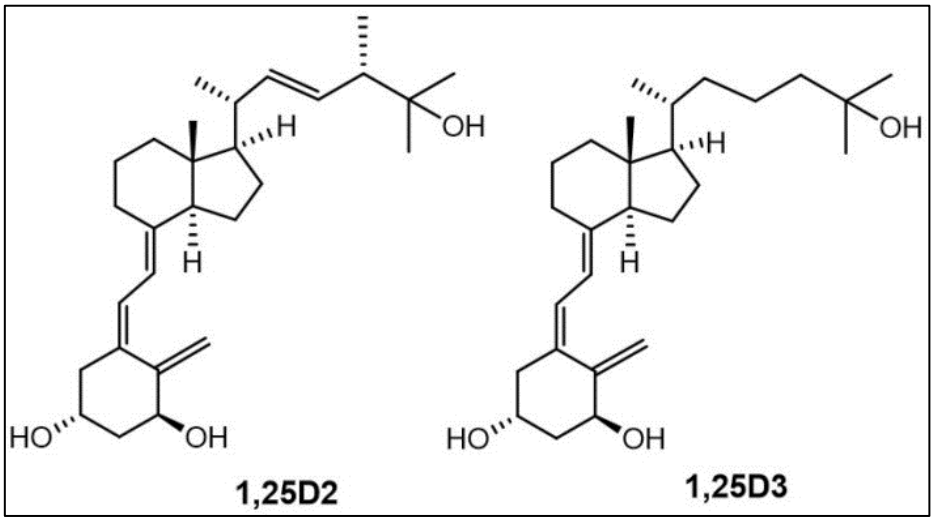

Figure (1): The structures of 1α, 25-dihydroxyvitamin D3 (1,25D3) and 1α, 25-dihydroxyvitamin D2 (1,25D2) ***(Kutner and Brown, 2018).***

Sources of vitamin D

There are two sources of delivering vitamin D: (1) cutaneous synthesis and (2) diet ***(Wintermeyer et al., 2016)***.

Most of it is supplied by cutaneous synthesis ***(Wacker and Holick, 2013)***. 7-Dehydrocholesterol (provitamin D_3, 7-DHC), which is synthesized inside the liver from cholesterol, converts to previtamin D_3 while absorbing solar energies (ultraviolet B wave length: 290–315 nm). Under the effect of heat, it immediately converts to vitamin D_3 (cholecalciferol) ***(Holick, 2011).***

Although the exposure to direct sunlight, depending on latitude, season and time, makes up the total amount of the

vitamin D_3 production, excessive exposure can also cause the formation of inactive photoproducts ***(Reuss-Borst, 2014).***

The smaller portion of vitamin D, whereof two forms exist, is ingested from diet ***(Reuss-Borst, 2014)*** together with calcium and phosphates. Ergocalciferol (vitamin D_2) is especially found in plants or plant products, while cholecalciferol (vitamin D_3) is mainly contained in animal products as fresh and canned salmon, mackerel and tuna as well as cod liver oil ***(Barvencik and Amling , 2015).***

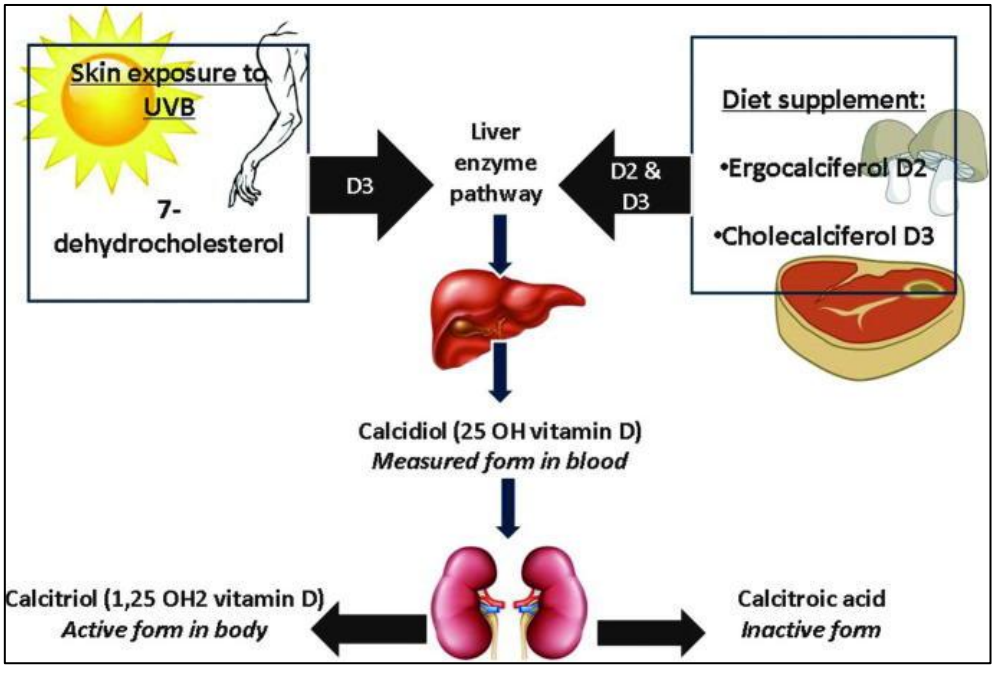

Figure (2): Different sources and forms of vitamin D ***(Mostafa and Hegazy, 2015).***

Dietary Sources of Vitamin D

Food sources of vitamin D are scarce. Although oily fish is considered to be a good source of vitamin D3 ***(Brown et al., 2013),*** its consumption and its vitamin D content is not high enough to significantly improve the vitamin D status of humans ***(Lehmann et al., 2015).***

Besides fish, mushrooms are often considered as another valuable source of vitamin D, in particular of vitamin D2. However, the major natural vitamin D metabolite in fungi and yeast is the vitamin D precursor ergosterol, which can be converted to vitamin D2 by UVB irradiation ***(Ko et al., 2008).***

In the United States (US), there are fortified food options, involving infant formula, milk, and orange juice, to help meet needs. Also, all infant formulas sold in the US contain at least 400 units/L of vitamin D ***(Lee et al., 2013).***

Table (1): Vitamin D content of foods ***(Lee et al., 2013)***

Food	Vitamin D Content, IU
Atlantic herring (raw)	1628/100 g
Butter	35/100 g
Canned pink salmon with bones in oil	624/100 g
Canned tuna/sardines/salmon/mackerel in oil	224–332/100 g
Cereal fortified	40/serving
Codfish (raw)	44/100 g
Cod liver oil	175/g; 1360/tablespoon
Cooked salmon/mackerel	345–360/100 g
Cow's milk	3–40/L
Dried shitake mushrooms (non-radiated)	1660/100 g
Egg yolk	20–25 per yolk
Fresh shitake mushrooms	100/100 g
Fortified milk/infant formulas*	400/L
Fortified orange juice/soy milk/rice milk	400/L
Margarine, fortified	60/tablespoon
Parmesan cheese	28/100 g
Shrimp	152/100 g
Swiss cheese	44/100 g
Yogurt (normal, low fat, or non-fat)	89/100 g

IU, international unit
**Infants consuming ≥ 1 L of formula daily do not require additional supplementation*

Seasonality of Vitamin D status

Because vitamin D levels had been shown to depend on season ***(Andersen et al., 2013),*** this factor should be taken into account when interpreting an individual's vitamin D status. Individual 25(OH) D levels reach their lowest levels after winter and their maximum at the summer end. Interestingly, this seasonal variation resembles the described seasonal variation of some infectious diseases including sepsis ***(Prietl et al., 2013).***

Vitamin D absorption and photobiogenesis

Vitamin D obtained from sun exposure, food, and supplements is biologically inactive (either the vitamin D2 or D3) and must undergo activation through 2 consecutive enzymatic hydroxylation reactions occurring in the liver and kidney ***(Gil et al., 2018)***.

Dietary vitamin D (either vitamin D2 or D3) is usually absorbed at the small intestine with other dietary fats ***(Silva and Furlanetto, 2018)***.

The acidic pH of gastric juice may affect vitamin D bioavailability. It is apparent that no data available on the susceptibility of major dietary forms of vitamin D to GIT pH conditions. A hypothesis can be made that protein digestive enzymes (pepsin and trypsin) are also intimately included in vitamin D absorption as they cleave vitamin D binding proteins present in food and thus facilitate its release. Further, in duodenum digestive enzyme (amylases, lipase and protease) continues the release of vitamin D from food matrix ***(Maurya and Aggarwal, 2017)***.

The presence of fats in the lumen triggers bile acids release, which initiate emulsification and support the formation of lipid-containing micelles, which diffuse into enterocytes ***(Mulligan and Licata, 2010)***. Once absorbed, exogenous vitamin D is packaged into chylomicrons, and thus is transported to the liver. A fraction of the vitamin D contained in the chylomicron can be taken up by adipose tissue and skeletal muscle ***(Gil et al., 2018)***.

Once remnant chylomicrons reach the liver, a specific carrier protein, the vitamin D binding protein (DBP) makes it possible for them to enter the hepatocytes and later facilitates their transport to different tissues that need them. Endogenously, vitamin D3 can be photosynthesized in the skin ***(Gil et al., 2018)***.

7-Dehydrocholesterol (provitamin D3) is converted to the pre vitamin D3 form (precalciferol) following its exposure to ultraviolet B (UVB) radiation ***(Valero-Zanuya and Hawkins-Carranza, 2007)***. Subsequently, it can suffer a thermal isomerization to vitamin D3 in the epidermis. Alternatively, pre vitamin D3 may be photoconverted to non active forms, such as tachysterol and lumisterol, which may exert different biological activities ***(Cisneros et al., 2017)***. Vitamin D3 production in the skin is due to the extent and quality of the UVB radiation reaching the dermis as well as the availability of 7-dehydrocholesterol and the characteristics of the skin ***(Gil et al., 2018)***.

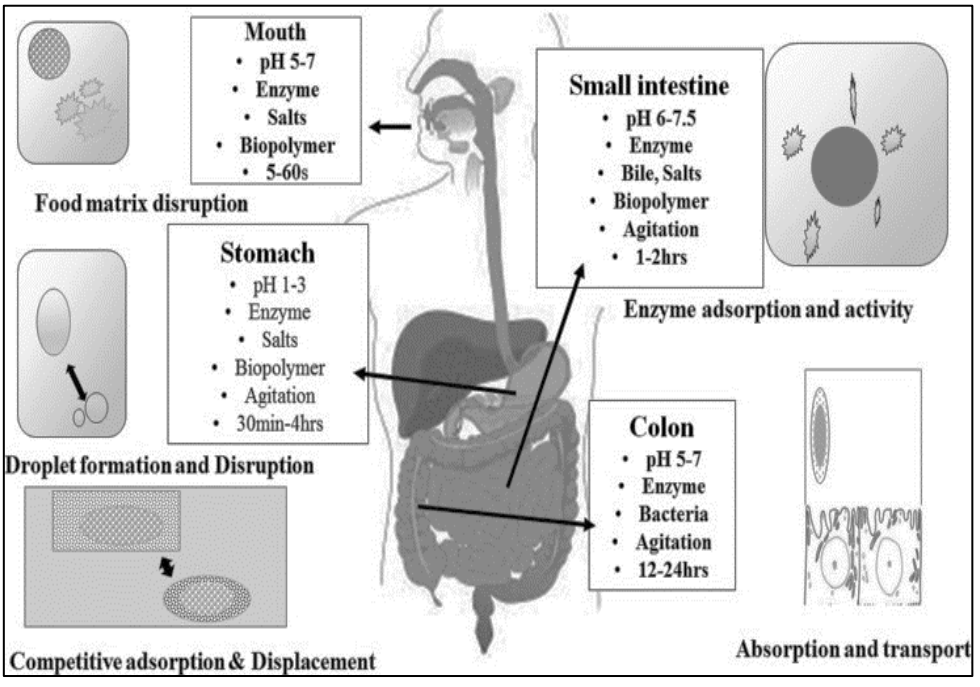

Figure (3): Schematic diagram of the human digestive system and the various physiochemical and physiological processes included in digestion and absorption of vitamin D ***(Maurya and Aggarwal, 2017)***.

Vitamin D metabolism

The three main steps in vitamin D metabolism, 25-hydroxylation, 1α-hydroxylation, and 24-hydroxylation are all performed by cytochrome P450 mixed-function oxidases (CYPs). These enzymes are located either in the endoplasmic reticulum (ER) (e.g., CYP2R1) or in the mitochondria (e.g., CYP27A1, CYP27B1, and CYP24A1). The electron donor for the ER enzymes is the reduced nicotinamide adenine dinucleotide phosphate (NADPH)-dependent P450 reductase. The electron donor chain for the mitochondrial enzymes is

comprised of ferredoxin and ferredoxin reductase. These are not specific for a given CYP—specificity lies within the CYP. Although of the CYPs included in vitamin D metabolism, only CYP2R1 and CYP24A1 were crystallized, it is likely that these enzymes contain a number of common structural features. These involve 12 helices (A–L) and loops and a common prosthetic group, namely the iron-containing protoporphyrin IX (heme) linked to the thiolate of cysteine. The I helix runs through the center of the enzyme above the heme where a thr(ser) and asp(glu) pair is essential for catalytic activity ***(Sugimoto and Shiro, 2012)***. CYP2R1, like other microsomal CYPs, contains two extra helices that appear to form a substrate channel in the bilayer of the ER ***(Sugimoto and Shiro, 2012)***. The B′ helix serves as a gate, closing on substrate binding. Whether a similar substrate channel exists for the mitochondrial CYPs is not clear.

Regulation of Vitamin D metabolism

1, 25-dihydroxyvitamin D (1, 25[OH] 2D) is compared to vitamin D, 25(OH) D has a much higher serum concentration and a longer half-life (about 3 weeks versus 1 day) and is so considered the best parameter to indicate vitamin D supply from all different sources. 1, 25-dihydroxyvitamin D (1, 25[OH] 2D) is the so-called active vitamin D hormone or calcitriol. Serum concentrations of 1, 25(OH) 2D are mainly derived from renal hydroxylation of 25(OH) D and are rather dependent on regulators of mineral metabolism (e.g.