



Vitamin D3 5000 IU 120 count

Supplement Facts		
Serving Size: 1 Softgel Servings per Container: 120		
	Amount per Serving:	DV%
Vitamin D3 (as Cholecalciferol) (from Lanolin)	125 mcg (5,000 IU)	625%
* Percent Daily Values are based on 2,000 calorie diet. † Daily Value not established.		
Other Ingredients: Softgel Capsule (bovine gelatin, water, glycerin) and Extra Virgin Olive Oil		
Not manufactured with yeast, wheat, gluten, soy, corn, milk, eggs, fish or shellfish ingredients		
Non-GMO		

Suggested usage: Take 1 softgel every two days with a fat containing meal

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The Scientific Basis:

Vitamin D may play various roles in human reproduction and several recently published studies indicate that vitamin D levels are predictive of implantation and ongoing pregnancy rates in *in vitro* fertilization (IVF).

Vitamin D is really not a “vitamin” but a small family of steroid hormones that increase the absorption of calcium, magnesium, phosphate, iron and zinc from the intestine and which also have effects on many other organ systems. Vitamin D is either consumed, as in certain fortified foods, e.g., dairy products, or synthesized from cholesterol in the skin, when there is sufficient sun exposure. A review article in the *New England Journal of Medicine* revealed that the majority of American women and more than one billion people worldwide may have Vitamin D insufficiency or deficiency.

Receptors for Vitamin D are present in the human uterus, ovary and placenta and low levels of vitamin D in pregnancy are associated with pre-eclampsia, gestational diabetes and intrauterine fetal growth retardation. When bound to its receptor, the active form of vitamin D (calcitriol) seems to be involved in estrogen production and implantation. In fact, calcitriol may regulate several genes involved in implantation. Vitamin D is involved in female reproduction including roles in IVF and polycystic ovary syndrome (PCOS). Primarily attributed to vitamin D effects on the endometrium, several observational studies suggest better IVF pregnancy rates in women with sufficient vitamin D levels (≥ 30 ng/ml).

An evaluation of 173 women undergoing IVF in Toronto revealed that women with sufficient vitamin D levels (> 75 nmol/L) had significantly higher pregnancy rates in IVF than women with insufficient levels (> 75 nmol/L). This prospective study showed that women with sufficient levels had a 52.5% clinical pregnancy rate compared to a 34.7% rate among those with insufficiency. Another investigation, published in *Human Reproduction*, measured vitamin D levels in 388 patients who underwent IVF/ICSI and a single embryo transfer. Clinical pregnancy rates were significantly lower in women with vitamin D levels < 20 ng/ml compared with those with higher concentrations (41 vs. 54%). When controlling for all potentially confounding factors, vitamin D was independently associated with lower clinical pregnancy rates.

In a prospective study of 335 IVF patients study from Milan, researchers found that women who had sufficient that levels of vitamin D (> 20 ng/ml) were significantly more likely to produce higher quality embryos and were more like to achieve a clinical pregnancy than women who were vitamin D deficient (< 20 ng/ml). This prospective study examined 154 women who were vitamin D deficient and 181 women who had sufficient vitamin D blood levels. The clinical pregnancy rates were 20% and 31%, respectively. Interestingly, a subgroup analysis showed that the group of women with the highest levels (> 30 ng/ml) had the highest chances of pregnancy.

It does appear, then, based upon these and a number of recent studies that Vitamin D plays a key role in human reproduction, maybe involving embryo quality as well as at the uterine lining, where it may facilitate implantation of the embryo. Vitamin D is readily available, inexpensive

and has few, if any side effects and may improve one's fertility potential. However, there are no adequate clinical studies on vitamin D supplementation and IVF outcome.

In PCOS women, low 25-hydroxyvitamin D levels are associated with obesity, metabolic, and endocrine disturbances and vitamin D supplementation might improve menstrual frequency and metabolic abnormalities in those women. One randomized controlled trial found an increased endometrial thickness in women with polycystic ovary syndrome (PCOS) receiving vitamin D during intrauterine insemination cycles. In addition, vitamin D supplementation had a beneficial effect on serum lipids in PCOS women.

Further, vitamin D might influence the metabolism of estrogen and progesterone in healthy women and high levels of 25-hydroxy vitamin D levels might be associated with endometriosis. Vitamin D was also favorably associated with primary dysmenorrhea, uterine leiomyoma, and ovarian reserve in late reproductive aged women. There may also be an association between low serum Vitamin D levels and miscarriage risk. In a prospective cohort study of 1683 pregnant women the association between maternal serum concentrations of serum 25-hydroxyvitamin D and the risk of subsequent miscarriage ($n = 58$) was studied. Low concentrations of 25-hydroxy Vitamin (D <50 nmol/L) were associated with a >2 -fold increased risk for first trimester miscarriage. Vitamin D levels were not associated with an increased risk of second-trimester miscarriage.

During pregnancy, low maternal serum Vitamin D levels have been associated with several maternal and fetal concerns. A systematic review of the world literature revealed that insufficient Vitamin D levels in pregnancy may be associated with an increased risk of preeclampsia, gestational diabetes mellitus, preterm birth and small for gestational age babies.

In men, vitamin D is positively correlated with sperm quality and androgen status. In fact, supplementation with vitamin D might increase testosterone levels. The role of Vitamin D in male reproduction includes Vitamin D receptors (VDR) and enzymes that metabolize vitamin D in testis, male reproductive tract and human spermatozoa. The expression levels of VDR and the enzyme which degrades 1, 25-dihydroxy Vitamin D in human spermatozoa serve as positive predictive markers of semen quality and VDR facilitate increases in intracellular calcium concentration that induce sperm motility. Animal models have demonstrated that vitamin D is important for estrogen signaling and sperm motility, whereas human studies support the positive association between serum 25-hydroxyvitamin D level and sperm motility in both fertile and infertile men.

Ultraviolet light from the sun causes a form of cholesterol (7-dehydrocholesterol) to be converted to an inactive form of Vitamin D (cholecalciferol, or Vitamin D₃). In the liver, D₃ is converted to 25-hydroxy D₃ (calcidiol). Likewise, dietary Vitamin D₂ (ergocalciferol) and Vitamin D₃ are incorporated into chylomicrons (large lipoprotein particles formed in cells of the small intestine following absorption of fatty foods) and travel to the liver, where they also are converted to 25-hydroxy Vitamin D₃. When stimulated by parathyroid hormone, this 25-hydroxy Vitamin D₃ from the liver is then converted in the kidney to 1,25-dihydroxy Vitamin D₃ or calcitriol. It is calcitriol that is the active form of Vitamin D in the human with it enhances the absorption of calcium and phosphorus from the small bowel and assists parathyroid hormone in

bone metabolism and regulation of serum calcium levels. Further, there are Vitamin D receptors found in various tissue types and it has been shown that Vitamin D inhibits cell proliferation and mediates cell differentiation.

References

1. Holick M: Vitamin D deficiency. *N Engl J Med* 2007 357: 266-281.
2. Garbedian K, Boggild M, Moody J, Liu KE: Effect of Vitamin D status on clinical pregnancy rates following in vitro fertilization *CMAJ Open* 2013 Jun 28;1(2):E77-82. doi: 10.9778/cmajo.20120032
3. Polyzos NP, Anckaert E, Guzman L, Schiettecatte J, et al: Vitamin D deficiency and pregnancy rates in women undergoing single embryo, blastocyst stage, transfer (SET) for IVF/ICSI. *Human Reprod* 2014 Sep;29(9):2032-40. doi: 10.1093/humrep/deu156.
4. Lerchbaum E, Obermayer-Pietsch: Mechanisms in endocrinology: vitamin D and fertility: a systematic review. *Eur J Endocrinol* 2012 **166**: 765-778
5. Anagnostis P, Karras S, Goulis DG: Vitamin D in human reproduction: a narrative review. *Int J Clin Pract* 67(3) 225-235.
6. Paffoni A, Ferrari S, Vigano P, Pagliardini L, et al: Vitamin D deficiency and infertility: insights from in vitro fertilization cycles. *J Clin Endocrinol Metab* 2014 99(11): E2372-E2376.
7. Jensen MB: Vitamin D and male reproduction. *Nat Rev Endocrinol* 2014 10 175-186.
8. Lerchbaum E, Rabe T: Vitamin D and female fertility. *Cur Opin Obstet Gynecol* 2014 26(3) 145-150.
9. Wei SQ, Qi HP, Luo ZC, Fraser WD: Maternal vitamin D status and adverse pregnancy outcomes: a systematic review and meta-analysis. *J Mat Fetal Neonat Med* 2013 26(9) 889-899.
10. Andersen LB, Jorgensen JS, Jensen TK, Dalgard C, et al: Vitamin D insufficiency is associated with increased risk of first-trimester miscarriage in the Odense Child Cohort. *Am J Clin Nutr* **September 2015** 102(3) **633-638**.

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