The future of vitamin D supplementation

The first high performance topical Vitamin D3 product to hit the market.

Only 15 years ago, doctors, scientists and the educated laymen thought of "vitamin D" as the "anti-rachitic vitamin", almost exclusively. The prevention of rickets, a defective mineralization of bones before epiphyseal closure in immature mammals that leads to fractures and deformity and post-menopausal bone loss (osteoporosis) is still among the most immediate health benefits of vitamin D supplementation and / or adequate sun exposure.

And still, the list of recently discovered and emerging beneficial effects of vitamin D on the endocrine, immune and musculoskeletal system continues to grow.

You don’t want to risk being deficient

Low levels of the vitamin D metabolite 25-OHD (<30ng/mL) have been linked to osteoporosis, cardiovascular disease, stroke, autoimmune diseases and cancer (see Figure 2).

<table>
<thead>
<tr>
<th>25(OH)D range</th>
<th>No. of experts</th>
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<tbody>
<tr>
<td>30–100</td>
<td>20</td>
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<tr>
<td>30–150</td>
<td>1</td>
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<tr>
<td>30–80</td>
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<tr>
<td>30–50</td>
<td>2</td>
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<tr>
<td>40–100</td>
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Table 1: Serum25(OH)D range (ng/mL) according to 25 experts Souberbille et al. questioned for their 2010 analysis of practical implications of recent insights into the role of vitamin D in musculoskeletal health, cardiovascular disease, autoimmunity and cancer (Souberbille. 2010).

No wonder that the group of published scientists who were surveyed for a 2010 paper on practical recommendations for the clinical practice agreed that 25OHD levels below 30ng/mL (>75 nmol/L) require immediate action on part of practicing physicians (see Table 1).

Good sources of vitamin D are scarce

The most abundant source of vitamin D for humans is exposure to sunlight (Holick. 2003). From an evolutionary perspective, foods are rather an alternative source of vitamin D. Most of the foods in our diets contain relatively little vitamin D.

In fact, oily fish, like salmon, mackerel, herring, and grandma’s cod liver oil are among the few food items that contain significant amounts of vitamin D. Yet while 3.5 ounces of while wild-caught salmon contain on average 500–1000 IU vitamin D, the same amount of its farmed counterpart contains only 100–250 IU vitamin D per serving (Chen. 2007).
It is thus only logical that the food industry is trying to make up for the lack of vitamin D in its products by fortifying milk, juice products, breads, yogurts, and cheeses.

Still, the latest evidence from epidemiological studies indicates that the amount of vitamin D the average Westerner gets from his / her diet is not enough to keep his / her levels of 25-OHD in the aforementioned range of 30-100ng/mL.

The downsides of low vitamin D levels are making the evening news

Frightening reports about the involvement of low vitamin D levels in the etiology of almost all diseases of civilization are in the news on an almost weekly basis.

As a consequence of the rising awareness of the ill health effects of low vitamin D levels, supplements containing anything from 400 IU to 50,000 IU vitamin D3 have become best-sellers at US and European drugstores; and that despite the fact that the results of randomized controlled trials draw a very ambiguous image of the net health benefits of these products:

"Despite a few hundred systematic reviews and meta-analyses, highly convincing evidence of a clear role of vitamin D does not exist for any outcome " (Theodoratou. 2014)

Scientists are still debating the potential causes of the confusing study results. Next to genetic polymorphisms, researchers are also looking at the route of administration and the role of vitamin D binding proteins (Chun.2013).

Does only free vitamin D matter? Probably not.

Chun et al., for example, argue that the 99.9% of 25(OH)D that circulates bound to vitamin D binding (VDBP) protein and or other carriers could have little to no influence on the "non-classical actions of vitamin D" (Chun. 2013). If this hypothesis was accurate, this would imply that a simple increase in 25-OHD, as it has been shown in response to dosages as low as 1,000IU of vitamin D3 per day will exert its beneficial effects on metabolic (diabetes, obesity, hyperlipidemia), immune (rheumatoid arthritis, multiple sclerosis, asthma, etc.), cardiovascular (stroke, CAD, CVD, etc.) and musculoskeletal health (sarcopenia, bone loss, etc.), only, if the 25-OHD is free and not bound by VDP or other carriers.

A similar mechanism has already been proposed for other hormones and is, just as it is the case for vitamin D, highly controversial. And there are in fact more than a handful of arguments against the "free vitamin D hypothesis". Decreasing vitamin D binding protein levels with age, for example, are associated with a significantly increased risk of vitamin D deficiency (Yousefzadeh. 2014). A similar association has been found for fatty liver disease (Malham. 2011) and type I diabetes (Blanton. 2011). Moreover, high levels of bound vitamin D have been associated with decreased pancreatic cancer and prostate cancer risks (Weinstein. 2012 & 2013) – a result that appears to be logical in view of the reduced biological activity of vitamin D analogues with an artificially binding affinity for vitamin D binding protein (Bouillon. 1991).

To finally answer the question if the amount of free 25(OH)D is a better marker of vitamin D activity we need more relevant data, data which
could have a major impact on our understanding of the optimal route of vitamin D supplementation, as well.

Different binding- and pharmacokinetics - The topical advantage

Scientists have been wondering for decades about the potential pharmacokinetic differences between endogenously produced vitamin D from the skin and the various forms of vitamin D in our diet.

In 1993 Haddad et al. published a paper in which they were able to show that dietary vitamin D will bind preferentially to other carriers than vitamin D binding protein (VDBP), such as chylomicron remnants or low density lipoprotein (LDL). The resulting vitamin D complexes are either stored (Holmes. 1983), as it appears to be the case in the fat tissue of obese individuals (Vimaleswaran. 2013) or taken up through liver membrane receptors and thus no longer available for the health-relevant interactions with vitamin D receptors on other organs (Haddad. 1993).

These pharmacokinetic differences and their consequences, such as the 2x higher half-life for cutaneously vs. orally delivered vitamin D (Wacker. 2013) and differences in vitamin D ⇔ vitamin D receptor interactions, are what makes topical vitamin D supplements so interesting.

Before our product developers at Super Human RX could make the important step from theory to practice, two important questions still had to be answered:

1. Is the topical delivery of vitamin D feasible and effective?
2. Does the topical delivery of vitamin D entail hitherto unknown health-risks?
The topical delivery of vitamin D is feasible and effective

In answering question #1, i.e. whether the topical delivery of vitamin D can effectively increase the serum levels of 25OHD and thus prevent the previously discussed ill-health effects that have been associated with low vitamin D levels, we can resort to a very recent study from the University of Dammam and the King Fahd University Hospital in Saudi Arabia.

Although, or rather because Saudi Arabia is a country with lots of sun, its citizens get little to no sun exposure. This is particularly true for women of whom more than 80% are classified as vitamin D deficient – independent of seasonal variability (Kanan. 2013).

As the results of the randomized-controlled trial by Sadat-Ali et al. shows, this is a problem which could easily be fixed if all the women used the topical vitamin D cream (5,000IU/day) the researchers used tested on 50 initially vitamin D deficient female study participants, all of whom reached sufficient vitamin D levels after only 90 days of treatment (see Figure 3).

The topical delivery of vitamin D is safe

In said peer-reviewed study from the March issue of the International Journal of Biomedical Science, the researchers didn’t just confirm that the administration of vitamin D through the skin "is possible" and "efficacious". They were also able to show that it is "safe" (Sadat-Ali. 2014). A fact that has been called into question by Michael Holick in the early 1980s.

In a 1982 patent Holick issued (US. Pat. No. 4,310,511; issued Jan. 12, 1982), he indicated that dermal uptake was inefficient and that there could be an "uncontrolled increase in absorption of vitamin D, with concomitant loss of concentration control, and the appearance of side effects such as vitamin D toxicity". A claim that was put into question roughly 18 years before the previously cited study by Sadat-Ali et al. was published.

In the patent application for a "method of delivering a nutritional or therapeutically amount of vitamin D to the blood of a mammal", who is still doing research in the field of vitamin D supplementation at the University of Toronto, points out that the earlier assumption was based on an incomplete understanding of the processes which govern the regulation and synthesis of vitamin D.

In said patent, Vieth also presents data from early animal experiments in which he was able to show that the "application to bare skin of a nutritionally effective amount of vitamin D dissolved in a suitable, pharmaceutically acceptable carrier, will produce an increase in 25-hydroxyvitamin D close to the increase attainable with the same dose given directly into the stomach." And that in spite of the fact that ethyl alcohol, the carrier Veith used, is vastly inferior to DMSO which is used as a carrier in Primal D.

The data in Figure 4 confirms that Vieth’s statements are more than marketing claims. His test-solution did in fact allow for a similar absorption of vitamin D3 through the skin as the classic intravascular (injection) or gastric (oral supplement) routes for vitamin D delivery.
Vieth's data does also confirm that the subcutaneously administered vitamin D3 is released only gradually into the blood stream, where it reaches its peak levels 2 days after the administration and thus at a time point, when the vitamin D3 levels that peaked rapidly after the intravascular injection and/or direct instillation into the stomach have already declined by more than 50%.

No wonder, the dreaded changes in calcium metabolism of which Holick speculated that they may entail a significant toxicity risk are significantly more pronounced in response to the oral, compared to the topical application of vitamin D at similar doses. A significant health risk, i.e. the potential of calcification of the kidneys as a consequence of an increase in urinary calcium excretion doesn’t exist for either of the two ways of administration, though.

The gist – The Top 3 Advantages of Primal D

- **Precise, individualized dosing**

With Primal D you decide how much vitamin D you want to apply without having to buy a new product. Your vitamin D test came out extremely high? No problem, with Primal D you can always adjust your daily dose.

- **Sustained release of vitamin D via the natural route, through the skin**

Just like cutaneously produced vitamin D, topically applied vitamin D will hit your blood stream much slower than oral vitamin D. The ensuing long-lasting elevation of vitamin D promotes vitamin D receptor interactions on target organs rather than vitamin D uptake and storage by the liver and fat depots (Holmes. 1983; Haddad. 1993; Sadat-Ali. 2014).

- **Reliable, scientifically proven ability to increase 25-OHD levels w/ out toxicity issues**

In contrast to oral vitamin D supplements, topical vitamin D will effectively increase the level of circulating 25-OHD into the normal range of >30ng/mL, even if you suffer from reduced bile-flow, liver problems, digestive problems, reflux disease, irritable bowel disease or the consequences of gastric bypass surgery (Basha. 2000; Holick. 2007; Aarts. 2011; Ulitsky. 2011)

Due to the sustained delivery and reduced peak serum levels of vitamin D3 the use of Primal D is associated with an even lower toxicity risk than regular vitamin D supplements at similar doses.
Are you really getting enough sun?

It’s often said that spending as little as 30 minutes of whole-body sun exposure will produce 10,000 IUs of vitamin D3. This is a misconception. 7-dehydrocholesterol is synthesized to Previtamin D3 by UV light. The Previtamin D3 must still convert to D3. This does not always occur for a variety of reasons.

For instance, the skin has a feedback loop and when large amounts of D3 are being synthesized it begins to degrade faster than it synthesizes it to maintain equilibrium. Another issue may be that Previtamin D3 can be washed out of the skin before it even converts into D3 if you don’t allow it to stay put long enough. One such study indicated that this can occur from swimming while sun bathing or showering immediately after sun bathing. While this is just one study and many among the scientific community feel it’s not conclusive there appears to be some evidence that not all sun exposure will lead to a surge in D3 levels.

So even if you’re not sun-phobic you may be surprised to find that all your time gardening or sun bathing is not having the effect you want on your D3 levels. And if you are sun-phobic and slather sunscreen on at every possible opportunity you’ll be surprised to know that a

References:


Ulitsky, Alex, et al. "Vitamin D Deficiency in Patients With Inflammatory Bowel Disease Association With Disease Activity and Quality of Life." Journal of Parenteral and Enteral Nutrition 35.3 (2011): 308-316.


