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1	Single high dose vitamin D3: a promising sunburn therapy
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- 20 Summer weekends often beckon us outdoors to bask in the sun's warmth, which, in
- 21 moderation, offers tangible benefits for our health and well-being. However, many of us
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have, at one time or another, stayed out a bit too long, resulting in that all-too-familiar red, painful, and swollen skin—sunburn. The aftermath of overexposure is more than just discomfort; it's a visible manifestation of the body's inflammatory response. Sunburn triggers an influx of neutrophils and macrophages to the affected skin, alongside a storm of pro-inflammatory mediators, including tumour necrosis factor alpha. These macrophages then differentiate into inflammatory macrophages, which release inducible nitric oxide synthase, prolonging inflammation and exacerbating tissue damage. The result? Painful, unsightly skin, and a desperate search through the bathroom cabinet for topical steroids, non-steroidal anti-inflammatories, aloe veragel, or indeed any remedy that might offer relief.

But what if there were a simpler, more effective solution? Enter single high-dose vitamin D3—an over-the-counter remedy that might just save your skin. Research suggests that taking a one-time oral dose of 100,000 to 200,000 IU of vitamin D3 (1,000 IU = 25  $\mu$ g) within hours of sunburn onset can significantly reduce skin inflammation. In some cases, it may even resolve the symptoms in time for you to enjoy the sun the next day.

So, how does it work? The large dose of vitamin D3 increases the levels of inactive vitamin D3 in the circulation and sunburnt skin. Keratinocytes and macrophages then convert this into its active form. This active vitamin D3 combines with endogenous retinoids—produced by UV radiation—to promote the differentiation of anti-inflammatory 'pro-resolution' macrophages, which express arginase-1 and markers of autophagy. In essence, this process extinguishes the inflammation caused by sunburn.

What evidence supports this approach in humans? While data are currently limited, a double-blind, placebo-controlled trial involving 20 subjects demonstrated that a single dose of 50,000 to 200,000 IU of vitamin D3 administered one hour after exposure to erythemogenic UVB significantly reduced skin redness, histological evidence of skin damage, and skin markers of inflammation. Not everyone experienced the same degree of benefit though, with the most significant responses observed in those whose serum vitamin D3 levels rose the most post-dosing. Importantly, the study reported no changes in serum calcium or phosphate levels, as the kidneys inherently protect against this, nor any other

adverse reactions. High-dose vitamin D3 (up to 600,000 IU) has been safely used in other clinical contexts, such as critical care in over 1360 patients, without toxicity.<sup>5</sup>

However, the pharmacokinetics of single high-dose vitamin D3 are complex, and optimal dosing levels for achieving immunomodulatory effects remain under investigation. Does taking vitamin D3 before sun exposure offer the same benefits? The answer remains unclear, though it is likely that vitamin D3's immunomodulatory effects are most potent after injury has occurred. Can we recommend single high-dose vitamin D3 for general sunburn treatment? Not just yet, although anecdotal and off-label use are increasing. The prudent course is to await further studies that replicate these findings across larger and more diverse populations before incorporating vitamin D3 into routine clinical practice for sunburn.

The potential of the anti-inflammatory effects of single high-dose vitamin D3 extends beyond sunburn. Emerging evidence suggests its benefits in other clinical scenarios, such as minimising radiation-induced dermatitis following breast cancer radiotherapy, alleviating acute radiation recall dermatitis after chemotherapy, and reducing toxic erythema from chemotherapy. For sunburn, a practical guide might be to consider taking a single oral dose of 100,000 IU taken 1-12 hours after the excessive sun exposure. Most over the counter vitamin D3 tablets sold come in 1000-10000 IU (25  $\mu$ g – 250  $\mu$ g) doses (though larger doses of 50000 IU are available), meaning you would take multiple tablets in one go. That may seem like a lot, but it is safe. Given the growing body of data supporting vitamin D3 as a therapeutic intervention for managing acute skin inflammation, it may well be worth it. As dermatologists, we now pack our vitamin D3 tablets alongside sunscreen when heading on sunny holidays. Perhaps soon, you will too.

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