CASE REPORT

DIM and PSA Reduction: Blocking Aromatization for Prostate Health: A Case Report

Danielle Arnold, MS, CNS, LDN; Oscar Coetzee, MS, DCN; Allyson LaGrutta, MS

ABSTRACT

This case study examines the effects of diindolylmethane (DIM) on lowering Prostate-specific antigen (PSA) levels and improving hormonal balance in a 78-year-old male patient. It further considers whether the timing of hormonal changes in relation to DIM use suggests a possible causal link. The patient presented with steadily rising PSA levels and declining testosterone, raising concerns about potential prostate pathology. Given his reluctance to undergo a prostate biopsy—due to concerns about its invasiveness and potential complications—a functional medicine approach was adopted to address the hormonal imbalances contributing to his condition. The intervention included discontinuing cholesterol-lowering supplements and introducing 100 mg per day of DIM-Evail™ for three months to modulate estrogen metabolism. Over the three months, the patient's PSA dropped from 4.6 to 2.4 ng/mL, while the total and free testosterone notably increased from 436 ng/dL to 615 ng/dL. This case highlights the potential of targeted nutraceutical interventions in modulating hormone metabolism and supporting prostate health, though, as a single case, the findings warrant further validation through larger clinical studies. (*Altern Ther Health Med.* [E-pub ahead of print.])

Keywords • Diindolylmethane (DIM), Prostate-specific antigen reduction, aromatase inhibition therapy, estrogen metabolism modulation, testosterone restoration, prostate cancer risk biomarkers, nutraceutical intervention for elevated prostate-specific antigen

Danielle Arnold, MS, CNS, LDN, Adjunct Professor, Purdue Global University. **Oscar Coetzee**, MS, DCN, University of Bridgeport, Bridgeport, CT, Associate Professor - Assistant Director, Doctor of Health Science, Natural Healthcare Center, Long Branch, NJ; Clinical Director, Functional Medicine. **Allyson LaGrutta**, MS, Warwick, NY, USA.

Corresponding author: Danielle Arnold, MS, CNS, LDN
E-mail: thesourcefn@gmail.com

INTRODUCTION

Prostate-specific antigen (PSA) is a key biomarker for monitoring prostate health, often used to assess conditions like benign prostatic hyperplasia (BPH) and prostate cancer.[1] While PSA levels are primarily linked to these conditions, fluctuations in testosterone and estrogen levels can also influence PSA dynamics. Some research suggests that lower testosterone levels are linked to higher Gleason scores, indicating more aggressive prostate cancer. This can result in falsely low PSA levels, which may delay diagnosis, as low PSA can itself be a predictor of low testosterone, particularly in men with high-grade prostate cancer (PC) (Gleason Sum ≥8).[2] What we do know is that as men age, their bodies naturally convert more testosterone into estrogen through a process called aromatization. This shift can contribute to prostate enlargement and hormonal imbalances.[1]

One approach to support a healthier hormonal balance is through diindolylmethane (DIM), a biologically active and natural compound derived from indole-3-carbinol (I3C), obtained from the dietary consumption of cruciferous vegetables like broccoli, cabbage, and Brussels sprouts. I3C is rapidly converted to DIM in the stomach via acid-catalyzed condensation.[8,17] Research shows that DIM helps the body metabolize estrogen more efficiently by induction of cytochrome P450 (CYP) enzymes, including CYP1A1, CYP1A2, and CYP1B1, which are crucial for the oxidative metabolism of estrogens.[6,8] This enzyme induction specifically promotes the conversion of estrone to 2-hydroxy-estrone (2OHE1), a form of estrogen linked to healthier cell function and described as antiproliferative and proapoptotic.[3] It has also been suggested to have a protective effect against certain cancers.[8] DIM supplementation has also been shown to enhance the 2-hydroxylation of estrogen and favorably increase the 2:16 OHE ratio.[3,8] By helping to optimize estrogen metabolism, DIM may contribute to a better testosterone-to-

estrogen balance, which could be beneficial for prostate health.[8,18,19] This support is multifaceted due to both effects on androgen signaling and estrogen metabolism, which is why it is increasingly used as a promising agent for the prevention of the recurrence of hormone-dependent cancers and in protocols for prostate cancer.[17] This improved hormonal balance may contribute to normalized PSA levels. While it is important to question whether DIM simply masks elevated PSA levels, research demonstrates that DIM actively suppresses PSA gene expression through its role as a strong and pure androgen receptor antagonist.[7,18] This involves inhibiting androgen receptor (AR) translocation and competing with dihydrotestosterone (DHT) for binding to the AR.[7,18] Furthermore, DIM favorably modulates estrogen metabolism through induction of cytochrome P450 (CYP) enzymes,[3,6,8] thereby enhancing the formation of protective antiproliferative and proapoptotic 2-hydroxyestrone (2OHE1) metabolites[3] and improving the 2:16 ratio.[8] These effects may reduce estrogen-driven prostatic inflammation, mediated in part by Estrogen Receptor alpha (Erα), which is the dominant estrogen receptor subtype mediating adverse effects, including inflammatory responses, in the prostate gland.[19] Beyond hormone metabolism, DIM also influences apoptosis, proliferation, and metastasis of prostate tumor cells,[17] and in androgen-independent prostate cancer models exerts antiproliferative effects via CB2 receptor simulation, associated with reduced pAKT and increased cleaved CASP-3.[17]

DIM's influence on hormone balance also extends to the testosterone–estrogen axis. While descriptions of estrogen metabolism are often in the context of estrogen-enhanced cancers, the underlying principles of less proliferative 2-hydroxyestrone (2OHE1) and proliferative 16-alpha-hydroxyestrone (16αOHE1) metabolites are directly applicable to any hormone-sensitive cell, including prostate cells.[3,6,9] This is because estrogens have direct and significant effects on prostate cells and tissue, influencing proliferation, inflammation, and potential for carcinogenesis.[19] By indirectly inhibiting aromatase, DIM reduces the conversion of testosterone to estrogen, helping maintain a more favorable testosterone-to-estrogen ratio.[8] This may decrease estrogenic stimulation of prostate cells without amplifying androgenic drive, adding another layer of protection against hormone-sensitive proliferation and inflammation in the prostate.[18]

5-alpha-reductase (5αR) is an enzyme that plays a crucial role in prostate health. Specifically, the type 2 enzyme, located in the prostatic stroma, converts testosterone into the more potent androgen dihydrotestosterone (DHT). DHT is a powerful androgen that binds to and activates the AR in prostate cells, stimulating prostate growth and increasing PSA expression. Its potent effects are significantly implicated in the development and progression of both BPH and prostate cancer.[2,19]

Although DIM is not a confirmed direct inhibitor of 5αR, it may influence androgenic activity through other mechanisms such as AR antagonism, potentially mitigating the effects of DHT, a potent androgen implicated in BPH and prostate cancer progression.[17,18,19] Beyond hormonal modulation, DIM exhibits anti-inflammatory effects[8] and may promote apoptosis[3] and inhibit angiogenesis in abnormal prostate cells.[8] These effects are critical in limiting chronic inflammation, cellular proliferation, and neovascularization, which are all drivers of elevated PSA and prostate pathology. Taken together, these mechanisms suggest that the observed reductions in PSA associated with DIM supplementation are unlikely to reflect mere biomarker suppression. Rather, they may indicate meaningful improvements in the underlying hormonal and inflammatory environment of the prostate.[2]

Why This Matters for Men with a History of Prostate Cancer

Concerns that increased testosterone may promote prostate cancer are being reevaluated. The saturation model suggests that prostate tissue is only responsive to androgens at very low testosterone levels; beyond that, additional testosterone appears not to stimulate cancer growth.[11] Lower testosterone has also been associated with more aggressive tumors.[2,10]

Given this hormonal context, DIM's modest increase in free testosterone, via reduced aromatization and suppression of Sex Hormone-Binding Globulin (SHBG), should not be viewed as harmful.[3] SHBG is a liver-derived protein that binds to sex hormones, including testosterone and estradiol, making them biologically inactive in circulation.[12] A reduction in SHBG, therefore, results in more "free" or biologically active testosterone being available in the body. This is consistent with the evidence that estradiol, which DIM can help reduce through aromatase inhibition, increases SHBG production.[12] When combined with DIM's effects on lowering DHT through AR antagonism,[7,17] curbing inflammation,[8] and promoting apoptosis,[3,8,17] DIM may support a more favorable hormonal and cellular environment in men with prior prostate pathology.

Although the mechanistic data surrounding DIM are robust, validation via larger clinical trials is essential to confirm its influence on PSA dynamics and safety in hormone-sensitive prostate conditions. This case report contributes novel clinical evidence by documenting DIM's integrated effects on stabilizing PSA levels, increasing testosterone, lowering estrogen levels, and modulating inflammatory pathways in an individual with rising PSA levels. These findings underscore DIM's translational relevance and highlight the need for larger controlled studies to define its role in prostate health management.

NARRATIVE

A 78-year-old male presented to the Natural Healthcare Center (Long Branch, NJ, USA) in December 2022 with concerns regarding rising PSA levels and declining testosterone. His past medical history included hyperlipidemia, hypertension, BPH, and coronary artery disease, for which he underwent coronary stent placement in 2023. He was a former smoker, consumed alcohol socially, and reported no family history of prostate cancer.

At presentation, his medications included Finasteride 5 mg/day (for BPH and alopecia, prescribed by urologist), Irbesartan 150 mg/day (for hypertension, prescribed by cardiologist), Rosuvastatin calcium 10 mg/day (for hyperlipidemia, prescribed by cardiologist), Bupropion 150 mg/day (for depression, prescribed by primary care physician), Tadalafil 20 mg/day (for erectile dysfunction), and Alfuzosin Hydrochloride (dose not specified) (for BPH). He also reported using an over-the-counter cholesterol-lowering supplement, CholestOff Complete® (Nature Made, USA).

Historical laboratory testing demonstrated a gradual rise in PSA and a decline in testosterone (Table 1). On April 12, 2021, his PSA measured 3.2 ng/mL, with concurrent elevations in LDL cholesterol (114 mg/dL) and glucose (100 mg/dL). By May 4, 2022, his PSA had increased to 4.0 ng/mL. On November 22, 2022, his PSA further rose to 4.2 ng/mL, at which time total testosterone was 585 ng/dL and free testosterone was 5.9 pg/mL.

At his initial consultation on December 7, 2022, laboratory results showed continued progression, with a PSA of 4.6 ng/mL (above the reference range of 0.0–4.0 ng/mL), total testosterone of 436 ng/dL, and free testosterone of 3.5 pg/mL (low, reference range: 6.6–18.1 pg/mL). Estradiol was measured at 20 pg/mL, luteinizing hormone (LH) at 11.2 mIU/mL (elevated), and follicle-stimulating hormone (FSH) at 19.8 mIU/mL (elevated). These findings indicated declining androgen status in the setting of rising PSA. It was at this point that care with the clinical nutritionist (author) began.

A targeted functional medicine intervention was initiated. The patient was prescribed DIM-Evail™ 100 mg/day (Designs for Health, USA) to support estrogen metabolism. He was also advised to discontinue CholestOff Complete® (Nature Made, USA), given concerns that suppression of cholesterol may have contributed to his declining testosterone, as cholesterol serves as the precursor for steroid hormone biosynthesis.

The patient was reviewed again on January 9, 2023, at which time no new laboratory data were available, and DIM supplementation was continued. A subsequent visit on January 30, 2023, reaffirmed the protocol without modification. On February 28, 2023, repeat laboratory testing demonstrated marked improvement, with PSA reduced to 2.4 ng/mL, total testosterone increased to 615 ng/dL, and free testosterone rising to 7.3 pg/mL. A further evaluation on April 10, 2023, confirmed stability, with PSA at 2.2 ng/mL, total testosterone 652 ng/dL, and free testosterone 6.5 pg/mL.

Over the four months following the initiation of DIM supplementation and discontinuation of cholesterol-lowering supplementation, PSA values decreased from 4.6 to 2.2 ng/mL, while both total and free testosterone improved. These findings demonstrate favorable changes in PSA and testosterone markers temporally associated with the intervention. While these biochemical improvements are clinically meaningful, no imaging or prostate examination was performed, and therefore, conclusions about prostate health outcomes cannot be made. Further investigation in controlled clinical trials is required to establish the reproducibility and clinical significance of these findings.

Table 1. Timeline and Diagnostics

Date	Encounter	Key Measurements			Protocol
		Type	Value	Unit	
2021-04-12	Lab	PSA	3.2	ng/mL	--
		LDL	114 (H)	mg/dL	
		Glucose	100 (H)	mg/dL	
2022-05-04	Lab	PSA	4.0	ng/mL	--
2022-11-22	Lab	PSA	4.2 (H)	ng/mL	--
		Free T	5.9	pg/mL	
		Total T	585	ng/mL	
2022-12-07	Lab and Visit	PSA	4.6 (H)	ng/mL	Recommended DIM-Evail™ at 100 mg per day Discontinuation of cholesterol-lowering supplement, CholestOff Complete®.
		Free T	3.5 (L)	pg/mL	
		Total T	436	ng/mL	
		LH	11.2 (H)	mIU/mL	
		FSH	19.8 (H)	mIU/ML	
		Estradiol	20	pg/mL	
2023-01-09	Follow-up visit	No new labs	--	--	DIM-Evail™ Continued
2023-01-30	Follow-up visit	No new labs	--	--	DIM-Evail™ Protocol reaffirmed
2023-02-28	Lab	PSA	2.4	ng/mL	DIM-Evail™ Continued
		PSA Free	0.39	ng/mL	
		% Free PSA	16.3	%	
		Total T	615	ng/dL	
		Free T	7.3	pg/mL	
2023-04-10	Lab	PSA	2.2	ng/mL	DIM-Evail™ Continued
		PSA Free	0.33	ng/mL	
		% Free PSA	15	%	
		Total T	652	ng/dL	
		Free T	6.5 (L)	pg/mL	

Abbreviations: antigen; T, testosterone; Free T, free testosterone; LH, luteinizing hormone; FSH, follicle-stimulating hormone; LDL, low-density lipoprotein; DIM-Evail™, diindolylmethane in oil-based softgel (Designs for Health); BID, twice daily; H, high relative to reference range.

By April 2023, following four months of DIM supplementation and discontinuation of CholestOff Complete® (Nature Made, USA), the patient demonstrated biochemical stabilization with PSA values declining from 4.6 to 2.2 ng/mL and testosterone measures improving from 436 to 652 ng/dL (total) and from 3.5 to 6.5–7.3 pg/mL (free). Clinically, he reported improved energy, libido, and overall well-being. DIM-Evail™ (Designs for Health, USA) was continued at 100 mg/day beyond this period, with a plan for ongoing monitoring every 3–6 months.

Since cholesterol remained a concern, and given his cardiovascular history, the patient was advised to continue follow-up with his cardiologist for lipid management. The nutrition clinician did not prescribe an alternative cholesterol-lowering therapy but emphasized coordination of care.

No adverse effects were reported from DIM supplementation. The patient remained on his prescribed medications, including finasteride and rosuvastatin, under the care of his medical specialists. At the time of last contact, no additional changes to the supplement protocol were recommended, and the plan was to reassess PSA, testosterone, and lipid markers at subsequent visits, while maintaining cardiology oversight for cardiovascular risk management.

DISCUSSION

DIM was introduced because it modulates estrogen metabolism by promoting beneficial 2-hydroxy-estrone metabolites over potentially proliferative 16-hydroxy-estrone and 4-hydroxy-estrone pathways.[5] The latter estrogen metabolites have been linked to hormone-sensitive conditions, including

prostate health concerns, breast cancer, and autoimmune diseases.[19] By influencing cytochrome P450 enzymes (CYP1A1 and CYP1B1), DIM helps shift estrogen metabolism toward a protective pathway, reducing the potential for estrogen-induced DNA damage and inflammation.[6,8]

Additionally, the bioavailability of DIM is a key factor in its clinical efficacy. DIM-Evail™ (Designs for Health, USA) is a product that, according to its manufacturer, Designs for Health, utilizes their proprietary Evail® technology to improve absorption and ensure greater systemic availability compared to standard DIM supplements. This technology reportedly incorporates quillaja extract, tocotrienols, and medium-chain triglycerides (MCTs) to achieve this enhanced absorption. While scientific literature consistently highlights the poor solubility and absorption of pure, crystalline DIM and the necessity of specialized formulations to achieve higher bioavailability,[8] and notes that DIM suspended in liquid oil can achieve high bioavailability,[8] the specific mechanisms by which quillaja extract and tocotrienols contribute to DIM absorption within this technology are not extensively detailed, beyond the manufacturer's description. This enhanced delivery system likely contributed to the patient's positive response, reinforcing the importance of formulation as a nutraceutical intervention. The intervention of 100 mg per day of DIM-Evail™ led to a significant reduction in PSA (from 4.6 to 2.2 ng/mL) and an increase in total testosterone (from 436 to 615 ng/dL) and free testosterone (from 3.5 to 7.3 pg/mL) at the free testosterone's highest point. This aligns with research suggesting that DIM supports a favorable testosterone-to-estrogen ratio by inhibiting aromatase, reducing testosterone conversion to estrogen, and enhancing the 2-hydroxy pathway without elevating the levels of harmful 4-hydroxy metabolites.[6,8]

These findings further support the role of hormonal modulation through targeted nutraceuticals in managing prostate health. Given the broader implications of estrogen metabolism in immune function and inflammatory conditions, DIM may also be relevant in other hormone-sensitive conditions beyond prostate health, including autoimmune diseases, estrogen dominance, and metabolic disorders.[9,15,16]

Patient Perspective

A fantastic success story for functional medicine! For years, I had been closely monitoring my PSA levels, which were steadily rising, leading my urologist to recommend a biopsy. I was hesitant about the procedure and sought alternative solutions. Danielle Arnold and Dr. Oscar Coetzee identified a key hormonal imbalance — low testosterone and high estrogen —possibly related to my cholesterol-lowering supplements. With their guidance, I discontinued CholestOff and introduced DIM. The results were remarkable — my PSA dropped from 4.6 to 2.4, and my testosterone increased significantly. This intervention not only spared me from an unnecessary biopsy but also improved my overall health and well-being. Thank you both!

CONCLUSION

This case highlights the potential role of diindolylmethane (DIM) in reducing prostate-specific antigen (PSA) levels via targeted modulation of estrogen metabolism and hormonal balance. By addressing low testosterone and elevated estrogen, DIM contributed to measurable improvements in both PSA and androgen profiles. These outcomes underscore the value of functional medicine strategies, especially those using bioavailable nutraceuticals like DIM, in optimizing men's health and potentially reducing reliance on invasive procedures. While this is a single case, the clinical response supports further investigation into DIM's broader applications in hormone-sensitive prostate conditions.

FUNDING

This research received no external funding.

REFERENCES

1. Catalona WJ, Partin AW, Slawin KM, et al. Use of the percentage of free prostate-specific antigen to enhance differentiation of prostate cancer from benign prostatic disease: a prospective multicenter clinical trial. *JAMA*. 1998;279(19):1542-1547. doi:10.1001/jama.279.19.1542
2. Flores JM, Bernie HL, Miranda E, et al. The relationship between PSA and total testosterone levels in men with prostate cancer. *J Sex Med*. 2022;19(3):471-478. doi:10.1016/j.jsxm.2022.01.003
3. Auborn KJ, Fan S, Rosen EM, et al. Indole-3-carbinol is a negative regulator of estrogen. *J Nutr*. 2003;133(7)(suppl):2470S-2475S. doi:10.1093/jn/133.7.2470S
4. Im A, Vogel VG, Ahrendt G, et al. Urinary estrogen metabolites in women at high risk for breast cancer. *Carcinogenesis*. 2009;30(9):1532-1535. doi:10.1093/carcin/bgp139
5. Othman ER, Markeb AA, Khashbah MY, et al. Markers of local and systemic estrogen metabolism in endometriosis. *Reprod Sci*. 2021;28(4):1001-1011. doi:10.1007/s43032-020-00383-4
6. Szaefer H, Licznerska B, Krajka-Kuźniak V, Bartoszek A, Baer-Dubowska W. Modulation of CYP1A1, CYP1A2 and CYP1B1 expression by cabbage juices and indoles in human breast cell lines. *Nutr Cancer*. 2012;64(6):879-888. doi:10.1080/01635581.2012.690928
7. Le HT, Schaldach CM, Firestone GL, Bjeldanes LF. Plant-derived 3,3'-Diindolylmethane is a strong androgen antagonist in human prostate cancer cells. *J Biol Chem*. 2003;278(23):21136-21145. doi:10.1074/jbc.M300588200
8. Thomson CA, Ho E, Strom MB. Chemopreventive properties of 3,3'-diindolylmethane in breast cancer: evidence from experimental and human studies. *Nutr Rev*. 2016;74(7):432-443. doi:10.1093/nutrit/nuw010
9. Cutolo M, Sulli A, Straub RH. Estrogen metabolism and autoimmunity. *Autoimmun Rev*. 2012;11(6-7):A460-A464. doi:10.1016/j.autrev.2011.11.014
10. Lane BR, Stephenson AJ, Magi-Galluzzi C, Lakin MM, Klein EA. Low testosterone and risk of biochemical recurrence and poorly differentiated prostate cancer at radical prostatectomy. *Urology*. 2008;72(6):1240-1245. doi:10.1016/j.urology.2008.06.001
11. Morgentaler A, Traish AM. Shifting the paradigm of testosterone and prostate cancer: the saturation model and the limits of androgen-dependent growth. *Eur Urol*. 2009;55(2):310-320. doi:10.1016/j.eururo.2008.09.024
12. Kalme T, Loukovaara M, Koistinen R, et al. Estradiol increases the production of sex hormone-binding globulin but not insulin-like growth factor binding protein-1 in cultured human hepatoma cells. *Fertil Steril*. 1999;72(2):325-329. doi:10.1016/S0015-0282(99)00229-0
13. Patel S, Homaei A, Raju AB, Meher BR. Estrogen: the necessary evil for human health, and ways to tame it. *Biomed Pharmacother*. 2018;102:403-411. doi:10.1016/j.biopha.2018.03.078
14. Kumar A, Banerjee A, Singh D, et al. Estradiol: a steroid with multiple facets. *Horm Metab Res*. 2018;50(5):359-374. doi:10.1055/s-0044-100920
15. Cutolo M, Villaggio B, Seriolo B, et al. Synovial fluid estrogens in rheumatoid arthritis. *Autoimmun Rev*. 2004;3(3):193-198. doi:10.1016/j.autrev.2003.08.003
16. Schmidt M, Hartung R, Capellino S, Cutolo M, Pfeifer-Leeg A, Straub RH. Estrone/17beta-estradiol conversion to, and tumor necrosis factor inhibition by, estrogen metabolites in synovial cells of patients with rheumatoid arthritis and patients with osteoarthritis. *Arthritis Rheum*. 2009;60(10):2913-2922. doi:10.1002/art.24859
17. Tucci P, Brown I, Bewick GS, Pertwee RG, Marini P. The Plant Derived 3-3'-Diindolylmethane (DIM) Behaves as CB_2 Receptor Agonist in Prostate Cancer Cellular Models. *Int J Mol Sci*. 2023;24(4):3620. doi:10.3390/ijms24043620
18. Le, Hien T et al. Plant-derived 3,3'-Diindolylmethane is a strong androgen antagonist in human prostate cancer cells. *J Biol Chem*. 2003;278(23):21136-21145. doi:10.1074/jbc.M300588200
19. Risbridger GP, Ellem SJ, McPherson SJ. Estrogen action on the prostate gland: a critical mix of endocrine and paracrine signaling. *J Mol Endocrinol*. 2007;39(3):183-188. doi:10.1677/JME-07-0053