

The Need for Sex Hormone Analysis in Addition to Long-Term Follow-Up of Phytosterol Supplementation

Heitor Oliveira Santos

Universidade Federal de Uberlândia, Uberlândia, MG - Brazil

Dear Editor,

I read with great interest the article entitled “Phytosterols in the Treatment of Hypercholesterolemia and Prevention of Cardiovascular Diseases”, by Cabral and Klein, published in the Brazilian Archives of Cardiology.¹ The authors discuss phytosterol doses in the treatment of hypercholesterolemia, showing the current consensus of renowned guidelines and approval by global regulatory agencies.

As already mentioned, the main phytosterol mechanism of action occurs through the reduction (30% to 50%) in the intestinal absorption of cholesterol.¹ The authors, however, make it clear that long-term follow-up is essential to assess the association of phytosterol supplementation with the risk of cardiovascular diseases. Additionally, I emphasize another

important investigation: analyses of serum sex hormones during randomized clinical trials based on phytosterol administration.

I recently showed that cholesterol intake may be related to increased total testosterone in men, whereas statin use may annul this potential.² Perhaps the use of phytosterols can also attenuate serum total testosterone levels in men (Figure 1).

In one test, the ingestion of 8.6 g/d of phytosterols reflected in the daily excretion of 28 mg cholesterol/g of fecal dry weight, resulting in an increase of 20 mg / g in comparison to the period prior to the test.³ These proportions reflect in the daily excretion of approximately 230 mg of fecal cholesterol without the ingestion of phytosterols and 810 mg with the ingestion of phytosterols, since the average daily fecal excretion in humans is 128 g of wet weight, which corresponds to 29 g of dry weight.⁴

I point out that daily intake of 500 to 1,000 mg of cholesterol may result in an approximate increase of 130 ng/dL of total testosterone in men. In rats, the ingestion of phytosterols for 22 days reduced serum testosterone by 33%, in comparison to controls.⁵ To the best of my knowledge, there are no studies that analyzed sex hormones in association with phytosterol administration in humans. Therefore, in addition to the aforementioned need to analyze the long-term administration of phytosterols, it is also important to consider sex hormone measurements in this context.

Keywords

Cardiovascular Diseases/prevention&control; Hypercholesterolemia; Phytosteroids; Steroids

Mailing Address: Heitor Oliveira Santos •

Av. Pará, 1720. CEP 38400-902, Umuarama, Uberlândia, MG – Brazil
E-mail: heitoroliveirasantos@gmail.com, heitor13cam@hotmail.com
Manuscript received January 07, 2018, revised manuscript May 23, 2018, accepted May 23, 2018

DOI: 10.5935/abc.20180132

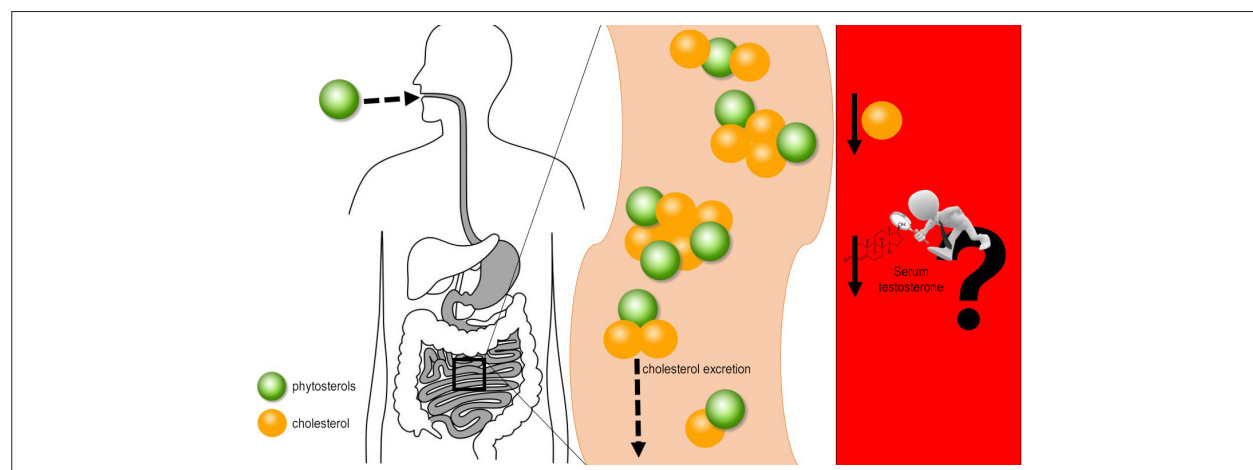


Figure 1 – Proposal to analyze serum testosterone levels during phytosterol supplementation. Phytosterols increase the excretion of cholesterol, resulting in serum cholesterol decrease. Since cholesterol is important for the synthesis of sex hormones, the decrease in serum testosterone combined with phytosterol supplementation is a hypothesis. Therefore, the testing of this concept is a useful and, at first, an innovative concept. Dotted arrows indicate the conduction of phytosterols; continuous arrows indicate decreased levels of serum cholesterol and testosterone.

References

1. Cabral CE, Klein MR. Phytosterols in the treatment of hypercholesterolemia and prevention of cardiovascular diseases. *Arq Bras Cardiol.* 2017;109(5):475-82.
2. Santos HO. Ketogenic diet and testosterone increase: Is the increased cholesterol intake responsible? To what extent and under what circumstances can there be benefits? *Hormones(Athens).* 2017;16(3):150-60.
3. Weststrate JA, Ayesha R, Bauer-Plank C, Drewitt PN. Safety evaluation of phytosterol esters. Part 4. Faecal concentrations of bile acids and neutral sterols in healthy, normallipidaemic volunteers consuming a controlled diet either with or without a phytosterol ester-enriched margarine. *Food Chem Toxicol.* 1999;37(11):1063-71.
4. Rose C, Parker A, Jefferson B, Cartmell E. The Characterization of feces and urine: A review of the Literature to Inform Advanced Treatment Technology. *Crit Rev Environ Sci Technol.* 2015;45(17):1827-79.
5. Awada AB, Hartatia MS, Finka CS. Phytosterol feeding induces alteration in testosterone metabolism in rat tissues. *J Nutr Biochem.* 1998;9(17):712-7.

Reply

We thank you for your interest and comments related to our recent review article entitled "Phytosterols in the Treatment of Hypercholesterolemia and Prevention of Cardiovascular Diseases,"¹ which aimed specifically to address the available evidence in the literature on the association between phytosterols and risk of cardiovascular diseases.

We agree that it is important to investigate the effects of phytosterols on serum levels of sex hormones, especially due to the potential risk of reducing plasma testosterone levels.

We are not aware of studies carried out in humans that have performed such an evaluation. Experimental animal studies are scarce, and a reduction in plasma testosterone levels has been observed in some,^{2,3} but not all of them.⁴

Sincerely,

Carlos Eduardo Cabral
Márcia Regina Simas Torres Klein

References

1. Cabral CE, Klein MR. Phytosterols in the Treatment of Hypercholesterolemia and Prevention of Cardiovascular Diseases. *Arq Bras Cardiol.* 2017;109(5):475-482.
2. Qasimi MI, Nagaoka K, Watanabe G. The effects of phytosterols on the sexual behavior and reproductive function in the Japanese quail (*Coturnix coturnix japonica*). *Poult Sci.* 2017;96(9):3436-44.
3. Awad AB, SriHartati M, Fink CS. Phytosterol feeding induces alteration in testosterone metabolism in rat tissues. *J Nutr Biochem.* 1998; 9(12):712-7
4. Ryökkynen A, Käyhkö UR, Mustonen AM, Kukkonen JV, Nieminen P. Multigenerational exposure to phytosterols in the mouse. *Reprod Toxicol.* 2005; 19(4): 535-40.

