

# The Role of Nutraceuticals in Male Fertility

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## KEYWORDS

• Nutraceutical • Antioxidant • Supplement • Diet • Male infertility

## KEY POINTS

- Nutraceuticals have become exceedingly popular for the treatment of male infertility as a result of widespread availability.
- Most nutraceuticals have antioxidant properties that may effect sperm production and function.
- The data present in the available English literature are mixed on the effects of nutraceuticals on male fertility because of the lack of standard dosing or control for dietary intake from various sources.
- Support is lacking for supplementation exceeding that obtained through a well-balanced diet.

## INTRODUCTION

Medically therapeutic nutraceuticals have become more popular as a result of public awareness and increasing interest by the scientific community and consumers. In addition, nutraceuticals have become an important part of replacing nutritional deficiencies caused by the consumption of over-processed junk foods that may make up a prevalent part of the Western diet.<sup>1</sup>

Different nutraceuticals, including herbs, fruits, vegetables, nutritional supplements, and vitamins, have been promoted to improve many aspects of male fertility.<sup>2</sup> These include sperm function and semen analysis parameters, erectile function, and libido.

Infertility affects 15% of couples and a male factor is found to be solely responsible or in conjunction with a female factor in 50% of cases.<sup>3,4</sup> These therapies are thus popular among infertile couples seeking alternatives to traditional assisted reproductive technologies (ART) because of their widespread availability, relatively harmless side effect profile, and comparatively low cost.

The purpose of this article is to review nutraceuticals and their effects on male fertility. The discussion begins with a review of the effect of oxidative stress on sperm production and function because the common pathway for most nutraceuticals relies on the antioxidant properties of these therapies. Understanding the effect of oxidative stress on sperm is an important part of reviewing the effects of nutraceuticals on male infertility.<sup>5</sup>

## OXIDATIVE STRESS

Oxidative stress in the testes or semen can be attributed to infection, inflammation, trauma, tobacco exposure, industrial exposure, strenuous exercise, chemotherapy, and exogenous (ie, hot tub, sauna, lap top, and so forth) or endogenous (ie, cryptorchidism, varicocele, febrile illness, and so forth) heat exposure.<sup>6</sup> Leukocytes and underdeveloped spermatozoa are the primary producers of endogenous oxidants in the semen, with immature and teratozoospermic forms producing more reactive oxygen species (ROS) compared with mature and morphologically normal spermatozoa.<sup>7</sup>

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Nothing to disclose.

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Urol Clin N Am 41 (2014) 181–193

<http://dx.doi.org/10.1016/j.ucl.2013.08.003>

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Physiologic ROS are also produced in response to chemical and bacterial stimuli.<sup>8</sup>

Some detrimental effects of ROS include free radical attack and lipid peroxidation on the unsaturated fatty acids of the sperm plasma membrane resulting in decreased sperm membrane integrity, sperm DNA damage,<sup>9</sup> decreased intrinsic ability to repair sperm DNA damage,<sup>10</sup> and decreased sperm motility.<sup>11</sup> Despite the negative effects of excessive oxidative stress, physiologic ROS is essential for certain sperm functions including capacitation and signal transduction events.<sup>12</sup>

## ANTIOXIDANTS

Antioxidants function as ROS scavengers to protect against oxidative stress and damage.<sup>13</sup> Physiologic antioxidants are produced intrinsically for normal physiologic functions and in response to chemical and bacterial stimuli<sup>8</sup> and are present in seminal plasma and spermatozoa.<sup>14</sup> The body is able to buffer ROS by using physiologic free radical scavengers.<sup>15</sup> Injury occurs when this fine balance is disrupted by an increased production or decreased clearance of ROS.

Physiologic antioxidants are enzymatic and nonenzymatic. Enzymatic physiologic antioxidants include catalase, superoxide dismutase, and glutathione peroxidase. Nonenzymatic physiologic antioxidants include carnitine, carotenoids, glutathione, hypotaurine, taurine, and vitamins C and E.<sup>16</sup>

Antioxidants are obtained through dietary intake including herbs, fruits, vegetables, nuts, legumes, dairy, and meat products. They can also be obtained through oral supplements including vitamins and minerals. Increased intake of dietary antioxidants from any source can potentially improve semen quality and intrinsic sperm properties.<sup>17</sup> In contrast, lower dietary intake may result in poor semen quality as a result of lower total body concentration of antioxidants.<sup>18</sup>

## DEFINITION OF NUTRACEUTICALS

Nutraceuticals are foods or food ingredients “that provides medical or health benefits, including the prevention and/or treatment of a disease.”<sup>19</sup> The medicinal benefits of plants have been known through many millennia in many historical civilizations. Hippocrates (460–377 BC) stated “let food be thy medicine and medicine be thy food” referring to the use of plants and their byproducts for prevention and treatment of diseases.<sup>20</sup>

Nutraceutical is a combination of the words nutrition and pharmaceutical coined by Stephen DeFelice, MD in 1989.<sup>21</sup> It is an inclusive term

that describes products derived from food that can provide extra health benefits beyond the basic nutritional value found in foods.<sup>1</sup> Used in its purest form, nutraceuticals bridge the world between food and pharmaceuticals. The term nutraceutical is therefore used as an all-encompassing term including plant-based foods and byproducts, supplements, minerals, and vitamins. Our discussion of nutraceuticals focuses on the common foods that contain the antioxidants that have an effect on fertility and their side effects with excess consumption (**Table 1**). Commercially available extracts of these antioxidants are not discussed, although they can be taken to supplement dietary shortages if needed.

## REVIEW OF NUTRACEUTICALS

### *Arginine*

Arginine is a precursor of nitric oxide and plays a role in augmenting the cellular inflammatory response by providing protection against oxidative damage.<sup>22</sup> Arginine is essential for sperm motility, metabolism, capacitation, acrosome reaction, and is a precursor for producing putrescine, spermine, and spermidine.<sup>23,24</sup>

Reports on the effect of arginine on semen parameters have been varied in the literature. Studies have reported daily arginine supplementation improves sperm concentration and motility.<sup>25–29</sup> Conversely, other studies have failed to demonstrate any improvement in sperm counts or pregnancy rates.<sup>30,31</sup> Other studies have demonstrated that excessive arginine concentrations can result in impaired sperm function.<sup>24</sup>

Arginine occurs naturally in many plant-based dietary sources including barley, brown rice, buckwheat, cereal, chocolate, coconut, dairy, nuts, and seeds. It can also be found in various meat products. The recommended daily allowance (RDA) is 20 g, with an upper limit of 30 g.<sup>32</sup> Potential side effects of excess consumption include increased bleeding risk, electrolyte abnormalities, gastrointestinal (GI) distress, increased glucose levels, hypotension, renal insufficiency, worsening symptoms of sickle cell disease, and asthma.<sup>22</sup>

### *Carnitines*

Carnitines are synthesized from the amino acids lysine and methionine. They are responsible for regulating intracellular metabolism through  $\beta$ -oxidation and buffer the acetyl-coenzyme A (CoA) to CoA ratio by transporting long-chain fatty acids into the mitochondria. Carnitines provide energy for spermatozoa and affect sperm motility and maturation.<sup>33</sup> They also function as antioxidants providing protection against ROS.<sup>34</sup>

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