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Review article

Testicular Oxidative Stress and Antioxidant Therapies in Male Infertility: An Evidence-Based Review

Bharath S, Vickram A S, Prasanth C, Jenila Rani D, Bhavani Sowndharya B

Department of Biotechnology, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences, Chennai, 602105, India.

Corresponding to:
Dr. Vickram A S.
Department of Biotechnology, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences, Chennai, 602105, India.

Email: vickramas.16@gmail.com

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Abstract:

Male infertility accounts for almost half of infertility cases among couples globally. One of the primary reasons for decreased male reproductive function is oxidative stress (OS), which occurs when the body's antioxidant Defense systems are overwhelmed by the synthesis of reactive oxygen species (ROS). An excess of ROS can harm sperm quality and reproductive capacity by causing lipid peroxidation, mitochondrial malfunction, and sperm DNA breakage, even while healthy ROS levels define optimal sperm activity. Testicular tissue is particularly vulnerable to oxidative damage due to its high metabolism and the high quantity of polyunsaturated lipids in sperm membranes. Numerous internal and external variables, including varicocele, infections, environmental contaminants, aging, and bad lifestyle choices, can accelerate the generation of ROS and overwhelm the testicular antioxidant system. The pathophysiological implications of testicles' oxidative stress on male fertility are addressed in this review, which also critically explores the fundamental sources and mechanisms of this stress. The laboratory procedures and diagnostic indications are now being applied to detect oxidative stress in the sperm. The focus is on antioxidant-based treatment options, which include both new and possibly helpful chemicals as well as established supplements like vitamins C and E, Coenzyme Q 10, carnitines, and N-acetylcysteine. This review supports a personalized strategy to antioxidant therapy as a viable adjuvant in the treatment of male infertility and underlines the importance of large-scale, properly planned trials.

Keywords: Reactive Oxygen Species, Personalized medicine, oxidative damage, sperm damage, assisted reproductive technology

Introduction

Infertility is among the most complicated disorders compromising the reproductive system. Its defining trait is not being able to conceive following a year or more of regular, unprotected sexual activity.[1] Though figures vary widely between countries and regions, infertility is thought to afflict 8–12% of couples of reproductive ages globally.[2] Male infertility is usually estimated to be the sole cause of about 20% of cases of infertility; another 30% to 40% are regarded as partially responsible.[3] Despite great progress in diagnosis and treatment, about half of all cases of male infertility remain idiopathic—that is, without a known etiological component. The overall rise in male infertility rates in recent years has aroused considerable alarm due to a global deterioration in semen quality over time and a corresponding rise in the frequency of male reproductive problems. Numerous environmental, nutritional, social, and economic factors have been hypothesized as contributing to the falling trend in semen quality, although the specific explanation of the increased prevalence of male infertility is nevertheless unknown. Additionally, in males with reproductive possibilities, frequent problems such as insulin resistance, arterial hypertension, obesity, dyslipidaemia, psychological stress, and anxiety disorders have also been connected to decreased fertility.[4] Male infertility and these complications seem to have a complex and poorly understood association. Nonetheless, studies have shown that oxidative damage is one of the essential processes behind the etiopathogenesis of several diseases. At the same time, a lot of focus has been devoted to the critical part that reactive oxygen species (OS) play in the establishment of male unsuccessful reproduction.[5]

The basic concept of oxidative stress is an imbalance between the body's ability to eliminate free radicals, also known as reactive oxygen species (ROS), and the creation of these harmful molecules. At normal physiological levels, ROS are important to manage a range of reproduction-related activities, including as fertilization, acrosome response, and sperm maturation and hyperactivation.[6,7] However, high ROS concentrations damage several cellular activities. Antioxidants and specific dietary components may be key in controlling spermatogenesis by reducing the ROS concentration in spermatozoa and semen plasma and restoring normal physiological levels.[8] Therefore, the objectives of this review are to: provide an overview of the primary causes of ROS in male infertility; update knowledge regarding the impact of elevated ROS levels and oxidative stress on the clinical outcomes of Assisted Reproductive Technology (ART), including In Vitro Fertilization (IVF)and intracytoplasmic sperm injection (ICSI); discuss in detail the role of antioxidants alone and in combination with other antioxidants; and explain why diet may be a more practical long-term solution for reducing oxidative stress and, consequently, sperm quality and fertility outcomes.

Testicular Oxidative Stress: Mechanisms and Pathophysiology

It is clear that 30–80% of infertile male cases have elevated levels of ROS in their ejaculate, the etiopathogenesis of male infertility is unknown in about half of the cases.

Endogenous ROS in human semen are mostly derived from leukocytes in the seminal fluid and undeveloped sperm with cytoplasmic retention and a morphologically defective head.[9,10] In addition to leukocyte activation and chemotaxis, inducing further inflammatory processes, male genital tract infections generate extrinsic ROS. Leukocytes initiate the myeloperoxidase system, which creates ROS, to combat infections.[11] OS in the seminal fluid may come from leukocytes creating too much ROS. Conversely, intrinsic ROS are created by defective and immature spermatozoa. Cytoplasm accumulates in the mid-piece during the typical spermiogenesis phase, causing cell expansion and condensation. The cytosolic glucose-6-phosphate dehydrogenase (G6PD) enzyme, which produces intracellular nicotinamide adenine dinucleotide phosphate (NADPH), is abundant in the excess residual body that immature spermatozoa with morphological defects (NADPH) retain.[12] The intramembrane oxidase enzyme nicotinamide adenine dinucleotide phosphate (NADPH) oxidase 5 (nox5) then transforms NADPH into ROS. When highly reactive ROS transgress antioxidant defence mechanisms, a change in the homeostatic balance between ROS and antioxidant defence systems may result in the development of OS, LPO (Lipid Peroxidation), sperm DNA fragmentation (SDF), and germ cell death are among the adverse effects on sperm that have been reported. Table 1 shows testicular oxidation stress and clinical consequences in male infertility.

Table 1. Testicular oxidation stress and clinical consequences

Si. No	Component	Mechanism	Effects on the Testis	Clinical Results	Reference
1.	Reactive oxygen species	Generated by leukocytes, mitochondria, and toxins	Damage caused by oxidation to sperm cells.	decreased sperm count and motility.	13
2.	Peroxidation of Lipids	ROS attacking on sperm membrane lipids	Loss of integrity in membranes	Impaired fertilization capacity	14
3.	Protein Oxidation	Protein oxidative modification in sperm	Defective receptors and enzymes	Ineffective sperm function	15
4.	DNA Breakdown	ROS cause sperm DNA strands to break.	instability of the genome	Embryo development failure	16
5.	Antioxidant Enzymes Deficit	reduced Superoxide Dismutase (SOD), Catalase (CAT), and Glutathione Peroxidase (GPx) activity	Insufficient neutralization of ROS	An increase in oxidative stress	17
6.	Apoptosis	ROS starts the cell death mitochondrial pathway	Germ cell loss	Degeneration of the testicles	18
7.	Hormonal Interruptions	Leydig and Sertoli cells are oxidatively damaged.	Change in the levels of inhibin and testosterone.	Reduced sperm production	19
8.	Inflammatory processes	NF-κB (Nuclear Factor kappa-light-chain-enhancer of activated B cells) and cytokine activation	Prolonged inflammation of the testicles	Subfertility and pain in the testicles	20
9.	Varicocele	ROS are created by venous stasis and hypoxia.	Testicular hypoperfusion	Infertility in men with varicocele	21
10.	Exposures to the Environment	ROS production is boosted by pesticides and heavy metals	Direct injury to testicular tissue caused by toxins.	Poor ART results and repeated failure	22

Generation of Reactive Oxygen Species (ROS)

Reactive oxygen species can cause inflammation by activating many signalling pathways, much like the response of inflammation can cause. According to a number of studies, hydroperoxyl radical and ROS can promote inflammation by stimulating the transcription factor NF-kB.(23) Additionally, it has been discovered that OS is essential for the activation of the NOD-like receptor protein 3 (NLRP3) inflammasome.(24) The NLRP3 inflammatory oligomeric molecular complex triggers innate immune responses by producing pro-inflammatory cytokines that involve interleukins IL-1β and IL-18. In a study conducted in 2022, a number of pathways for ROS-mediated NLRP3, have been found. It has been shown that ROS created by damaged mitochondria activate NLRP3 inflammatory cells, which in turn causes the generation of IL1 and the development of localized inflammation.(25) It has also been established that NLRP3 inflammasomes are induced during apoptosis in response to the oxidation of mitochondrial DNA. Additionally, when OS is generated, ROS triggers the thioredoxin-interacting protein, which initially suppresses endogenous thioredoxin. This enables the protein to separate from thioredoxin and attach to the NLRP3 inflammasome, thereby inducing its activation.(26)

Impact of ROS on Spermatogenesis and Sperm Function

ROS-mediated harm to both the functional and structural integrity of SPZ (spermatozoa), that renders them especially vulnerable to oxidative assaults among germ cells, is one of the primary causes of male infertility. Damaged or insufficient SPZ has a detrimental effect on the result of a pregnancy and the health pathways of the progeny.(27) It is generally documented that spermatids drastically alter the way their DNA folds during spermiogenesis, replacing transition proteins for histones first, followed by protamines. Instead of dislodging histones, transition proteins enhance the recruitment and processing of protamines, which in turn cause histone eviction. This shows that protamines and transition proteins act together rather than as a result of one another.(28) Interestingly, telomeres and promoters of genes critical in early embryonic development are found in the small fraction (~5–10%) of DNA that is still ordered in nucleosomes by residual histones, even though the majority of the sperm genome is linked to protamines.(29) Oxidative stress is extremely hazardous for this chromosomal compartment. Furthermore, the sperm nucleus in mice has a regionalized sensitivity to oxidative DNA alterations, with the basal and peripheral nuclear regions—the latter of which is positioned around the midpiece—being more vulnerable.(30) Given the concept of chromosomal territories and the non-random insertion of chromosomes into the sperm nucleus, it makes sense that certain autosomes, notably chromosomal references (Chr19, Chr18, and Chr17), would be particularly prone to oxidative damage.(31) Sex chromosomes, on the other hand, seem to be especially well-protected. Fig 1 demonstrates how oxidative stress kicks off a cascade of biochemical events that include mitochondrial failure, DNA damage, and lipid peroxidation. These alterations affect sperm motility, viability, and ultimately fertilization capacity by triggering the apoptotic pathway.

Table 2. Male infertility etiological causes for testicular oxidative stress.

SI. No	Reasons	Description	Mechanism	Effect on the Testis	Reference
1.	Varicocele	Unusual testicular vein dilatation	Heat stress and hypoxia elevate ROS.	Germ cell apoptosis, decreased sperm quality	34
2.	Infections	Sexually Transmitted Infections and bacterial or viral orchitis	Cytokine and immune cell activation	Inflammation, ROS burst, DNA damage	35
3.	Toxins in the environment	Endocrine disruptors, insecticides, and heavy metals (lead, cadmium)	Hormonal disturbance and direct ROS generation	Testicular atrophy, poor spermatogenesis	36
4.	Smoking	Cadmium, nicotine, and oxidants are all present in tobacco.	Boosts both local and systemic ROS	Decreased sperm motility and count.	37
5.	Drinking alcohol	Chronic use compromises endocrine and hepatic function.	Reduces testosterone and generates ROS	Spermatogenic arrest, sperm DNA fragmentation	38
6.	Obesity	Too much adipose tissue alters hormones and metabolism.	Elevates oxidative load and pro-inflammatory cytokines	Hormonal imbalance, oxidative sperm damage	39
7.	Diabetes mellitus	Insulin resistance and chronic hyperglycemia	Produce more AGEs (Advanced Glycation End-products) in the context of ROS (Reactive Oxygen Species) in the mitochondria to produce more AGE and ROS.	Leydig/Sertoli cell dysfunction	40
8.	Radiation exposure	Ionizing radiation from medicine or the workplace	DNA strand breakage and direct ROS production	Loss of germ cells, testicular fibrosis	41
9.	Exposure to heat	Extended scrotal warmth (from laptops or tight clothing)	Uses oxidative stress to disrupt with spermatogenesis	Reduced sperm production and function	42
10.	Aging	Testicular function naturally falls.	Decreases in antioxidant enzymes and mitochondrial dysfunction	Increased DNA fragmentation, lower sperm quality	43

Etiological Factors Contributing To Testicular Oxidative Stress

Male infertility has a complex etiopathology that encompasses several interrelated causes. The male reproductive system may be impacted by environmental and lifestyle variables, nutrition, radiation exposure, and several other factors. It is clear that the majority of these factors cause oxidative stress (OS), which in turn leads to male infertility.[32] Oxidative stress (OS) in the male reproductive tract occurs when the production of reactive oxygen species (ROS) exceeds the body's antioxidant defence capacity, due to either internal (endogenous) factors or external (environmental or lifestyle-related) influences. Through lipid peroxidation, deoxyribonucleic acid fragmentation, and germ cell apoptosis, OS causes altered sperm shape and functionality.[33] These changes are reflected in poor semen parameters and fertilizing capacity, leading to male subfertility or infertility. This review discusses the generation of reactive oxygen species (ROS) in the male reproductive system, their involvement in the pathophysiology of male infertility, the impact of oxidative stress (OS) on reproductive function, current methods for measuring ROS levels, and the therapeutic potential of antioxidant treatments for OS-induced male infertility Table 2 highlights male infertility etiological causes for testicular oxidative stress.

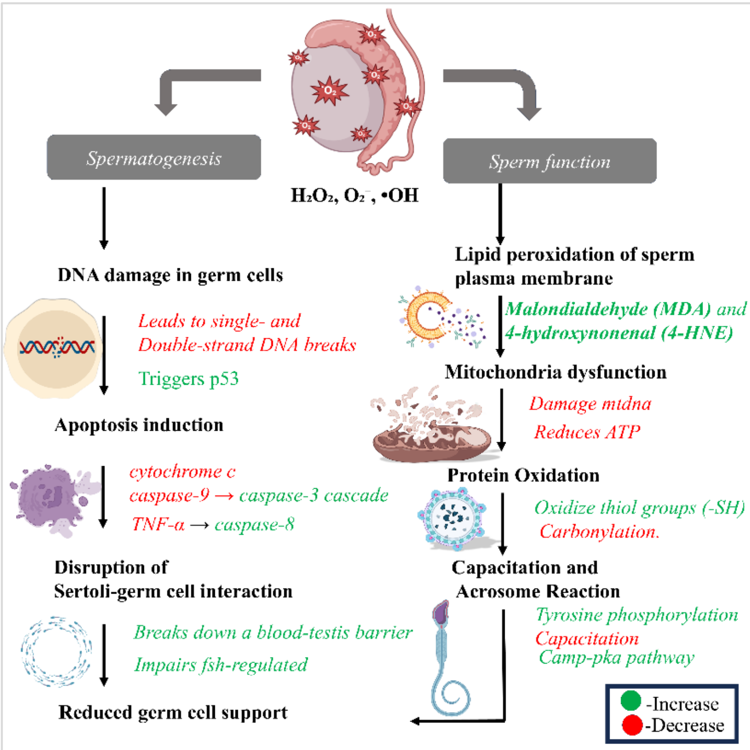

Figure 1: Oxidative stress's effect on DNA integrity and sperm function

Lifestyle Risk Factors: Smoking Cigarettes, Alcohol Consumption, and Obesity.

Lifestyle factors like smoking, alcohol consumption, and obesity have a significant impact on male fertility. Smoking-related toxins damage sperm DNA and cause oxidative stress. Because it disrupts hormonal balance and encourages the production of ROS, alcohol has an impact on sperm quality.[44] Because obesity alters endocrine function and causes inflammation, it has an impact on ART success rates. Abnormalities in the nuclear and plasma membranes of sperm cells are exacerbated by alcohol consumption.[45] Alcohol consumption raises the proportion of sperm cells with aberrant chromatin, according to an experimental study. NADH (Nicotinamide Adenine Dinucleotide, reduced form) and acetaldehyde are produced during metabolism. While NADH raises the respiratory chain activity in mitochondria, acetaldehyde interacts with proteins and lipids to produce ROS.[46] Both the number and motility of healthy sperm can be reduced by cigarette smoking. Additionally, it may cause lipid peroxidation, which results in the production of reactive oxygen species. Additionally, it can raise the amount of ROS and decrease the amount of antioxidants like vitamin C and E in seminal plasma. Cigarette smoking can also cause an inflammatory response and increase the quantity of leukocytes in the testicles.[47] The other issues found in smokers are linked to sperm count decrease, DNA fragmentation, and axonemal damage. Obese men's low semen quality is caused by aberrant hormone control and excessive ROS generation. It is thought that adipocytokine dysregulation and ROS production cause oxidative stress in these patients.[48] Excess ROS generation in obese males may be caused by elevated metabolic rates and blood coagulation. Furthermore, an increase in temperature and the production of ROS can change the enzymes involved in spermatogenesis in the testicles. decrease in sperm concentration to raise the scrotal skin's temperature. Pollutants in the environment could be one of the main causes of ROS production. It has been demonstrated that lead and NO diminish seminal quality, and that motor vehicles that generate NO (nitric oxide) have a detrimental effect on male fertility.[49] It has been discovered that lead (Pb) affects sperm viability, count, and normal morphology. Additionally, it has been demonstrated that butylbenzyl phthalate damages testicles and reduces serum testosterone levels. Electromagnetic radiation from cell phones damages sperm due to ROS formation. When the semen samples were exposed to radiofrequency electromagnetic waves, the ROS–TAC (Total Antioxidant Capacity) score decreased, ROS levels rose, and sperm motility and viability significantly decreased.[50] Figure 2 highlights environmental and physiological factors affecting infertility

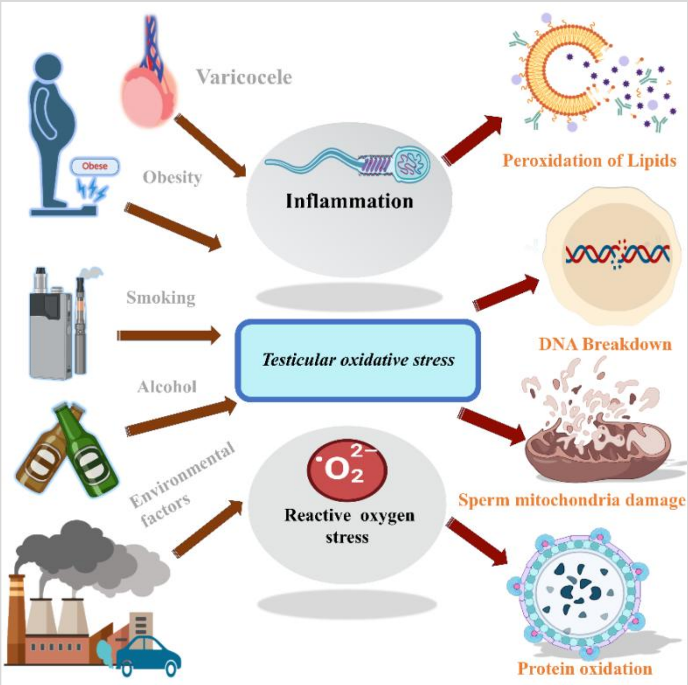

Figure 2: Environmental and physiological factors affecting male infertility

Antioxidant Therapies In Male Infertility: Evidence-Based Review

Oxidative stress can be exacerbated by a variety of environmental and internal conditions that impact antioxidant defense.[51] Despite the fact that antioxidant molecules are essential for maintaining the testicles during spermatogenesis. Under normal conditions, the male reproductive system's ROS generation and antioxidant activity are in balance. However, excessive ROS formation in semen can lead to oxidative stress and interfere with the antioxidant defence systems of sperm or seminal plasma.[52] The body has developed an antioxidant defence system that scavenges and restricts the production of oxygen-derived radicals in order to prevent oxidative damage.[53] Despite ROS's physiological and pathological effects, the human body has a defence mechanism against them to keep this level within a safe range. Actually, antioxidant activity kicks in to reduce ROS oxidative damage when the level of free radicals grows abnormally.[54]

Spermatozoa are safeguarded from oxidative damage by the endogenous antioxidants in seminal plasma.[55] These antioxidants can be classed as either enzymatic or non-enzymatic, and both are found in the male reproductive system. Superoxide dismutase, catalase, and peroxidase are enzyme antioxidants that catalytically remove reactive oxygen species from biological systems.[56] This enzymatic antioxidant is predominantly processed by sperm itself. Fig 3 shows the important activities of selenium and Sertoli cells in enhancing spermatogenesis using the antioxidant qualities of selenium and the nutritional aid supplied by Sertoli cells improves sperm maturation and capacitation, assuring reproductive competence.

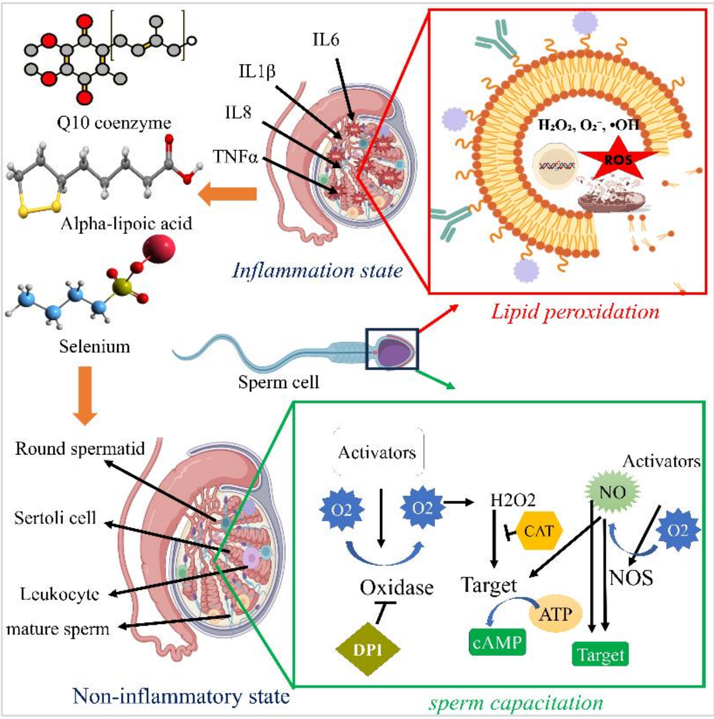

Figure 3: The interaction between selenium and Sertoli cells in sperm maturation

The total seminal antioxidant activity is also influenced by the non-enzymatic antioxidants found in semen.[57] Semen often contains non-enzymatic antioxidants such as beta carotene, carotenoids, flavonoids, vitamin C and E, and metal-binding proteins such as albumin, ferritin, and myoglobin. Through deactivating pro-oxidant transitional metal ions, these proteins function as antioxidants. Using non-enzymatic scavengers found in semen, seminal plasma's main antioxidant role is to shield spermatozoa against ROS produced by underdeveloped sperm cells and leukocytes.[58] However, there are very few antioxidant enzymes in spermatozoa. Moreover, peroxidation of lipids in the acrosome and tails membrane cannot be stopped by sperm antioxidant enzymes. In other words, the sperm cells need an extra layer of antioxidant defence.

Antioxidant therapy is generally accepted to increase male fertility and sperm quality. As an antioxidant, vitamin C reduces oxidative stress and improves sperm quality, according to numerous studies.[59] It is known that adding vitamins C and E to the sperm of guys who are normozoospermic and asthenozoospermic reduces the amount of DNA damage caused by ROS.[60] For asthenozoospermic patients, a 6-month course of vitamin E treatment can decrease lipid peroxidation in spermatozoa and increase the chance of pregnancy.[61] Additionally, supplying antioxidant E and selenium at the same time increases the motility of sperm in infertile males. Zinc, vitamin C, and vitamin E have also been shown to reduce sperm DNA fragment index, oxidant stress, and apoptosis in patients with asthenozoospermia.[62] Several studies have indicated that carnitine intake enhances the motility and the sperm count of oligospermic and asthenozoospermic patients.[63,64] Zinc and folic acid, separately or in combination, boost the amount of sperm in infertile men but not in fertile ones.

Micronutrient-Based Mitochondrial Antioxidants in Oxidative Stress-Driven Infertility

In a triple-blind, placebo-controlled, randomized clinical trial, alpha-lipoic acid (ALA) was tested for its effect on male infertility. The treated group showed significant improvements in sperm concentration, total sperm count, and overall sperm motility after approximately three months of treatment. Alpha-lipoic acid (ALA), a naturally occurring antioxidant that plays a vital role in mitochondrial energy metabolism and free radical scavenging, is transformed inside cells and tissues into dihydrolipoic acid (DHLA), which has even stronger antioxidant activity. Inside cells and tissues, alpha-lipoic acid (ALA) is converted to dihydrolipoic acid (DHLA), which has even greater antioxidant activity. Both ALA and DHLA can bind to metals, which blocks metals from causing oxidative damage and keeps proteins from losing their structure and function. Within cells and tissues, alpha-lipoic acid (ALA) is reduced to dihydrolipoic acid (DHLA), which possesses potent antioxidant properties. Both ALA and DHLA act as metal chelators, neutralizing reactive oxygen species (ROS) and transition metals, thereby preventing protein degradation and lipid peroxidation by enzymes. This study assessed the fraction of DNA fragmentation related with intracellular oxidative stress (OS) in sperm samples from infertile individuals .[67] In vitro synthesis of ALA considerably lowered both the levels of oxidative stress indicators and sperm DNA fragmentation.. Most likely, this was achieved via lowering ROS production. ALA may protect against ROS damage and improve semen properties like spermatozoa count, motility, and morphology.[68]

For males undergoing varicocelectomy for varicocele-induced infertility (varicocele has been associated to the formation of sperm OS), an 80-day triple-blind randomized control experiment was performed to assess the advantages of ALA versus placebo treatment.[69] ALA therapy produced higher-quality sperm at the end of the study than the control when varicocele was surgically repaired.[70]

Furthermore, as a cryoprotective agent, ALA was assessed during the freezing-thawing phase of assisted reproductive technology (ART). Numerous changes that sperm may undergo during cryopreservation could result in cryodamage and incremental OS. This is demonstrated by increased sperm viability and motility, less DNA damage, and consequently less apoptosis.[71]

Coenzyme Q10 (CoQ10) is a crucial component for energy production and possesses strong antioxidant properties. It is a part of the respiratory system in the mitochondrial system that controls ROS generation, protecting the cell membranes from lipid peroxidation-induced damage.[72]

For efficient movement, sperm cells need a high energy viability, which mitochondria supply through oxidative phosphorylation. Free radicals produced during the mitochondria's electron transport chain are neutralized by CoQ10. Infertile men have low quantities of CoQ10. Impaired sperm features, notably motility, have been associated to reduced seminal plasma levels of CoQ10.[73] Consequently, studies demonstrated that CoQ10 enhances sperm motility and count in infertile men.[74] A randomized clinical trial was done to determine how CoQ10 supplementation affects seminal parameters in males with oligoasthenoteratozoospermia (OAT) . They discovered that most OAT men have more OS in their semen, which changes semen parameters and causes sperm functions to fail. Additionally, breakthrough plasma analysis confirmed the previously found substantial direct correlation between CoQ10 concentrations and sperm motility and shape.[75] CoQ10 supplements for at least three months enhanced antioxidant enzyme activity and reduced OS in seminal plasma. Overall motility, progressive motility, and sperm concentration were all significantly increased after 3 months of CoQ10 supplementation administration.[76] The seminal level of CoQ10 was linked to several of the most important characteristics of semen, such as sperm level, motility, and morphology, by increasing the overall antioxidant capacity. CoQ10 is one of the most promising compounds for the treatment of idiopathic male infertility.

Selenium (Se) is a constituent of many proteins called selenoproteins, which are involved in a number of metabolic processes related to antioxidant defence, redox state management, and cancer prevention.[77] Se is a cofactor of antioxidative enzymes that neutralize and inhibit the generation of ROS during proper spermatogenesis, mitochondrial function, and capacitation.[78] Glutathione peroxidase is one of the selenoproteins (SePP) that are required for various redox processes in male reproduction. It is integrated into the mitochondrial membrane of spermatozoa, which balances the formation of ROS during the motility phase.[79] Furthermore, normal spermatogenesis is dependent on SePP. The testis and seminal fluid contain substantial amounts of SePP, which is critical for preserving sperm during storage, genital tract passage, and modifications leading up to sperm–oocyte interaction.[80] It is true that sperm density and the in proportion of vital sperm are positively related to seminal plasma SePP concentration. The effects of daily supplemental selenium intake on the quantity, concentration, shape, and motility of sperm as well as the overall quality of semen. Table 3 contains the mechanisms, dosage recommendations, and clinical outcomes of antioxidant therapy for male infertility.

Table 3. The mechanisms, dosage recommendations, and clinical outcomes of antioxidant therapy

Si. No	Supplements	Dose & Duration	Action Mechanism	Male Fertility Role	Reference
1.	L-acetyl carnitine and L-carnitine	2 g + 1 g daily for 3–6 months:	Enhances mitochondrial energy generation, reduces ROS	increases the number and motility of sperm	81
2.	Ascorbic acid	500 mg per day for three months	destroys free radicals and restores vitamin E.	avoids oxidative damage to sperm DNA	82
3.	Alpha-tocopherol or tocopherol	600 mg daily for three to twelve months	Lipid-soluble antioxidant that safeguards the lipids in sperm membranes	enhances the membrane integrity and motility of sperm	83
4.	Q10 Coenzyme (CoQ10)	200–400 mg every day for three months,	increases the synthesis of ATP in the mitochondria and has an antioxidant action.	enhances the density and motility of sperm.	84
5.	L-arginine and arginine	500 mg per day for three months	Nitric oxide precursor that improves blood flow and antioxidant	increases erectile function and sperm motility.	85
6.	Cysteine N-acetyl (NAC)	600 mg per day for three to six months	Glutathione precursor that cleanses cells	increases motility and lowers sperm DNA fragmentation.	86
7.	Folate (vitamin B9)	5 mg per day for six months	implicated in the synthesis and repair of DNA	increases DNA stability and sperm morphology	87
8.	Selenium	200 g every day for three months	Cofactor for antioxidant defense and glutathione peroxidase	enhances the viability and motility of sperm	88
9.	Zinc	66 mg per day for three months	Stabilizes sperm chromatin and helps in the activity of antioxidant enzymes	Enhances testosterone and sperm quality.	89
10.	B-12 and methylcobalamin	Methyl: 1500–6000 µg/day (3–6 months); B12: 25 µg/day (4 months)	implicated in cell division, DNA synthesis, and methylation correspondingly	enhances DNA integrity and sperm concentration.	90

Challenges and Future Perspective

Male infertility is one of the several disease conditions whose genesis is exclusively dependent on OS. Therefore, a balance of ROS and antioxidants is crucial for optimal sperm cell synthesis, function, and vitality. Antioxidant-rich supplementation may help men improve the overall quality of their sperm by reducing OS-induced sperm damage and improving hormone synthesis, spermatozoa quantity, motility, and morphology.(91) Although antioxidant therapy for male infertility is gaining popularity, its use in the clinic is complicated by many issues. Clinical studies employ various antioxidant treatments, dosages, and durations, which makes the outcomes difficult to replicate and variable. It is more difficult to diagnose and monitor when there is no defined reference range for total antioxidant capacity (TAC) or threshold for seminal reactive oxygen species (ROS).(92) Because of their poor absorption and hazy distribution to testicular tissues, the value of many antioxidants is questioned. Reductive stress brought on by excessive drug use may prevent crucial ROS-dependent sperm functions, such as capacitation.(93) Future therapeutic trials should focus on interactions between different antioxidants to take advantage of their mixed mechanisms of action.

Conclusion

In conclusion, certain antioxidants, particularly zinc, selenium, alpha-lipoic acid, coenzyme Q10, have been found to have a favourable correlation with sperm quality and, as a result, can aid in enhancing male fertility . Although the body of research on this subject has steadily grown, high-quality, carefully planned prospective and randomized controlled trials with larger patient samples and a strong methodological design that considers some confounding variables are still needed to validate the potential positive effects of supplementation therapy on infertile couples. Furthermore, many over-the-counter supplements have not been scientifically shown to increase fertility, and excessive antioxidant use may be harmful to spermatic function. A balanced diet, which utilizes the synergy of several antioxidants, may be a long-term and safe option. The ideal nutritional traits for attaining fertility require further research in fertile populations.

References

1. Carson SA, Kallen AN. Diagnosis and Management of Infertility: A Review. JAMA 2021;326(1):65–76. DOI: 10.1001/jama.2021.4788
2. Huang B, Wang Z, Kong Y, Jin M, Ma L. Global, regional and national burden of male infertility in 204 countries and territories between 1990 and 2019: an analysis of global burden of disease study. BMC Public Health 2023;23(1):2195. DOI: 10.1186/s12889-023-16793-3
3. Eisenberg ML, Esteves SC, Lamb DJ, Hotaling JM, Giwercman A, Hwang K, et al. Male infertility. Nat Rev Dis Prim 2023;9(1):49. DOI: 10.1038/s41572-023-00459-w
4. Kaltsas A, Koumenis A, Stavropoulos M, Kratiras Z, Deligiannis D, Adamos K, et al. Male Infertility and Reduced Life Expectancy: Epidemiology, Mechanisms, and Clinical Implications. J Clin Med 2025;14(11):3930. DOI: 10.3390/jcm14113930
5. Baskaran S, Finelli R, Agarwal A, Henkel R. Reactive oxygen species in male reproduction: A boon or a bane? Andrologia 2021;53(1): e13577. DOI: 10.1111/and.13577
6. Moustakli E, Zikopoulos A, Skentou C, Katopodis P, Domali E, Potiris A, et al. Impact of Reductive Stress on Human Infertility: Underlying Mechanisms and Perspectives. Int J Mol Sci 2024;25(21):11802. DOI: 10.3390/ijms252111802
7. Kumaresan A, Yadav P, Sinha MK, Nag P, John Peter ESK, Mishra JS, et al. Male infertility and perfluoroalkyl and poly-fluoroalkyl substances: evidence for alterations in phosphorylation of proteins and fertility-related functional attributes in bull spermatozoa. Biol Reprod 2024;111(3):723–39. DOI: 10.1093/biolre/ioae089
8. Pascoal GD, Geraldi MV, Maróstica Jr MR, Ong TP. Effect of paternal diet on spermatogenesis and offspring health: focus on epigenetics and interventions with food bioactive compounds. Nutrients

2022;14(10):2150. DOI: 10.3390/nu14102150
9. Becatti M, Cito G, Argento FR, Fini E, Bettiol A, Borghi S, et al. Blood leukocyte ROS production reflects seminal fluid oxidative stress and spermatozoa dysfunction in idiopathic infertile men. Antioxidants 2023;12(2):479. DOI: 10.3390/antiox12020479
10. Sudhakaran G, Kesavan D, Kandaswamy K, Guru A, Arockiaraj J. Unravelling the epigenetic impact: Oxidative stress and its role in male infertility-associated sperm dysfunction. Reprod Toxicol 2024; 124:108531. DOI: 10.1016/j.reprotox.2023.108531
11. Henkel R, Offor U, Fisher D. The role of infections and leukocytes in male infertility. Andrologia 2021;53(1): e13743. DOI: 10.1111/and.13743
12. Sengupta P, Roychoudhury S, Nath M, Dutta S. Oxidative stress and idiopathic male infertility. Oxidative stress and toxicity in reproductive biology and medicine: a comprehensive update on male infertility 2022:181-204. DOI: 10.1007/978-3-030-89340-8_9
13. Liu KS, Mao XD, Pan F, An RF. Effect and mechanisms of reproductive tract infection on oxidative stress parameters, sperm DNA fragmentation, and semen quality in infertile males. Reprod Biol Endocrinol 2021;19(1):97. DOI: 10.1186/s12958-021-00781-6
14. O'Flaherty C, Scarlata E. OXIDATIVE STRESS AND REPRODUCTIVE FUNCTION: The protection of mammalian spermatozoa against oxidative stress. Reproduction 2022;164(6): F67–78. DOI: 10.1530/REP-22-0200
15. Caroppo E, Dattilo M. Sperm redox biology challenges the role of antioxidants as a treatment for male factor infertility. F&S Rev 2022;3(1):90–104. DOI: 10.1016/j.xfnr.2021.12.001
16. Newman H, Catt S, Vining B, Vollenhoven B, Horta F. DNA repair and response to sperm DNA damage in oocytes and embryos, and the potential consequences in ART: a systematic review. Mol Hum Reprod 2022;28(1): gaab071. DOI: 10.1093/molehr/gaab071
17. Gusti AMT, Qusti SY, Alshammari EM, Toraih EA, Fawzy MS. Antioxidants-Related Superoxide Dismutase (SOD), Catalase (CAT), Glutathione Peroxidase (GPX), Glutathione-S-Transferase (GST), and Nitric Oxide Synthase (NOS) Gene Variants Analysis in an Obese Population: A Preliminary Case-Control Study. Antioxidants 2021;10(4):595. DOI: 10.3390/antiox10040595
18. Sharma P, Kaushal N, Saleth LR, Ghavami S, Dhingra S, Kaur P, et al. Oxidative stress-induced apoptosis and autophagy: Balancing the contrary forces in spermatogenesis. Biochim Biophys Acta - Mol Basis Dis 2023;1869(6):166742. DOI: 10.1016/j.bbadis.2023.166742
19. Rotimi DE, Acho MA, Falana BM, Olaolu TD, Mgbojikwe I, Ojo OA, et al. Oxidative Stress-induced Hormonal Disruption in Male Reproduction. Reprod Sci 2024;31(10):2943–56. DOI: 10.1007/s43032-024-01662-0
20. Kong EQZ, Subramaniyan V, Lubau NSA. Uncovering the impact of alcohol on internal organs and reproductive health: Exploring TLR4/NF-kB and CYP2E1/ROS/Nrf2 pathways. Anim Model Exp Med 2024;7(4):444–59. DOI: 10.1002/ame2.12436
21. Toprak T, Kulaksiz D. Oxidative stress, varicocele, and disorders of male reproduction. In: Alam F, Rehman RBTFP of OS in M and R, editors. Academic Press 2024:215–32. DOI: 10.1016/B978-0-443-18807-7.00014-4
22. Gautam R, Eepsita P, Arbind Kumar P, and Arora T. Assessing the impact and mechanisms of environmental pollutants (heavy metals and pesticides) on the male reproductive system: a comprehensive review. J Environ Sci Heal 2024;42(2):126–53. DOI: 10.1080/26896583.2024.2302738
23. Ali I, Li C, Kuang M, Shah AU, Shafiq M, Ahmad MA, et al. Nrf2 Activation and NF-Kb & caspase/bax signaling inhibition by sodium butyrate alleviates LPS-induced cell injury in bovine mammary epithelial cells. Mol Immunol 2022; 148:54–67. DOI: 10.1016/j.molimm.2022.05.121
24. Wang C, Yang T, Xiao J, Xu C, Alippe Y, Sun K, et al. NLRP3 inflammasome activation triggers gasdermin D–independent inflammation. Sci Immunol 2025;6(64): eabj3859. DOI: 10.1126/sciimmunol. abj3859
25. Dominic A, Le NT, Takahashi M. Loop Between NLRP3 Inflammasome and Reactive Oxygen Species. Antioxid Redox Signal 2022;36(10–12):784–96. DOI: 10.1089/ars.2020.8257
26. Qayyum N, Haseeb M, Kim MS, Choi S. Role of Thioredoxin-Interacting Protein in Diseases and Its Therapeutic Outlook. Int J Mol Sci 2021;22(5):2754. DOI: 10.3390/ijms22052754
27. Peng Y, He Q. Reproductive toxicity and related mechanisms of micro(nano)plastics in terrestrial mammals: Review of current evidence. Ecotoxicol Environ Saf 2024; 279:116505. DOI: 10.1016/j.ecoenv.2024.116505
28. Arévalo L, Esther Merges G, Schneider S, Schorle H. Protamines: lessons learned from mouse models. Reproduction 2022;164(3): R57–74. DOI: 10.1530/REP-22-0107
29. Odroniec A, Olszewska M, Kurpisz M. Epigenetic markers in the embryonal germ cell development and spermatogenesis. Basic Clin Androl 2023;33(1):6. DOI: 10.1186/s12610-

022-00179-3

30. Oehninger S, Kruger TF. Sperm morphology and its disorders in the context of infertility. F&S Rev 2021;2(1):75–92. DOI: 10.1016/j.xfnr.2020.09.002
31. Drevet JR, Hallak J, Nasr-Esfahani MH, Aitken RJ. Reactive Oxygen Species and Their Consequences on the Structure and Function of Mammalian Spermatozoa. Antioxid Redox Signal 2021;37(7–9):481–500. DOI: 10.1089/ars.2021.0235
32. Chen L, Mori Y, Nishii S, Sakamoto M, Ohara M, Yamagishi SI, et al. Impact of Oxidative Stress on Sperm Quality in Oligozoospermia and Normozoospermia Males Without Obvious Causes of Infertility. J clin med 2024;13(23):7158. DOI: 10.1016/j.cels.2019.08.004
33. Gualtieri R, Kalthur G, Barbato V, Longobardi S, Di Rella F, Adiga SK, et al. Sperm Oxidative Stress during In Vitro Manipulation and Its Effects on Sperm Function and Embryo Development. Antioxidants 2021;10(7):1025. DOI: 10.3390/antiox10071025
34. Wang LH, Zheng L, Jiang H, Jiang T. Research advances in inflammation and oxidative stress in varicocele-induced male infertility: a narrative review. Asian J Androl 2025;27(2). DOI: 10.4103/aja202488
35. Fomichova O, Oliveira PF, Bernardino RL. Exploring the interplay between inflammation and male fertility. FEBS J 2024. DOI: 10.1111/febs.17366
36. Bhardwaj JK, Panchal H, Saraf P. Cadmium as a testicular toxicant: A Review. J Appl Toxicol 2021;41(1):105–17. DOI: 10.1002/jat.4055
37. Parameswari R, and Sridharan TB. Cigarette smoking and its toxicological overview on human male fertility—a prospective review. Toxin Rev 2021;40(2):145–61. DOI: 10.1080/15569543.2019.1579229
38. Finelli R, Mottola F, Agarwal A. Impact of Alcohol Consumption on Male Fertility Potential: A Narrative Review. Int J Environ Res Public Health 2022;19(1):328. DOI: 10.3390/ijerph19010328
39. Peel A, Saini A, Deluao JC, McPherson NO. Sperm DNA damage: The possible link between obesity and male infertility, an update of the current literature. Andrology 2023;11(8):1635–52. DOI: 10.1111/andr.13409
40. Roshanfekr Rad M, Sheibani MT, Razi M. A Comparative Study on the Adverse Effects of a High-Fat Diet on Testicular Tissue: Exploring the Difference Between Obesity-Prone and Obesity-Resistant Mice. Reprod Sci 2025;32(4):1013–32. DOI: 10.1007/s43032-025-01799-6
41. Bektas H, and Dasdag S. The effects of radiofrequency radiation on male reproductive health and potential mechanisms. Electromagn Biol Med 2025:1–26. DOI: 10.1080/15368378.2025.2480664
42. Gao Y, Chen W, Kaixian W, Chaofan H, Ke H, Liang M, et al. The effects and molecular mechanism of heat stress on spermatogenesis and the mitigation measures. Syst Biol Reprod Med 2022;68(5–6):331–47. DOI: 10.1080/19396368.2022.2074325
43. Romano M, Cirillo F, Spadaro D, Busnelli A, Castellano S, Albani E, et al. High sperm DNA fragmentation: do we have robust evidence to support antioxidants and testicular sperm extraction to improve fertility outcomes? a narrative review. Front Endocrinol 2023; 14:1150951. DOI: 10.3389/fendo.2023.1150951
44. Wang Y, Fu X, Li H. Mechanisms of oxidative stress-induced sperm dysfunction. Front Endocrinol 2025; 16:1520835. DOI: 10.3389/fendo.2025.1520835
45. Amor H, Hammadeh ME, Mohd I, Jankowski PM. Impact of heavy alcohol consumption and cigarette smoking on sperm DNA integrity. Andrologia 2022;54(7): e14434. DOI: 10.1111/and.14434
46. Subramaiyam N. Insights of mitochondrial involvement in alcoholic fatty liver disease. J Cell Physiol 2023;238(10):2175–90. DOI: 10.1002/jcp.31100
47. Fang Y, Su Y, Xu J, Hu Z, Zhao K, Liu C, et al. Varicocele-Mediated Male Infertility: From the Perspective of Testicular Immunity and Inflammation. Front Immunol 2021; 12:729539. DOI: 10.3389/fimmu.2021.729539
48. Leisegang K. Oxidative stress in men with obesity, metabolic syndrome and type 2 diabetes mellitus: Mechanisms and management of reproductive dysfunction. InOxidative Stress and Toxicity in Reproductive Biology and Medicine: A Comprehensive Update on Male Infertility 2022:237-256. DOI: 10.1007/978-3-030-89340-8_11
49. Kumar N, Singh AK. Impact of environmental factors on human semen quality and male fertility: a narrative review. Environ Sci Eur 2022;34(1):6. DOI: 10.1186/s12302-021-00585-w
50. Keskin İ, Karabulut S, Kaplan AA, Alagöz M, Akdeniz M, Tüfekci KK, et al. Preliminary study on the impact of 900 MHz radiation on human sperm: An in vitro molecular approach. Reprod Toxicol 2024; 130:108744. DOI: 10.1016/j.reprotox.2024.108744
51. Sonali J MI, Gayathri KV, Kumar PS, Rangasamy G. A study of potent biofertiliser and its degradation ability of monocrotophos and its in silico analysis. Chemosphere 2023; 312:137304. DOI: 10.1016/j.chemosphere.2022.137304
52. Takeshima T, Usui K, Mori K, Asai T, Yasuda

K, Kuroda S, et al. Oxidative stress and male infertility. Reprod Med Biol 2021;20(1):41–52. DOI: 10.1002/rmb2.12353

53. Kumar S, Saxena J, Srivastava VK, Kaushik S, Singh H, Abo-EL-Sooud K, et al. The Interplay of Oxidative Stress and ROS Scavenging: Antioxidants as a Therapeutic Potential in Sepsis. Vaccines 2022;10(10):1575. DOI: 10.3390/vaccines10101575
54. Nasreldin N, EL-Shoukary RD, Abdel-Raheem GSE, Gharib HS, Zigo F, Farkašová Z, et al. Effect of mineral-vitamin premix supplementation on behavioral, performance, hormonal, oxidative stress, and serum biochemical profiles on rutting male Camelus dromedarius in Egypt. Front Vet Sci 2023; 10:1221830. DOI: 10.3389/fvets.2023.1221830
55. Eini F, kutenaei MA, Shirzeyli MH, Dastjerdi ZS, Omidi M, Novin MG. Normal seminal plasma could preserve human spermatozoa against cryopreservation damages in Oligozoospermic patients. BMC Mol Cell Biol 2021;22(1):50. DOI: 10.1186/s12860-021-00390-6
56. Jomova K, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, Valko M, et al. Several lines of antioxidant defense against oxidative stress: antioxidant enzymes, nanomaterials with multiple enzyme-mimicking activities, and low-molecular-weight antioxidants. Arch Toxicol 2024;98(5):1323–67. DOI: 10.1007/s00204-024-03696-4
57. Sakhdary H, Farshad A, Rostamzadeh J, Binabaj FB, Sobhani K. Effects of enzymatic and non-enzymatic antioxidants in diluents on cryopreserved bull epididymal sperm. Asian Pacific J Reprod 2022;11(1). DOI: 10.4103/2305-0500.335861
58. Tvrdá E, Benko F, Slanina T, du Plessis SS. The Role of Selected Natural Biomolecules in Sperm Production and Functionality. Molecules 2021;26(17):5196. DOI: 10.3390/molecules26175196
59. Li K peng, Yang X song, Wu T. The Effect of Antioxidants on Sperm Quality Parameters and Pregnancy Rates for Idiopathic Male Infertility: A Network Meta-Analysis of Randomized Controlled Trials. Front Endocrinol 2022; 13:810242. DOI: 10.3389/fendo.2022.810242
60. Su L, Qu H, Cao Y, Zhu J, Zhang S zheng, Wu J, et al. Effect of Antioxidants on Sperm Quality Parameters in Subfertile Men: A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials. Adv Nutr 2022;13(2):586–94. DOI: 10.1093/advances/nmab127
61. Ogawa S, Nishizawa K, Shinagawa M, Katagiri M, Kikuchi H, Kobayashi H, et al. Micronutrient Antioxidants for Men (Menevit®) Improve Sperm Function by Reducing Oxidative Stress, Resulting in Improved Assisted Reproductive Technology Outcomes. Antioxidants 2024;13(6):635. DOI: 10.3390/antiox13121569
62. Ziamajidi N, Khajvand-Abedini M, Daei S, Abbasalipourkabir R, Nourian A. Ameliorative Effects of Vitamins A, C, and E on Sperm Parameters, Testis Histopathology, and Oxidative Stress Status in Zinc Oxide Nanoparticle-Treated Rats. Biomed Res Int 2023;(1):4371611. DOI: 10.1155/2023/4371611
63. Ranneh Y, Hamsho M, Fadel A, Ali Osman HM, Ali EW, Mohammed Kambal NH, et al. Therapeutic potential of carnitine and N-Acetyl-Cysteine supplementation on sperm parameters and pregnancy outcomes in idiopathic male infertility: A systematic review and meta-analysis of randomized control trials. Reprod Breed 2025;5(1):74–83. DOI: 10.1016/j.repbre.2025.02.002
64. Moghadam AM, Javid-Naderi MJ, Fathi-karkan S, Sabz FT kalate, Abbasi Z, Rahdar A, et al. Nanoparticle-mediated L-carnitine delivery for improved male fertility. J Drug Deliv Sci Technol 2024; 102:106420. DOI: 10.1016/j.jddst.2024.106420
65. Tripathi AK, Ray AK, Mishra SK, Bishen SM, Mishra H, Khurana A, et al. Molecular and Therapeutic Insights of Alpha-Lipoic Acid as a Potential Molecule for Disease Prevention. Rev Bras Farmacogn 2023;33(2):272–87. DOI: 10.1007/s43450-023-00370-1
66. Monika G, Melanie Kim SR, Kumar PS, Gayathri KV, Rangasamy G, Saravanan A, et al. Biofortification: A long-term solution to improve global health- a review. Chemosphere 2023; 314:137713. DOI: 10.1016/j.chemosphere.2022.137713
67. Cilio S, Rienzo M, Villano G, Mirto BF, Giampaglia G, Capone F, et al. Beneficial Effects of Antioxidants in Male Infertility Management: A Narrative Review. Oxygen 2022;2(1):1-1. DOI: 10.3390/oxygen2010001
68. Ye N, Lv Z, Dai H, Huang Z, Shi F. Dietary alpha-lipoic acid supplementation improves spermatogenesis and semen quality via antioxidant and anti-apoptotic effects in aged breeder roosters. Theriogenology 2021; 159:20–7. DOI: 10.1016/j.theriogenology.2020.10.017
69. Superti F, Russo R. Alpha-Lipoic Acid: Biological Mechanisms and Health Benefits. Antioxidants 2024;13(10):1228. DOI: 10.3390/antiox13101228
70. Cannarella R, Shah R, Ko E, Kavoussi P, Rambhatla A, Hamoda TAAAM, et al. Effects of Varicocele Repair on Testicular Endocrine Function: A Systematic Review and Meta-Analysis. World J Mens Heal 2024;42. DOI: 10.5534/wjmh.240109
71. Vasilescu SA, Ding L, Parast FY, Nosrati R,

Warkiani ME. Sperm quality metrics were improved by a biomimetic microfluidic selection platform compared to swim-up methods. Microsystems Nanoeng 2023;9(1):37. DOI: 10.1038/s41378-023-00501-7

72. El-Sayed AI, Ahmed-Farid O, Radwan AA, Halawa EH, Elokil AA. The capability of coenzyme Q10 to enhance heat tolerance in male rabbits: evidence from improved semen quality factor (SQF), testicular oxidative defense, and expression of testicular melatonin receptor MT1. Domest Anim Endocrinol 2021; 74:106403. DOI: 10.1016/j.domaniend.2019.106403
73. Akhigbe TM, Fidelis FB, Adekunle AO, Ashonibare VJ, Akorede BA, Shuaibu MS, et al. Does coenzyme Q10 improve semen quality and circulating testosterone level? a systematic review and meta-analysis of randomized controlled trials. Front Pharmacol 2025; 15:1497930. DOI: 10.3389/fphar.2024.1497930
74. Gharakhani Bahar T, Masoumi SZ, Pilehvari S, Kazemi F, Moradkhani S, Mahmoudi S, et al. Effect of CoQ10 Supplement on Spermogram Parameters and Sexual Function of Infertile Men Referred to The Infertility Center of Fatemieh Hospital, Hamadan, Iran, 2019: A Randomized Controlled Trial Study. Int J Fertil Steril 2023;17(2):99–106. DOI: 10.22074/ijfs.2022.544330.1234
75. El-Sherbiny HR, Abdelnaby EA, El-Shahat KH, Salem NY, Ramadan ES, Yehia SG, et al. Coenzyme Q10 Supplementation enhances testicular volume and hemodynamics, reproductive hormones, sperm quality, and seminal antioxidant capacity in goat bucks under summer hot humid conditions. Vet Res Commun 2022;46(4):1245–57. DOI: 10.1007/s11259-022-09991-8
76. Higazy A, Waleed M, M. E, and Samir M. Evaluation of monotherapy of Coenzyme Q10, L-carnitine or combined therapy on semen parameters in idiopathic male infertility: A placebo-controlled double blind randomized clinical trial. Arab J Urol 2025:1–7. DOI: 10.1080/20905998.2025.2509424
77. Kamala K, Santhosh K, Pavithra T, Sivaperumal P. Therapeutic potential of selenium nanoparticles synthesized by mangrove plant: Combatting oral pathogens and exploring additional biological properties. J Trace Elem Miner 2024; 9:100167. DOI: 10.1016/j.jtemin.2024.100167
78. Wróblewski M, Wróblewska W, Sobiesiak M. The Role of Selected Elements in Oxidative Stress Protection: Key to Healthy Fertility and Reproduction. Int J Mol Sci 2024;25(17): 9409. DOI: 10.3390/ijms25179409
79. Rattanawong K, Koiso N, Toda E, Kinoshita A, Tanaka M, Tsuji H, et al. Regulatory functions of ROS dynamics via glutathione metabolism and glutathione peroxidase activity in developing rice zygote. Plant J 2021;108(4):1097–115. DOI: 10.1111/tpj.15497
80. Khademzade O, Kochanian P, Zakeri M, Alavi SMH, Mozanzadeh MT. Oxidative Stress-Related Semen Quality and Fertility in the Male Arabian Yellowfin Sea Bream (Acanthopagrus arabicus) Fed a Selenium Nanoparticle-Supplemented Plant Protein-Rich Diet. Aquac Nutr 2022;2022(1):3979203. DOI: 10.1155/2022/3979203
81. Mateus FG, Moreira S, Martins AD, Oliveira PF, Alves MG, Pereira MD, et al. L-Carnitine and Male Fertility: Is Supplementation Beneficial? J Clin Med 2023;12(18):5796. DOI: 10.3390/jcm12185796
82. Kowalczyk A. The Role of the Natural Antioxidant Mechanism in Sperm Cells. Reprod Sci 2022;29(5):1387–94. DOI: 10.1007/s43032-021-00795-w
83. Bolarin A, Berndtson J, Tejerina F, Cobos S, Pomarino C, D'Alessio F, et al. Boar semen cryopreservation: State of the art, and international trade vision. Anim Reprod Sci 2024; 269:107496. DOI: 10.1016/j.anireprosci.2024.107496
84. Salvio G, Cutini M, Ciarloni A, Giovannini L, Perrone M, Balercia G, et al. Coenzyme Q10 and Male Infertility: A Systematic Review. Antioxidants 2021;10(6):874. DOI: 10.3390/antiox10060874
85. Oyovwi MO, Atere AD. Exploring the medicinal significance of l-Arginine mediated nitric oxide in preventing health disorders. Eur J Med Chem Reports 2024; 12:100175. DOI: 10.1016/j.ejmcr.2024.100175
86. Elgar K. Nutritional medicine reviews N-acetylcysteine: A review of clinical use and efficacy. J Australas Coll Nutr Environ Med 2023;42(3):14–27. DOI: 10.3316/informit. T2024051000007191887604512
87. Martinez M, Majzoub A. Best laboratory practices and therapeutic interventions to reduce sperm DNA damage. Andrologia 2021;53(2): e13736. DOI: 10.1111/and.13736
88. Yilmazer Y, Moshfeghi E, Cetin F, Findikli N. In vitro effects of the combination of serotonin, selenium, zinc, and vitamins D and E supplementation on human sperm motility and reactive oxygen species production. Zygote 2024;32(2):154–60. DOI: 10.1017/S0967199424000029
89. Chao HH, Zhang Y, Dong PY, Gurunathan S, Zhang XF. Comprehensive review on the positive and negative effects of various important regulators on male spermatogenesis and fertility. Front Nutr 2023; 9:1063510. DOI: 10.3389/fnut.2022.1063510
90. Rastegar Panah M, Jarvi K, Lo K, El-Sohemy

A. Vitamin B12 Is Associated with Higher Serum Testosterone Concentrations and Improved Androgenic Profiles Among Men with Infertility. J Nutr 2024;154(9):2680–7. DOI: 10.1016/j.tjnut.2024.06.013
91. Palla A, Ahmed W. Overview of prevention and management of oxidative stress. Fundamental Principles of Oxidative Stress in Metabolism and Reproduction 2024:243-76. DOI: 10.1016/B978-0-443-18807-7.00016-8
92. Gupta S, Finelli R, Agarwal A, Henkel R. Total antioxidant capacity—Relevance, methods and clinical implications. Andrologia 2021;53(2): e13624. DOI: 10.1111/and.13624
93. Hamed MA, Ekundina VO, Akhigbe RE. Psychoactive drugs and male fertility: impacts and mechanisms. Reprod Biol Endocrinol 2023;21(1):69. DOI: 10.1186/s12958-023-01098-2

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