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Review

Interventions Using Various Natural Antioxidant Therapies to Manage Male Fertility: A Review

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Abstract

The male reproductive system has an antioxidant defense system that protects against oxidative stress. Oxidative stress causes male reproductive dysfunction, including impaired spermatogenesis, steroidogenesis, and sperm function. Natural antioxidants are vital to reproductive function and normal semen quality. This review highlights new insights into the physiological role of antioxidants in male infertility and examines the latest and ongoing research integrating male fertility and natural antioxidants to improve understanding of their role in male infertility. To compile research on the effects of antioxidants on sperm quality, a comprehensive literature review was conducted in the electronic databases PubMed and Google Scholar, using keywords such as plant extract antioxidants, vitamins, minerals, and nutrients associated with male infertility and fertility. Evidence indicates that antioxidants such as vitamins, polyphenols, and trace elements improve sperm health, reduce DNA damage, and support testicular function by modulating apoptosis, mitochondrial dysfunction and inflammation, ultimately promoting male reproductive health. Overall, antioxidant therapy shows promise in reducing oxidative stress-related reproductive damage and boosting male fertility.

Keywords: male infertility; oxidative stress; plant-derived antioxidants; antioxidant therapy; semen quality parameters

1. Introduction

Infertility affects about 8–12% of couples and is a serious clinical problem today worldwide. A couple is considered infertile if they fail to conceive after having unprotected intercourse for 1 year. Approximately 10% to 15% of couples worldwide of which either the male partner, the female partner, or both partners are affected. The cause of infertility or subfertility in some of them is unidentified, and is called unexplained subfertility by American Society for Reproductive Medicine [1]. A single or a combination of low sperm concentration, low sperm motility, or defective sperm morphology can cause a fertility issue. Male factors contribute to 40%–50% of all infertility cases, and of all the men worldwide approximately 7% are affected by infertility [2,3].

Male infertility is caused mainly by varicocele (unilateral or bilateral), ductal obstruction, genital tract infections and inflammation [4]. There is evidence that both female and male infertility are commonly caused by the oxidative stress where it interferes in sperm capacitation, damaging sperm DNA, and membrane which directly results in impairment of sperm fertilizing ability thereby affecting the embryo development [5]. The presence of reactive oxygen species (ROS) in the semen leads to oxidative stress. There is high polyunsaturated fatty acid concentration in the sperm membranes disposing them to lipid peroxidation.

Human body can naturally neutralize excess Reactive Oxygen Species (ROS) due to endogenous and exogenous factors [1] and these ROS are one of the important factors for sperm maturation and fertilization at physiological level, but their production in excess leads to oxidative stress. Oxidative stress is also increased in men having anomalous parameters in their semen and occurs when there is excess production of ROS on the way of neutralizing toxic products [6,7]. Thus, its excess is a critical factor that leads to the pathophysiology of male infertility, with high levels of seminal reactive oxygen species present in 30% to 80% of infertile men [5]. Both intrinsic and extrinsic mechanisms contribute to spermatic ROS (Fig. 1). Intrinsic causes include a redox process that takes place in the mitochondria, where ROS act as byproducts, and cytoplasmic glucose-6-phosphate dehydrogenase (G-6-PDH) is the product of reduction. In addition to these, ROS are also caused by spermatic leucocytes, male accessory gland infections, varicocele, and hyperglycemia [8]. Extrinsic causes arise from heavy metals, insecticides, and pollution that come from industrial exposure. In addition, ROS are produced by radiation exposure, smoking, tobacco usage, biological risks, toxins, heat exposure, and excessive intake of alcohol [9].

It has been well documented that antioxidants have a significant impact on male infertility [10,11]. The therapy for infertility in men can be done by administration of

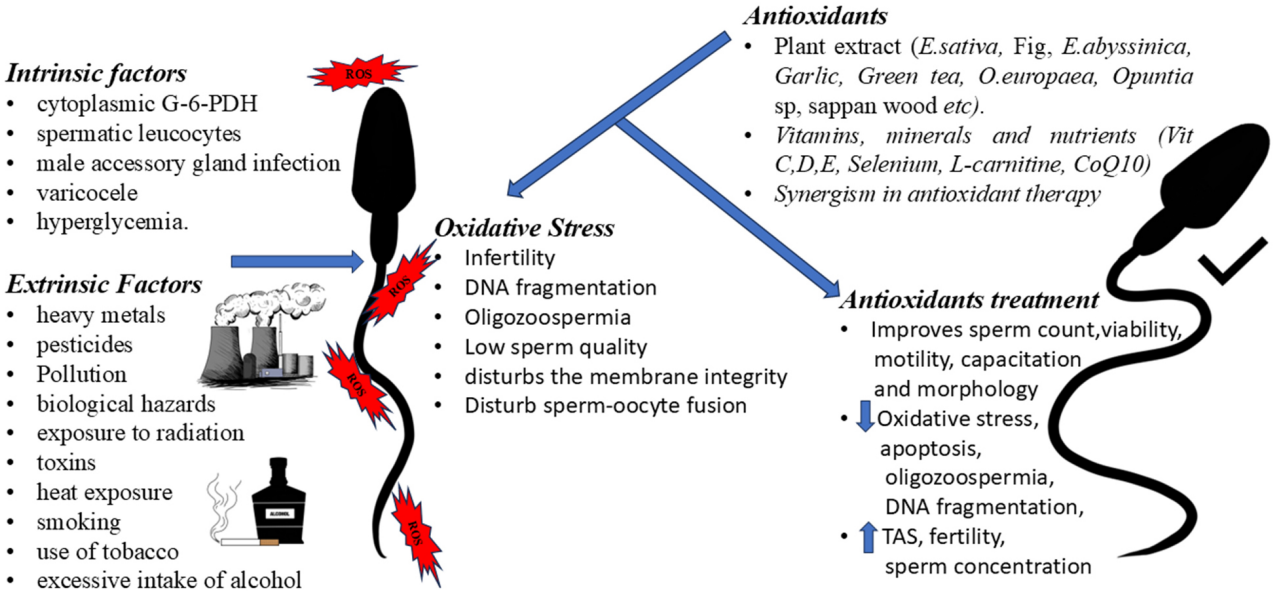

Fig. 1. Shows the graphical representation of Reactive Oxygen Species (ROS) factors and their mitigation by antioxidants (created using Adobe Fresco and Sketchbook).

appropriate and suitable antioxidants [12]. It can improve sperm quality by reducing oxidative damage by oral supplementation [1]. Antioxidants play a key role in fertilization potential by maintaining the cellular redox homeostasis in the reproductive tract of male and improving the sperm parameters [13]. Natural antioxidants are also present in the body in both the forms; enzyme- and non-enzyme-based. Glutathione peroxidase, superoxide dismutase, catalase, heme peroxidase, and glutathione reductase are examples of antioxidant enzymes. The antioxidants without enzymes are vitamin E, vitamin C, ferritin, transferrin, carotenes, beta carotenoids, flavonoids etc [14]. These antioxidants protect against ROS and also have positive effects on semen parameters concerned with many fertility problems [14].

Environmental toxicants, nanoparticles, heavy metals, pharmaceuticals, and metabolic disorders trigger testicular oxidative damage via lipid peroxidation, protein oxidation, DNA fragmentation, and apoptosis. Consequently, therapeutic antioxidants have gained attention as protective agents capable of restoring redox balance and improving reproductive function. This systematic review evaluates evidence supporting antioxidant-mediated protection against testicular damage and highlights mechanistic pathways underlying improved male reproductive outcomes.

2. Methods

Data related to the intervention of antioxidant intake on sperm quality were investigated from papers published during January 2015 to September 2025 in electronic databases from two sites, PubMed and Google Scholar using the following keywords like: causes of ROS, pathological role of ROS, various types of antioxidants used for treatment of male fertility, plant extract antioxidants, vitamins, antioxidants, minerals, nutrients associated with infertility and fertility in male, sperm and also semen. Original research, including human and animal experiments, were selected the site's many findings. The plant extract exclusively from leaves, fruits and stems used as male infertility therapy and natural antioxidants eliminating their comparison on their antioxidants level were included in this review.

2.1 Synergism in Antioxidant Therapy

Numerous antioxidants namely vitamin E, vitamin D, selenium, coenzyme Q10, L. carnitine, and vitamin C exhibited beneficial effects in the management of male infertility [15] (Fig. 2). Evidence suggests that combined antioxidant therapy is more effective than single-agent supplementation, particularly in improving semen quality and reducing oxidative stress. A clinical study has evaluated the impact of antioxidant therapy on both conventional semen parameters and advanced sperm function tests in men undergoing fertility treatment [16]. In a clinical investigation by Arafa et al. [16], infertile men were categorized into idiopathic and unexplained infertility groups and received a three-month course of the multivitamin antioxidant formulation FH PRO (FH PRO Fertility Multivitamin For Men). Post-treatment analysis revealed significant improvements in sperm concentration, motility, morphology, total seminal oxidation–reduction potential, and sperm DNA fragmentation (SDF), particularly among idiopathic cases. The findings supported the therapeutic utility of antioxidant supplementation in the clinical management of idiopathic male infertility.

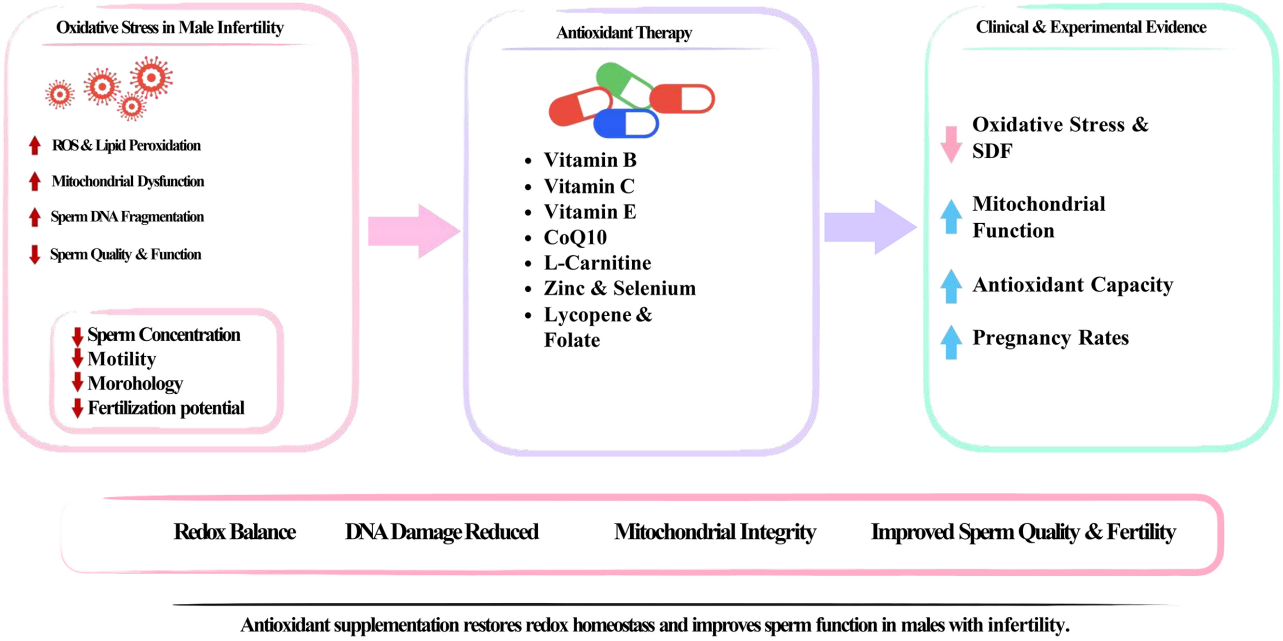

Fig. 2. Shows a graphical representation of the antioxidant therapy mechanism of action. ROS, Reactive Oxygen Species; SDF, Sperm DNA Fragmentation, up arrow = increase, down arrow = decrease (created using Adobe Fresco and Sketchbook).

An earlier study has similarly reported that altered seminal parameters contribute to idiopathic oligoasthenozoospermia, and the antioxidant therapy improves sperm quality [17]. In a randomized trial involving 32 infertile men with idiopathic oligoasthenozoospermia, a daily antioxidant combination containing vitamin C (90 mg), vitamin E (15 mg), CoQ10 (4 mg), selenium (30 µg), and zinc (5 mg) for three months significantly enhanced sperm concentration and motility. Furthermore, oxidative stress, particularly elevated Reactive Oxygen Species (ROS) has been implicated in idiopathic infertility, and six months of combined antioxidant therapy significantly improved sperm concentration and motility while reducing ROS levels and increasing antioxidant capacity [18]. Apart from that, similar improvements in semen quality, reduced lipid peroxidation, and enhanced total antioxidant capacity were observed with multi-antioxidant regimens containing L-carnitine, lycopene, glutathione, CoQ10, selenium, and zinc [15].

The therapeutic efficacy of antioxidant and vitamin combinations has also been evaluated in comparative studies. Terai et al. [19] assessed men with oligozoospermia and asthenozoospermia using a Makler counting chamber and compared antioxidant supplementation (L-carnitine, astaxanthin, zinc, CoQ10, vitamin B12, and vitamin E) with the herbal formulation hochuekkito (HET). Both interventions improved sperm concentration, motility, total motile sperm count, and serum endocrinological profiles. Experimental evidence further supports the protective role of antioxidants against chemically induced reproductive toxicity. For example, El-Rahman et al. [20] demonstrated that co-treatment with vitamin C and cranberry extract mitigated phenobarbital-induced testicular dysfunction in rats by enhancing antioxidant enzyme activity, reducing malondialdehyde (MDA) levels, decreasing caspase-3 expression, and restoring normal testicular histology.

Dietary antioxidant supplementation has also been shown to improve functional sperm parameters. Suárez et al. [21] reported that a multinutrients fertility supplement containing vitamins A, C, E, B-complex vitamins, folate, zinc, selenium, acetyl-L-carnitine, CoQ10, methionine, and lycopene significantly improved sperm concentration, mitochondrial membrane potential, and seminal antioxidant capacity, while reducing lipid peroxidation, chromatin fragmentation, and ROS generation. Similarly, Gvozdjáková et al. [22] evaluated the antioxidant formulation Carni-Q-Nol (L-carnitine fumarate, ubiquinol, vitamin E, and vitamin C) in infertile men. Three to six months of supplementation improved sperm density, reduced pathological forms, increased CoQ10-TOTAL and α-tocopherol levels, and lowered oxidative stress markers in both blood plasma and seminal fluid. Notably, pregnancy occurred in 45% of partners, highlighting the clinical relevance of oxidative stress

biomarkers in infertility management. Preclinical studies further demonstrate rapid improvements in sperm quality following micronutrient supplementation. McPherson et al. [23] showed that 12-day supplementation with zinc, lycopene, selenium, folic acid, green tea extract, and vitamin E in obese male mice significantly enhanced sperm quality and fetal outcomes, suggesting that short-term nutritional intervention during epididymal sperm transit can restore subfertility associated with obesity.

Collectively, the literature supports combined antioxidant therapy as a mechanistically plausible and clinically beneficial strategy for improving redox balance, mitochondrial integrity, genomic stability, and reproductive outcomes in male infertility.

2.2 Vitamins, Minerals and Nutrients as Antioxidants for Male Fertility

Although combined antioxidant therapy appears superior to single-agent supplementation in improving semen quality and reducing oxidative stress, substantial evidence supports the independent efficacy of individual vitamins, minerals, and bioactive nutrients in male reproductive function. The following described the importance of various vitamins, minerals and nutrients in male reproduction.

2.2.1 Vitamin B

Vitamin B12 has demonstrated protective effects on sperm preservation and mitochondrial function. Supplementation in cryopreservation media significantly improved post-thaw sperm motility, ATP preservation, antioxidant enzyme activity, and *in vitro* fertilization outcomes in buffalo models, highlighting its role in maintaining mitochondrial integrity during oxidative stress [24].

2.2.2 Vitamin C

Vitamin C (ascorbic acid), a potent water-soluble antioxidant, is abundant in testicular tissue and plays a critical role in spermatogenesis [25]. Clinical supplementation has been associated with significant improvements in sperm count, motility, and morphology [26]. Experimental models further demonstrate its capacity to mitigate oxidative and inflammatory damage induced by sleep deprivation [27], antidepressants (citalopram, fluoxetine) [28,29] and alcohol [30], by reducing malondialdehyde (MDA) and nitric oxide levels, enhancing total antioxidant capacity (TAC), restoring spermatogenesis, and normalizing testicular histology.

Evidence from both clinical and experimental studies supports a context-dependent role of vitamin C in male reproductive function. A randomized controlled trial by Cyrus et al. [31] demonstrated that vitamin C supplementation (250 mg/day for three months) following varicocelectomy significantly improved sperm motility and morphology, although sperm concentration remained unchanged. Observational findings by Kothari et al. [32] further indicated that seminal plasma ascorbic acid levels were significantly lower in men with abnormal ejaculates and positively correlated with circulating free testosterone, suggesting a relationship between antioxidant status and endocrine function. Besides, Shabanian et al. [33] demonstrated that vitamin C mitigated cyclophosphamide-induced reproductive toxicity, improving sperm motility, viability, and count. More recently, Raspa et al. [34] showed that supplementation with ascorbic acid 2-glucoside during cryopreservation enhanced sperm capacitation, acrosome reaction, and *in vitro* fertilization outcomes in C57BL/6 mouse strains.

Additionally, experimental animal studies provide mechanistic insight. Juniatiningrum et al. [35] reported that high-dose vitamin C administration in Wistar rats adversely affected Sertoli and Leydig cell populations and reduced sperm quality, indicating potential dose-dependent toxicity.

2.2.3 Vitamin E

Vitamin E is a lipid-soluble antioxidant that shields the cellular membrane from oxygen free radical damage and neutralizes free radicals and is one of the best known antioxidants. Out of all the eight isoforms of this vitamin, only α-tocopherol is important for human health and has the highest *in vivo* bioactivity. It improves functions of other antioxidants as well as prevents lipid peroxidation and inhibits ROS production in infertile males [36,37].

Accumulating evidence indicates that vitamin E (α-tocopherol) exerts beneficial effects on male reproductive function, particularly under oxidative stress conditions. Some clinical evidence has suggested that vitamin E supplementation may be associated with improved live birth rates [38]. In animal models, Bovula et al. [39] demonstrated dose-dependent improvements in testicular development, semen quality, and live spermatozoa counts in Windsnyer boars following α-tocopherol supplementation. Similarly, combined vitamin E and selenium therapy enhanced semen quality and fertility in subfertile rabbits Fadl et al. [40].

Clinical trials in assisted reproduction settings show mixed but generally favourable outcomes. Matorras et al. [41] reported a significant increase in live birth rate among infertile couples undergoing IVF after male partners received 400 mg/day vitamin E for three months, although improvements in progressive motility were comparable to placebo. In contrast, Sabetian et al. [42] found no significant enhancement in semen parameters, though vitamin E appeared to prevent deterioration observed in the placebo group. *In vitro* evidence from Ghafarizadeh et al. [43] further supports a protective role of vitamin E against oxidative damage in asthenoteratozoospermic samples.

An experimental study reinforces its anti-oxidant mechanism where Arjmand et al. [44] demonstrated that higher doses (200–300 mg/kg) mitigated morphine-induced reproductive toxicity by reducing lipid peroxidation (MDA) and improving sperm parameters. Protective effects were

also observed against heat-induced testicular damage when vitamin E was administered alone or in combination with vitamin C [25]. Moreover, Zarei et al. [45] reported improved sperm quality, chromatin integrity, and gene expression profiles in aged mice following vitamin E supplementation.

The available evidence suggests that vitamin E improves sperm functional parameters and may enhance reproductive outcomes, particularly in oxidative stress–mediated infertility. However, clinical findings remain heterogeneous, highlighting the need for standardized dosing and well-powered randomized trials.

2.2.4 Vitamin D

Emerging evidence supports a regulatory role of vitamin D in male reproductive function, with both deficient and excessive serum levels adversely affecting sperm quality. Observational studies suggest that optimal serum 25-hydroxyvitamin D [25(OH)D] concentrations are necessary for maintaining sperm count, motility, and normal morphology [46,47]. Clinical data from Rehman et al. [48] demonstrated that infertile men with normal semen parameters exhibited significantly higher serum 25(OH)D levels compared with those presenting abnormal semen profiles, alongside improved motility, concentration, and morphology. Experimental findings further corroborate these associations. In a murine model, Fu et al. [49] reported that vitamin D deficiency impaired testicular development and disrupted spermatogenesis, indicating a mechanistic role in germ cell maturation and endocrine regulation.

The evidence suggests that vitamin D exerts a dose-dependent influence on spermatogenesis and sperm functional parameters, highlighting the importance of maintaining physiological serum levels for optimal male fertility outcomes.

2.3 Alpha-lipoic Acid (ALA)

Alpha-lipoic acid (ALA), a potent mitochondrial antioxidant, has demonstrated beneficial effects on sperm quality in both clinical and experimental settings. In a triple-blind randomized controlled trial, Abbasi et al. [50] evaluated men undergoing microsurgical varicocelectomy, who received either 600 mg/day ALA or placebo for 80 days. Post-intervention analysis revealed significant improvements in sperm parameters, accompanied by reduced malondialdehyde (MDA) levels and increased total antioxidant capacity, suggesting that ALA may serve as an effective adjunct to surgical management by mitigating oxidative stress.

Supporting experimental evidence from Behnamifar et al. [51] demonstrated the dietary ALA supplementation (≥95 mg) in aging broiler breeder roosters where it improved sperm characteristics and antioxidant status, although hatchability rates remained unchanged. These findings indicate that ALA enhances sperm functional quality primarily through redox modulation, supporting its potential role as an adjunct antioxidant therapy in oxidative stress–associated male infertility.

2.4 Coenzyme Q10

Coenzyme Q10 (CoQ10), a key component of mitochondrial bioenergetics and a potent lipophilic antioxidant, has demonstrated consistent benefits in male infertility management. From the various studies it is known that CoQ10 enhances sperm function, endocrine parameters, and fertility outcomes, particularly in idiopathic and oxidative stress–associated male infertility. Clinical evidence indicates that ubiquinone supplementation improves seminal CoQ10 concentrations, sperm motility, and overall semen quality in men with idiopathic infertility [22]. Similarly, Thakur et al. [52] reported that administration of 150 mg/day ubiquinol for six months significantly improved sperm parameters and serum testosterone levels in oligoasthenozoospermic men.

Experimental studies further support its therapeutic role. El-Sayed et al. [53] demonstrated that dietary CoQ10 supplementation enhanced semen quality, testosterone levels, DNA integrity, and melatonin receptor expression in Sinai Gabali rabbits, particularly under heat stress conditions, suggesting improved oxidative stress resilience. In a large clinical cohort, Alahmar and Naemi [54] reported that 200 mg/day CoQ10 for six months significantly increased seminal CoQ10 levels, improved antioxidant capacity and sperm DNA fragmentation (SDF), and achieved a 24.2% pregnancy rate in men with idiopathic oligoasthenozoospermia. Additionally, Ahmed et al. [55] showed that CoQ10 supplementation during cryopreservation improved post-thaw sperm quality and *in vitro* fertility in buffalo models.

2.4.1 L-carnitine

L-carnitine (LC), a semi-essential amino acid derivative involved in mitochondrial fatty acid transport and energy metabolism, has demonstrated therapeutic potential in idiopathic male infertility. Clinical evidence indicates that LC-based supplementation improves sperm concentration, motility, and overall semen quality. In a cohort of 180 men with idiopathic oligoasthenoteratozoospermia (OAT), Nazari et al. [56] reported significant improvements in sperm concentration following three months of treatment with a multi-nutrient antioxidant formulation (Androferti) containing 1500 mg L-carnitine alongside vitamins and trace elements.

Similarly, Busetto et al. [57] demonstrated that six months of supplementation with L-carnitine and acetyl-L-carnitine, combined with antioxidants, significantly increased sperm concentration and total sperm count in men with oligo-, astheno-, and teratozoospermia, irrespective of varicocele status. Supporting these findings, Kopets et al. [58] showed that a multi-nutrient formulation including L-carnitine/L-acetyl-carnitine improved sperm quality and pregnancy rates in idiopathic male infertility.

Further mechanistic evidence is provided by Micic et al. [59], who reported that treatment with a carnitine-based formulation (Proxeed Plus) significantly enhanced sperm concentration, progressive motility, and vitality while reducing sperm DNA fragmentation index (DFI). Increases in seminal carnitine and α-glucosidase levels further suggest improved epididymal function and sperm maturation.

Overall, the evidence supports L-carnitine and its derivatives as effective metabolic and antioxidant adjuncts that enhance sperm bioenergetics, reduce DNA damage, and improve fertility outcomes, particularly in idiopathic OAT.

2.4.2 Selenium

Selenium (Se), an essential trace element, exerts critical biological functions through its incorporation into selenoproteins, which are involved in antioxidant defence, redox regulation, and catalytic processes [60]. Given its role in glutathione peroxidase activity and protection against oxidative stress, selenium has been investigated as a therapeutic agent in male reproductive dysfunction. It has been shown that Selenium plays a protective role in maintaining sperm integrity and mitigating oxidative stress–induced reproductive damage.

Experimental studies suggest a protective role of selenium, particularly in combination with other antioxidants. Baqir Al-Dhalimy et al. [61] evaluated the effects of vitamin C and selenium supplementation separately in stress-induced rat models and reported improvements in sperm parameters and reductions in acrosomal abnormalities following treatment with vitamin C or selenium. Similarly, Shams et al. [62] demonstrated that combined vitamin C and selenium supplementation mitigated penconazole-induced reproductive toxicity in male rats, preserving sperm quality and overall testicular function.

Across the available randomized and controlled clinical trials evaluating antioxidant supplementation in male infertility, pooled evidence indicates that combination of antioxidant therapy demonstrates superior efficacy compared with single-agent interventions, particularly in men with idiopathic oligoasthenoteratozoospermia and elevated oxidative stress markers. Multi-nutrient formulations incorporating mitochondrial enhancers (e.g., CoQ10, L-carnitine), lipid-phase antioxidants (vitamin E), water-soluble antioxidants (vitamin C), and enzymatic cofactors (selenium) have been associated with improvements in parameters such as progressive motility, sperm concentration, total antioxidant capacity, and sperm DNA fragmentation males. Table 1 shows the comparative antioxidant efficacy of these supplements in the reproductive functioning of male. Overall, the available evidence suggests that combination antioxidant therapy may represent a promising approach for redox modulation in male infertility, although individualized, biomarker-guided approaches remain important for optimizing clinical outcomes and minimizing unintended redox imbalance.

2.5 Plants Extract as Antioxidants for Male Fertility

Male infertility conditions-including reduced libido, azoospermia, oligospermia, erectile dysfunction, and sexual asthenia have historically been managed using medicinal plants and their bioactive derivatives. A substantial body of evidence indicates that many of these phytotherapeutic agents exert biological activity relevant to male reproductive function. Their efficacy has been investigated through *in vitro* assays, *in vivo* animal experiments, and clinical studies, demonstrating antioxidant, anti-inflammatory, androgenic, and spermatogenic properties [63]. In order to cure fertility issues and enhance both animal and human reproductive performance, plants and the substances they extract have been employed as dietary supplements.

A wide range of medicinal plants and phytochemical-rich extracts have been investigated for their protective and fertility-enhancing effects in male reproductive dysfunction. Here are a few plant extracts that are significant antioxidants in the treatment of infertility (Fig. 3).

2.6 Allium sativum (Garlic)

Allium sativum L., a member of the Alliaceae family and one of the most extensively cultivated species of the genus *Allium*, has been used in traditional medicine for centuries due to its broad pharmacological properties, including antioxidant, anti-inflammatory, and antimicrobial effects. Its reproductive benefits are largely attributed to sulfur-containing bioactive compounds such as allicin, diallyl sulfide, and S-allyl cysteine, which contribute to redox modulation and cytoprotection.

Ghalehkandi [64] evaluated the protective effect of fresh garlic juice on oxidative stress markers in male rats exposed to chromium chloride ($CrCl_3$)-induced reproductive toxicity. Administration of garlic juice at a dose of 120 mg/kg body weight significantly reduced malondialdehyde (MDA) and increased the levels of glutathione peroxidase (GPx), superoxide dismutase (SOD), and total antioxidant status (TAS). These findings suggest that garlic exerts a protective effect against heavy metal–induced oxidative damage in testicular tissue, likely through enhancement of endogenous antioxidant defense mechanisms and attenuation of reactive oxygen species (ROS)-mediated injury.

Mohammadzadeh et al. [65] investigated the therapeutic effects of *A. sativum* alone and in combination with *Citrullus colocynthis* in a diabetes mellitus (DM)-induced male reproductive damage model in Wistar rats and found that both garlic and *C. colocynthis* independently improved sperm parameters and attenuated oxidative stress but combination phytotherapy may enhance therapeutic ef-

Table 1. Comparative table of antioxidants efficacy in male reproductive functions.

Antioxidant/strategy	Model type	Main outcomes improved	Evidence strength	Overall efficacy
Combination Multi-Antioxidant Therapy (Vit C, E, Zn, Se, CoQ10 ± L-carnitine, B vitamins)	Human (idiopathic OAT, varicocel)	↑ Sperm concentration, ↑ motility, ↓ SDF, ↓ ROS, ↑ TAC, ↑ pregnancy rate	Strong (RCTs included)	Best
Coenzyme Q10/Ubiquinol	Human + animal	↑ Total sperm count (up to 53%), ↑ motility, ↓ DNA fragmentation, ↑ antioxidant status	Strong	Very good
L-Carnitine (± Acetyl-L-Carnitine)	Human RCTs	↑ Progressive motility, ↑ vitality, ↓ DNA fragmentation	Strong (multiple controlled studies)	Good
Vitamin E (α-tocopherol)	Human + animal	↓ Lipid peroxidation (MDA), ↑ motility, ↑ IVF live birth rate	Moderate–Strong	Good
Alpha-Lipoic Acid (ALA)	Human + animal	↑ Motility (post-varicocelectomy), ↑ semen quality	Moderate	Good
Vitamin C (Ascorbic Acid)	Human + extensive animal models	Protective in toxicant/stress models; ↑ motility (post-varicocele); ↓ oxidative stress	Moderate (dose dependent; mixed)	Very good
Vitamin B12	Animal	Sperm and mitochondrial preservation	Limited	Good
Selenium (alone)	Mostly animal	Protective in stress/toxic models	Limited	Good
Vitamin D	Observational + deficiency models	Associated with hormone levels & spermatogenesis	Associative (not interventional)	Good

OAT, oligoasthenoteratozoospermia; SDF, sperm DNA fragmentation; ROS, Reactive Oxygen Species; TAC, total antioxidant capacity; RCTs, randomized controlled trials (up arrow = increase, down arrow = decrease).

ficacy, suggesting a potential role for multi-target antioxidant strategies in the management of male infertility associated with oxidative stress.

2.6.1 Ashrasi Date Palm

Since Ashrasi date palm (ADP) is known to have strong antioxidant qualities, Hosseinipour et al. [66] investigated the antioxidant effects of its hydroalcoholic extract on sperm parameters and DNA fragmentation in diabetic rats. After administering different doses of ADP extracts to the induced diabetic rats for five weeks, it was shown that the higher dose groups showed a substantial therapeutic benefit with an improvement in sperm motility and viability as well as a decrease in sperm DNA fragmentation. According to the study, ADP hydroalcoholic extract can enhance sperm parameters and preserve sperm DNA integrity while also having antioxidant and protective properties against oxidative stress brought on by diabetes.

2.6.2 *Achillea tenuifolia* Lam.

Achillea tenuifolia Lam. (family Asteraceae) is a medicinal plant recognized for its antioxidant, anxiolytic, anti-inflammatory, and endocrine-modulating properties. Phytochemical analyses indicate the presence of flavonoids, phenolic acids, and terpenoids, which contribute to its biological activity.

Bagheri et al. [67] evaluated the effects of a hydroalcoholic extract of *A. tenuifolia* in a rat model of chronic restraint stress (CRS), a well-established paradigm for inducing oxidative stress–mediated reproductive and behavioral impairments. The experimental evidence suggested that *A. tenuifolia* exhibits antioxidant and neuroendocrine regulatory effects in stress-induced reproductive dysfunction. It is further suggested that by attenuating oxidative stress and restoring hormonal balance, the extract may improve reproductive performance under chronic stress conditions.

2.6.3 *Cardiospermum halicacabum* (L.)

Cardiospermum halicacabum (family Sapindaceae), commonly known as balloon vine, is traditionally used in ethnomedicine for its anti-inflammatory and restorative properties. Phytochemical studies indicate the presence of flavonoids, saponins, alkaloids, and phenolic compounds, which may contribute to its antioxidant and androgenic activities.

Peiris et al. [68] evaluated the effects of an aqueous leaf extract (ALE) of *C. halicacabum* on male rat fertility. In this experimental study, male rats received oral administration of ALE at doses of 100 mg/kg and 200 mg/kg body weight for 30 days and found that it exerts both spermatogenic and androgenic effects, contributing to improved male reproductive performance. The dose-dependent improvements in sperm parameters and serum testosterone levels indicate *C. halicacabum* potential as a phytotherapeutic agent in male infertility management.

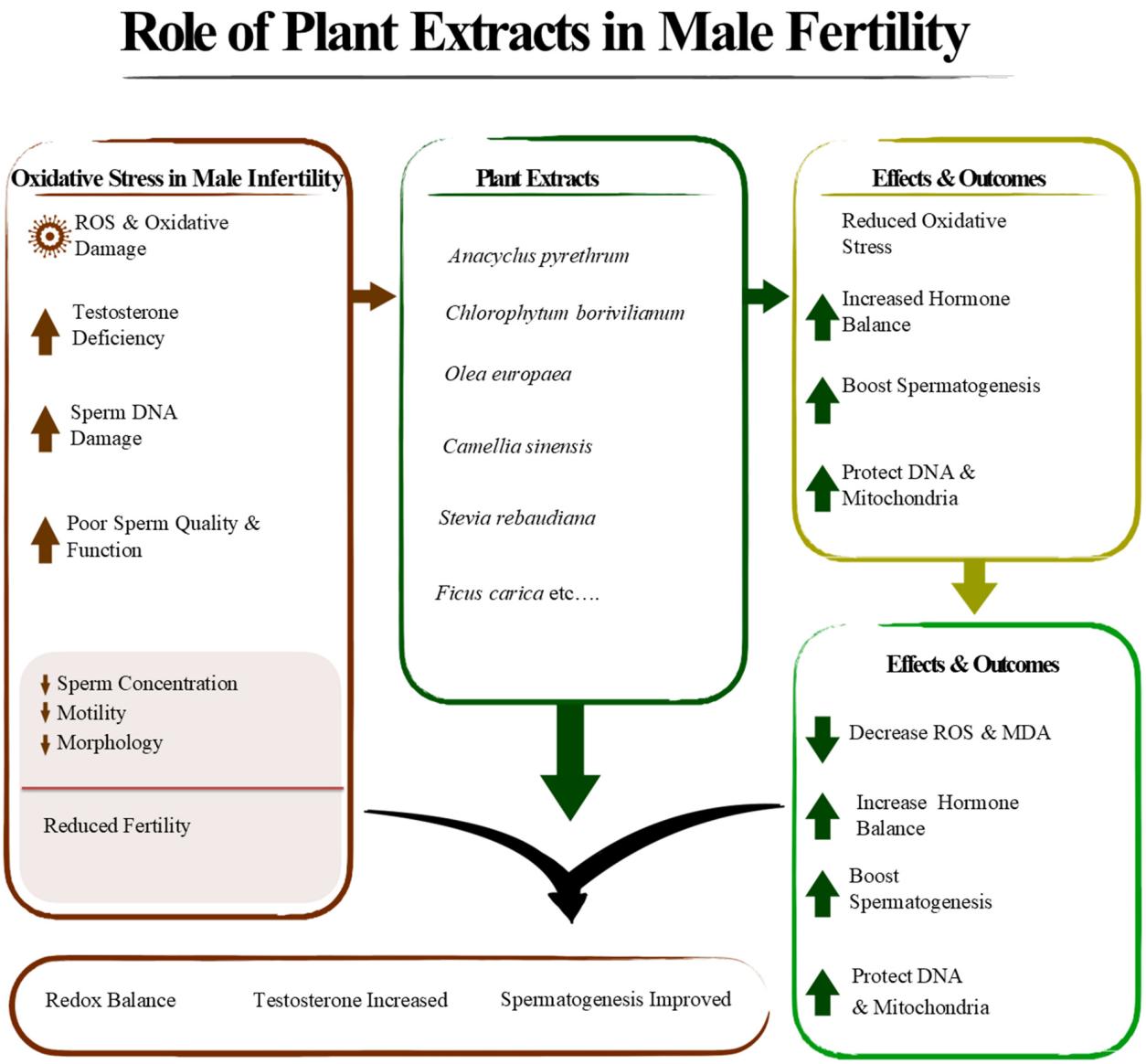

Fig. 3. Shows graphical representation of the summary of plant-derived antioxidants and their reported effects on male reproductive function. ROS, Reactive Oxygen Species; MDA, Malondialdehyde; up arrow = increase, down arrow = decrease (created using Adobe Fresco and Sketchbook).

2.6.4 *Camellia sinensis* L.

Camellia sinensis L. (family Theaceae), the plant source of green and black tea, contains several bioactive compounds, primarily caffeine, epigallocatechin-3-gallate (EGCG), and L-theanine. These constituents exhibit antioxidant, anti-inflammatory, and cytoprotective properties and have been investigated for their potential role in male reproductive function.

Dias et al. [69] evaluated the individual and combined effects of caffeine (71 µg/mL), EGCG (82 µg/mL), and L-theanine (19 µg/mL) on spermatozoa *in vitro*. Sperm were incubated either with single compounds or in combination. While individual components exerted protective antioxidant effects and improved sperm viability, prolonged combined exposure resulted in oxidative protein modifications, suggesting potential dose- and duration-dependent effects.

Opuwari and Monsees [70] examined the impact of green tea administration on the reproductive system of male rats. Organ weights remained largely unchanged, except for the kidney. Serum alanine transaminase (ALT) and aspartate transaminase (AST) levels decreased, and spontaneous acrosome reaction increased. Histologically, caudal

epididymal epithelial height increased, while seminiferous tubule diameter decreased. Overall, green tea consumption improved sperm parameters without evident systemic toxicity.

In an obesity-associated model, Han et al. [71] investigated the effects of green and black tea supplementation in high-fat diet (HF)-fed male mice. Experimental groups included HF controls and HF animals supplemented with either green or black tea (5% powder). Both teas mitigated obesity-induced reproductive dysfunction; however, black tea demonstrated a comparatively greater potential in enhancing fertility parameters.

The evidences suggests that *C. sinensis*–derived beverages exert protective effects on male reproductive function, although outcomes may vary depending on dosage, formulation, metabolic status, and exposure duration.

2.7 Caesalpinia sappan L.

Nadiyah et al. [72] evaluated the effects of ethanol extract of *Caesalpinia sappan* (sappan wood) on sperm quality parameters in male Wistar rats. Administration of the extract resulted in significant improvements in sperm concentration, motility, and viability compared with controls.

These findings suggest that *C. sappan* possesses bioactive compounds capable of enhancing male fertility, potentially through antioxidant-mediated mechanisms.

2.7.1 *Codonopsis pilosula* (Dangseng)

Wang et al. [73] investigated the protective effects of water extract of *Codonopsis pilosula* (CPWE) in a D-galactose–induced aging mouse model associated with testicular inflammation. Aging was induced via intra-peritoneal injection of D-galactose, after which mice received CPWE at low, medium, and high doses. CPWE administration significantly reduced testicular levels of malondialdehyde (MDA) and pro-inflammatory cytokines (IL-6 and IL-1β), while increasing serum superoxide dismutase (SOD) activity and testosterone concentrations. Histopathological examination revealed attenuation of age-related degenerative changes in testicular tissue. CPWE demonstrated marked antioxidant and anti-inflammatory effects, providing substantial protection against age-associated testicular inflammatory injury.

2.7.2 *Chlorophytum borivilianum*

The antioxidant potential of *Chlorophytum borivilianum* root extract (CRE) has been evaluated using DPPH (2,2-diphenylpicrylhydrazyl) and nitric oxide (NO) scavenging assays. Vyas et al. [74] investigated its protective effects in Swiss albino mice exposed to gamma (Gy) irradiation. Mice were pre-treated with CRE before and after irradiation and observed for 30 days. CRE demonstrated strong antioxidant activity; pretreated groups showed protection of sperm during epididymal maturation, whereas non-pretreated irradiated mice exhibited reduced sperm parameters and altered sperm morphology. These findings indicate that CRE mitigates radiation-induced oxidative damage in male germ cells.

Similarly, Mararajah et al. [75] reported that the aqueous root extract of *C. borivilianum* preserves testicular function in mice and protects human sperm against hydrogen peroxide (H_2O_2)-induced oxidative stress. *In vivo*, male mice were orally pre-exposed to 2% H_2O_2 for seven consecutive days to induce oxidative stress, followed by treatment with CB extract (100 and 200 mg/kg body weight) for an additional seven days. CB administration attenuated oxidative stress, restored antioxidant enzyme balance, and improved sperm parameters, testicular steroidogenesis, and spermatogenesis. Serum levels of FSH, LH, and testosterone were also restored toward near-normal values. *In vitro*, sperm samples from 32 healthy fertile men were co-incubated with 200 μM H_2O_2 and CB extract (100 and 200 μg/mL). CB treatment prevented the decline in sperm functional parameters following oxidative challenge.

Collectively, these findings support the potent antioxidant and testiculo-protective properties of *C. borivilianum*, highlighting its potential role in mitigating oxidative stress–mediated reproductive dysfunction.

2.8 Cannabis

Nwonuma et al. [76] investigated the effects of ethanolic leaf extract of *Cannabis sativa* on testicular function and sperm quality in rats. Animals were divided into five groups and administered varying concentrations of the extract for 60 days. Treatment resulted in significant improvements in sperm quality parameters compared with controls. Additionally, serum levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), triglycerides, cholesterol, and total protein were significantly increased.

The findings suggest that controlled administration of *C. sativa* leaf extract may enhance testicular function and sperm quality, potentially through antioxidant-mediated protection against oxidative damage.

2.9 Capparis spinosa L

Khojasteh Rad et al. [77] investigated the *in vitro* effects of hydroalcoholic extracts of *Capparis spinosa* leaves and fruits on oxidative stress, DNA fragmentation, and functional parameters of human sperm. Semen samples from 50 healthy men (20–45 years) were allocated into control and treatment groups exposed to 15, 30, and 45 ppm of leaf extract. Treatment with *C. spinosa* extract significantly reduced sperm DNA fragmentation and improved sperm motility and viability compared with controls.

These findings suggest that *C. spinosa* possesses antioxidant properties capable of enhancing human sperm functional integrity *in vitro*.

2.10 Dried White Mulberry Extract

Inanc et al. [78] evaluated the protective effects of dried white mulberry extract (DWME) against carmustine (Crm)-induced reproductive toxicity in Wistar albino rats. Carmustine exposure significantly impaired spermatological parameters and fertility, accompanied by increased oxidative stress, elevated DNA damage, and reduced sperm quality. Co-administration of DWME markedly attenuated these effects. The Crm + DWME group demonstrated significantly higher glutathione (GSH) levels and the greatest reproductive success, reflected by increased offspring numbers.

These findings indicate that dried white mulberry extract exerts protective effects against chemotherapeutic-induced reproductive damage, primarily through enhancement of antioxidant defense mechanisms.

2.11 Eruca sativa

Eruca sativa is rich in polyphenolic compounds that confer strong antioxidant potential. Grami et al. [79] evaluated the protective effects of *E. sativa* aqueous extract (ESAE) against bisphenol A (BPA)-induced reproductive toxicity in Wistar rats. Animals received oral doses for 30 consecutive days. BPA exposure reduced sperm viability, motility, and density, disrupted sperm morphology, and induced histological alterations in the testes and epididymis. ESAE administration ameliorated these impairments, restoring sperm parameters and improving gonadal histoarchitecture. The protective effect was attributed to its phenolic bioactive constituents and enhanced antioxidant capacity.

In a related study, Khalaf et al. [80] investigated a traditional polyherbal formulation containing extracts of *E. sativa* along with *Lepidium sativum*, *Origanum majorana*, and *Ferula hermonis* in Sprague–Dawley rats. Oral administration of individual or combined aqueous extracts enhanced sperm count, antioxidant enzyme activity, testosterone and LH levels, and improved seminiferous tubule morphology.

Collectively, these findings suggest that *E. sativa*, alone or in combination with other medicinal plants, improves male reproductive function primarily through antioxidant and endocrine-modulatory mechanisms.

2.12 Entada abyssinica

Sobeh et al. [81] investigated the phytochemical profile and protective effects of *Entada abyssinica* bark extract on cryopreserved ram spermatozoa. Secondary metabolites were characterized using LC–MS analysis, identifying 28 compounds, predominantly tannins and gallic acid derivatives. Supplementation of the freezing medium at 375 µg/mL significantly improved post-thaw semen quality and reduced hydrogen peroxide levels, indicating decreased oxidative stress. Molecular docking analysis further suggested that bioactive constituents of the extract may interfere with the Bcl-2–mediated apoptotic signalling cascade.

These findings demonstrate that *E. abyssinica* bark extract enhances cryosurvival of ram sperm through antioxidant activity and modulation of apoptosis-related pathways.

2.13 Ferulago angulata

Naderi et al. [82] investigated the protective effects of *Ferulago angulata* extract (FAE) against oxidative damage induced by lead acetate (LA) and diazinon (DZN) in NMRI mice. Exposure to LA and DZN significantly impaired the quality of cryopreserved spermatozoa through increased reactive oxygen species (ROS) generation. Supplementation with FAE markedly improved sperm motility, vitality, membrane integrity, fertilization capacity, and embryonic developmental competence. Additionally, FAE significantly reduced ROS levels in spermatozoa, both in the presence and absence of LA and DZN exposure.

These findings suggest that *F. angulata* extract enhances cryosurvival and functional competence of sperm under toxicant-induced oxidative stress, supporting its potential application in managing male infertility associated with environmental reproductive toxins.

2.14 Ficus carica

Ficus carica (Moraceae), commonly known as Fig, contains diverse phytochemicals, including phenolics, organic acids, and volatile compounds, which contribute to its biological activity.

Naghdi et al. [83] investigated the effects of *F. carica* leaf extract on testicular and sperm parameters in mice exposed to formaldehyde-induced toxicity. Formaldehyde exposure caused significant histopathological alterations, including vacuolated and disorganized seminiferous epithelium, spermatogenic arrest, and lumens filled with immature germ cells, along with a reduction in the gonadosomatic index. Treatment with *F. carica* extract improved sperm count and positively influenced overall sperm parameters, despite persistent structural alterations in testicular tissue.

These findings suggest that *F. carica* leaf extract exerts partial protective effects on sperm quality under chemically induced testicular stress, likely mediated by its phytochemical antioxidant properties.

2.15 Hygrophila spinosa T.

Vyas and Raval [84] evaluated the spermatogenic and aphrodisiac potential of the alkaloid-enriched fraction of *Hygrophila spinosa* in rats. The fraction was isolated and tested using both *in vitro* assays on isolated rat Leydig cells and *in vivo* experimental models. Results from both experimental approaches demonstrated a significant increase in testosterone levels in treated animals. Additionally, treatment improved testicular histoarchitecture and increased testicular weight compared to controls.

These findings suggest that the alkaloidal fraction of *H. spinosa* enhances steroidogenesis and supports spermatogenic activity, indicating potential utility in managing male reproductive dysfunction.

2.16 *Lycium barbarum*

Lycium barbarum polysaccharide (LBP) is widely used in traditional Chinese medicine and is recognized for its antioxidant, anti-apoptotic, anti-inflammatory, and fertility-enhancing properties.

Shi et al. [85] investigated the effects of LBP on spermatogenesis in streptozotocin-induced diabetic male mice. Animals were treated orally for 62 days with saline, sildenafil citrate (5 mg/kg), or LBP (10, 20, or 40 mg/kg). Diabetes significantly impaired sperm parameters, organ weights, and antioxidant status, with elevated malondialdehyde (MDA) levels. LBP administration improved sperm quality, enhanced antioxidant capacity, reduced lipid peroxidation, and inhibited apoptosis, thereby protecting against diabetes-induced spermatogenic dysfunction.

Similarly, Liu et al. [86] demonstrated that LBP (10 mg/kg) protected Immp2l+/− mice from ethanol-induced reproductive toxicity. Treatment enhanced antioxidant enzyme activity, scavenged reactive oxygen species, and preserved spermatogenic epithelium integrity by reducing collagen expression and stabilizing protein biosynthesis during spermatogenesis.

In a clinical context, Mehdikhanloo et al. [87] conducted a double-blind randomized trial involving 80 varicocele patients. Participants received either placebo or 400 mg/day of *L. barbarum* extract for two months. The intervention group exhibited significantly reduced MDA levels, increased antioxidant enzyme activity, and improved semen parameters, including sperm count, motility, morphology, semen volume, and testosterone levels.

Collectively, these experimental and clinical findings indicate that *L. barbarum* polysaccharides exert protective and restorative effects on male reproductive function through antioxidant enhancement, anti-apoptotic activity, and preservation of spermatogenic integrity.

2.17 Lavender

Farhadi et al. [88] evaluated the protective effects of ethanolic extract of *Lavandula angustifolia* on ram epididymal sperm during the freeze–thaw process. Different concentrations (0, 75, 150, and 300 µg/dL) were assessed for their impact on microscopic characteristics, oxidative stress markers, structural integrity, and fertility parameters. Among the tested doses, 150 µg/dL significantly improved post-thaw semen quality by reducing malondialdehyde (MDA) levels and decreasing sperm abnormalities. This concentration yielded the most favorable outcomes in terms of sperm viability and fertility potential.

These findings suggest that optimal-dose lavender extract supplementation enhances cryosurvival of ram sperm, primarily through attenuation of oxidative stress.

2.18 *Mucuna pruriens (Linn.)*

Murugesan et al. [89] evaluated the therapeutic potential of *Mucuna pruriens* in a high-fat diet–induced hypercholesterolemia rat model. Hypercholesterolemic rats exhibited impaired chromatin integrity, significant deterioration of sperm structural and functional parameters, and marked reductions in follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone levels. Treatment with *M. pruriens* significantly improved spermatogenesis, restored sperm quality, and normalized reproductive hormone levels.

These findings suggest that *M. pruriens* mitigates hyperlipidemia-associated reproductive dysfunction, likely through modulation of endocrine balance and improvement of testicular function.

2.19 *Momordica charantia*

Arun et al. [90] investigated the protective effects of *Momordica charantia* fruit extract against chronic unpredictable stress (CUS)-induced epididymal dysfunction in adult male rats. Animals were divided into four groups: control, CUS, and two CUS groups treated with MC extract (40 or 80 mg/kg). Stress was induced for 60 consecutive days using a randomized sequence of nine stressors.

CUS exposure disrupted antioxidant balance, altered epididymal protein secretion—particularly tyrosine-phosphorylated proteins—and impaired hormonal homeostasis, evidenced by elevated corticosterone and reduced testosterone levels.

MC extract administration restored antioxidant activity, improved the secretion of functional proteins from both the caput and cauda epididymis, normalized corticosterone levels, and significantly increased testosterone. Notably, the 80 mg/kg dose effectively preserved HSP-70 and tyrosine-phosphorylated protein expression in epididymal luminal fluid.

These findings indicate that *M. charantia* mitigates stress-induced epididymal and hormonal dysfunction through antioxidant and protein-regulatory mechanisms.

2.20 *Moringa oleifera*

Moringa oleifera, commonly known as the “miracle tree”, has traditionally been used as an aphrodisiac and to manage sexual dysfunction. Opuwari et al. [91] evaluated the effects of its aqueous leaf extract on Leydig TM3 cells, which are central to testosterone synthesis. Cells were treated with varying concentrations of the extract, with or without human chorionic gonadotropin. At the highest concentration (1000 µg/mL), the extract exhibited antioxidant activity by significantly increasing intracellular glutathione levels, although other antioxidant markers and lipid peroxidation remained unchanged.

In an *in vivo* model, Ghadimi et al. [92] investigated the effects of different doses of *Moringa oleifera* leaf extract (MOLE) on semen quality and fertility in aged broiler breeder roosters. Supplementation, particularly at 200 mg/kg (MOLE-200), significantly improved sperm motility, membrane integrity, and testosterone levels. This group

also exhibited the highest fertility rate, measured by the proportion of fertilized eggs, along with the lowest malondialdehyde levels, indicating reduced lipid peroxidation.

Collectively, these findings demonstrate that *M. oleifera* enhances reproductive function through antioxidant modulation and support of steroidogenic activity.

2.21 Olea europaea

Olea europaea, a member of the Oleaceae family, is widely recognized for its pharmacological properties, including antioxidant, anti-inflammatory, antihyperlipidemic, and cardioprotective effects.

Sarbishegi et al. [93] evaluated the protective role of olive leaf extract (OLE) against rotenone (ROT)-induced testicular toxicity in rats. Rotenone exposure significantly increased malondialdehyde (MDA) levels while reducing total antioxidant capacity (TAC) and impairing sperm parameters. Administration of OLE mitigated oxidative stress by lowering MDA levels, enhancing antioxidant capacity, and improving sperm quality. These findings suggest that *O. europaea* leaf extract exerts protective effects against pesticide-induced reproductive toxicity primarily through its antioxidant mechanisms.

2.22 Opuntia sp

Contino et al. [94] investigated the effects of fruit extracts from *Opuntia ficus-indica* and *Opuntia dillenii* on sperm quality and cryopreservation outcomes. *Opuntia* species are rich in antioxidant phytochemicals capable of neutralizing reactive oxygen species (ROS); however, excessive concentrations may adversely affect fertilization processes.

In the first experiment, exposure of spermatozoa to the fruit extracts significantly increased motility compared with controls and reduced oxidative stress and DNA fragmentation. In the second experiment, supplementation of the freezing medium with 50 µL of the extracts improved post-thaw sperm vitality and increased the proportion of intact acrosomes.

Overall, *Opuntia* fruit extracts enhance both fresh and cryopreserved sperm quality by mitigating oxidative damage, although optimal dosing is critical to avoid potential adverse effects.

2.23 Opuntia ficus-indica

Akacha et al. [95] investigated the protective effects of *Opuntia ficus-indica* cladode extract against methotrexate (MTX)-induced testicular toxicity in rats. MTX administration resulted in impaired sperm parameters, reduced serum testosterone levels, oxidative stress, and histopathological damage to testicular tissue. Treatment with *O. ficus-indica* extract significantly improved sperm count and motility, restored testosterone levels, reduced oxidative stress markers, and preserved gonadal histoarchitecture.

These findings indicate that *O. ficus-indica* cladode extract exerts protective effects against chemotherapeutic-induced reproductive toxicity, primarily through antioxidant and steroidogenic-supportive mechanisms.

2.24 Origanum vulgare

Chen et al. [96] evaluated the anti-inflammatory, anti-apoptotic, and antioxidant effects of *Origanum vulgare* in BALB/c mice subjected to finasteride-induced testicular toxicity for 35 days. Finasteride markedly disrupted testicular architecture, decreased antioxidant enzyme activity, and increased lipid peroxidation. Administration of *O. vulgare* extract, particularly at higher doses, restored antioxidant defence mechanisms, improved hormonal profiles, and ameliorated histological damage. The study demonstrated that *O. vulgare* protects testicular structure and function against finasteride-induced reproductive impairment.

In a separate *in-vitro* investigation, Alenezy et al. [97] assessed the effects of *O. vulgare* extract supplementation in *in-vitro* capacitation sperm medium (IVCSM) on sheep spermatozoa. Various concentrations (0.3, 0.6, 1.2 µg/mL and 25, 50, 100 µg/mL) were tested. Semen quality parameters showed significant improvement, particularly at concentrations of 1.2 µg/mL and above.

Collectively, these findings indicate that *O. vulgare* enhances sperm functional competence both *in vivo* and *in vitro*, primarily through antioxidant and cytoprotective mechanisms.

2.25 Palm Pollen and Pomegranate Peel

Abdulameer et al. [98] evaluated the effects of palm pollen and pomegranate peel, both recognized for their antioxidant, anti-inflammatory, and antimicrobial properties, on male rabbit fertility.

Supplementation with these herbal extracts significantly improved sperm quality parameters and enhanced reproductive performance. Histological findings demonstrated increased angiogenesis and spermatogenesis in treated animals compared with controls.

Overall, the results indicate that palm pollen and pomegranate peel exert beneficial effects on male reproductive health, supporting their potential role as adjunctive therapies for managing reproductive dysfunction.

2.26 Rumex hastatus

Ain et al. [99] investigated the therapeutic potential of *Rumex hastatus* leaf methanolic extract against triclosan (TCS)-induced testicular toxicity in male rats. TCS exposure significantly impaired testicular function, reduced sperm DNA integrity, disrupted hormonal balance, and deteriorated sperm parameters. Fertility assessment further revealed reduced litter size and poor pregnancy outcomes in females mated with TCS-exposed males. Co-administration of *R. hastatus* extract restored antioxidant enzyme activities, improved sperm quality, normalized hor-

monal levels, and re-established testicular histoarchitecture. Notably, fertility outcomes improved, with increased litter sizes and enhanced pregnancy rates in the extract-treated groups.

These findings suggest that *R. hastatus* exerts protective and restorative effects against triclosan-induced reproductive toxicity through antioxidant and endocrine-modulatory mechanisms.

2.27 Panax ginseng

Yeni et al. [100] demonstrated the protective effects of *Panax ginseng* against doxorubicin (DOX)-induced testicular toxicity in adult male Sprague–Dawley rats. DOX administration induced oxidative stress, inflammation, hormonal imbalance, and histological damage in testicular tissue. Treatment with *P. ginseng* extract significantly reduced lipid peroxidation and enhanced antioxidant defense mechanisms. Serum levels of FSH, LH, testosterone, TNF-α, IL-1β, MDA, SOD, LDH, GSH, and CAT were markedly improved in DOX-treated rats receiving ginseng compared to DOX-only controls.

Moreover, ginseng administration restored spermatogenesis and improved testicular histoarchitecture. These findings indicate that *P. ginseng* exerts a strong ameliorative effect against DOX-induced male reproductive toxicity through antioxidant and anti-inflammatory mechanisms.

2.28 Petroselinum crispum

Shipa et al. [101] evaluated the protective effects of *Petroselinum crispum* methanolic extract against acrylamide-induced reproductive toxicity in male rats. Acrylamide exposure triggered oxidative stress, inflammatory activation, impaired spermatogenesis, and disruption of steroidogenic pathways. Treatment with *P. crispum* extract mitigated these effects by restoring antioxidant enzyme activity and improving sperm parameters. It normalized the expression of inflammatory mediators (TNF-α, IL-6, IL-10, iNOS, NF-κB) and key steroidogenic genes (STAR, CYP17A1, 17β-HSD, and P450scc). Furthermore, the extract corrected acrylamide-induced alterations in NF-κB p65 and kinesin immune-expression and restored normal testicular histoarchitecture.

These findings indicate that *P. crispum* exerts protective effects against acrylamide-induced testicular injury through coordinated antioxidant, anti-inflammatory, and steroidogenic regulatory mechanisms.

2.29 Portulaca oleracea

Farag et al. [102] investigated the protective effects of *Portulaca oleracea* seed extract (POS) against acrylamide (ACR)-induced testicular dysfunction in rats. Acrylamide exposure induced marked oxidative stress, Leydig cell apoptosis, disrupted expression of proliferative (PCNA) and apoptotic (caspase-3) markers, testicular degeneration, reduced semen quality and sperm count, and impaired steroidogenesis. POS administration exerted dose-dependent protective effects by reducing oxidative stress, inhibiting apoptosis, modulating steroidogenic pathways, and improving testicular lesion grading. Treatment restored normal spermatogenesis, preserved Sertoli and Leydig cell architecture, increased testosterone levels and steroidogenic gene expression, and significantly improved overall testicular histology.

These findings demonstrate that *P. oleracea* seed extract mitigates acrylamide-induced reproductive toxicity through antioxidant, anti-apoptotic, and steroidogenic regulatory mechanisms.

2.30 Rubus apetalus

Alumeti Munyali et al. [103] investigated the antioxidant and protective effects of *Rubus apetalus* in a rat model of cryptorchidism (CPT), a major cause of male infertility. Induction of CPT resulted in reduced reproductive organ weights, impaired sperm parameters, altered testicular protein expression, disrupted sex hormone levels, compromised reproductive potential, histomorphometric abnormalities, and elevated oxidative stress. Treatment with *R. apetalus* mitigated these alterations by improving sperm quality, restoring testicular protein levels, and enhancing overall reproductive potential.

These findings suggest that *R. apetalus* exerts protective effects against cryptorchidism-induced reproductive dysfunction, primarily through its antioxidant properties.

2.31 Rhus tripartite (Ucria)

Mosaoa et al. [104] investigated the protective effects of *Rhus tripartite* methanolic extract (RTME) against reproductive toxicity induced by the endocrine disruptor propylparaben (PrP) in Wistar albino rats. Animals were allocated into four groups: control, RTME alone, PrP alone, and RTME + PrP co-treatment.

Propylparaben exposure impaired reproductive parameters and induced oxidative stress and inflammation. RTME co-administration attenuated these adverse effects by enhancing antioxidant status, reducing inflammatory markers, and increasing 5-α reductase activity. However, reproductive parameters were not fully restored to baseline levels. But the overall investigation on RTME demonstrates partial protective effects against PrP-induced reproductive toxicity, primarily through antioxidant and anti-inflammatory mechanisms.

2.32 Salvia miltiorrhiza

Salvia miltiorrhiza (red sage), a traditional Chinese medicinal herb, has been investigated for its protective effects against testicular ischemia–reperfusion (I/R) injury. Davoodi et al. [105] evaluated the hydroalcoholic extract of *S. miltiorrhiza* (SM) in adult male Wistar rats divided into three groups: control, I/R (torsion followed by detorsion after 2 hours), and SM-treated I/R (200 mg/kg intra-

peritoneal administered 30 minutes prior to detorsion). I/R injury markedly impaired sperm parameters and induced testicular tissue damage. Pre-treatment with *S. miltiorrhiza* significantly improved sperm quality, reduced histopathological alterations, and enhanced antioxidant enzyme activity.

These findings suggest that SM exerts protective effects against I/R-induced testicular damage, likely through antioxidative and cytoprotective mechanisms.

2.33 Stevia rebaudiana

Hanna et al. [106] investigated the protective effects of *Stevia rebaudiana* aqueous extract on male fertility following tartrazine-induced oxidative stress in Wistar rats. Animals were allocated into four groups: control (distilled water for 56 days), *Stevia* (1000 mg/kg), tartrazine (300 mg/kg), and a combined treatment group receiving stevia one hour prior to tartrazine administration. Tartrazine exposure impaired sperm quality and reduced testosterone, antioxidant enzyme levels, and CREM protein expression. In contrast, the combined stevia–tartrazine group demonstrated significant improvement in sperm parameters, restoration of testosterone levels, enhanced antioxidant status, and increased CREM protein expression compared to the tartrazine-only group.

These findings indicate that *S. rebaudiana* supplementation mitigates tartrazine-induced testicular oxidative damage and preserves sperm functional integrity.

2.34 Syzygium cumini

Suleman et al. [107] evaluated the ameliorative potential of *Syzygium cumini* fruit pulp extract (SPE) in bovine semen cryopreservation. Because mitochondria and plasma membranes of thawed spermatozoa are highly susceptible to oxidative stress, SPE was incorporated into the semen cryopreservation extender at varying concentrations following dilution of semen samples. Semen quality parameters were assessed before and after cryopreservation. SPE supplementation significantly improved sperm membrane integrity, motility, and fertilizing capacity compared with controls.

Overall, SPE enhanced both fresh and frozen–thawed semen quality, likely due to its rich composition of antioxidants and phytosterols that mitigate cryo-induced oxidative damage.

2.35 Syzygium aromaticum

Mishra and Singh [108], investigated the biphasic effects of *Syzygium aromaticum* flower bud aqueous extract, traditionally used to manage male sexual dysfunction. Male mice were administered 15, 30, or 60 mg/kg body weight of the extract daily for 35 days. The lowest dose enhanced male fertility parameters, whereas higher doses adversely affected reproductive organ physiology.

These findings indicate a dose-dependent biphasic response, where low-dose *S. aromaticum* exerts fertility-enhancing effects, while higher doses may induce reproductive toxicity.

2.36 Tomato

Luis Heriberto et al. [109] evaluated the therapeutic effects of whole tomato lipid extract in a diet-induced obesity model. Obesity was induced by administering a 30% (w/v) sucrose solution for three months, resulting in reduced testicular size, impaired sperm quality parameters, elevated testicular oxidative stress, and histopathological alterations in seminiferous tubules. Treatment with whole tomato lipid extract significantly reduced gonadal adipose tissue mass and oxidative stress levels, preserved testicular size, improved sperm quality indices, and restored seminiferous tubule architecture.

These findings indicate that tomato-derived lipid extracts exert protective effects against obesity-associated testicular dysfunction, likely through antioxidative and metabolic regulatory mechanisms.

2.37 Turnera diffusa

Turnera diffusa Willd. ex Schult. is traditionally recognized for its aphrodisiac properties and use in managing male reproductive dysfunction. Kumar et al. [110] demonstrated its therapeutic potential in a type 2 diabetes mellitus rat model. Administration of low and high doses of *T. diffusa* extract improved testicular steroidogenesis and spermatogenesis, thereby restoring overall testicular function and male fertility. In diabetic rats, treatment significantly reduced sperm morphological abnormalities and sperm DNA fragmentation, while restoring sperm count, motility, and viability toward near-normal levels. *T. diffusa* reduced testicular NOX-2 expression and lipid peroxidation, enhanced antioxidant enzyme activities (SOD, CAT, and GPx), and attenuated testicular inflammation. These findings support its antioxidative and anti-inflammatory role in mitigating diabetes-induced reproductive dysfunction.

2.38 Tribulus terrestris

Khaleghi et al. [111] evaluated the *in vitro* effects of *Tribulus terrestris* extract on human sperm parameters. Semen samples from healthy donors were allocated into four groups: an untreated control and three treatment groups incubated with 20, 40, and 50 mg/mL of the extract. Assessment of sperm motility, viability, and DNA fragmentation demonstrated that concentrations of 40 and 50 mg/mL significantly improved motility and viability compared with controls, without adversely affecting DNA integrity.

Overall, *T. terrestris* extract appears to enhance sperm functional competence *in vitro*, indicating potential utility in assisted reproductive technologies to improve male fertility outcomes.

Table 2. Comparative summary of plant-derived antioxidants in male reproductive function.

Plant extract	Model type	Experimental condition	Reproductive outcomes	Oxidative/mechanistic findings	Overall interpretation
Allium sativum (Garlic)	Wistar rats	Chromium toxicity; diabetes model	Improved sperm quality; reduced damage	Reduced MDA	Antioxidant and anti-diabetic reproductive protection
Ashrasi date palm	Wistar rats	Diabetes-induced damage	Improved sperm parameters and DNA integrity	Antioxidant protection	Preserves sperm DNA under hyperglycemia
Achillea tenuifolia Lam.	*In vivo* (rat)	Chronic restraint stress	↑ LH, FSH, testosterone; improved fertility parameters	↑ Total antioxidant capacity; ↓ MDA	Ameliorates stress-induced reproductive dysfunction
Cardiospermum halicacabum (L.)	*In vivo* (rat)	Normal fertility model	↑ Sperm concentration, motility; ↑ testosterone; ↑ pregnancy rate	Antioxidant-mediated mechanism	Dose-dependent fertility enhancement
Camellia sinensis L.	*In vitro* (rat sperm)	Incubation study	↑ Sperm viability (24–72 h)	EGCG-mediated antioxidant effect; prolonged exposure ↑ protein oxidation	Improves viability; high exposure may induce oxidative protein modification
Camellia sinensis (Green tea)	Rats; Mice	*In vitro* incubation; Obesity model	Improved sperm parameters (dose-dependent)	Antioxidant; protein oxidation at high exposure	Beneficial at physiological doses
Caesalpinia sappan	Wistar rats	Oral supplementation	Increased sperm motility, viability, concentration	Antioxidant activity	Dose-dependent spermatogenic enhancement
Codonopsis pilosula	Aging mice	D-galactose-induced aging	Reduced inflammatory testicular damage	Inhibited inflammasome activation	Anti-aging and anti-inflammatory testicular protection
Chlorophytum borivilianum	Mice; Human sperm (*in vitro*)	Gamma irradiation; H_2O_2-induced oxidative stress	Preserved sperm integrity and function	Radical scavenging; reduced oxidative damage	Strong antioxidant protection of sperm under oxidative stress
Citrullus colocynthis	Wistar rats	Diabetic reproductive damage	Reduced reproductive injury	Modulated oxidative and diabetic pathways	Synergistic protection with garlic
Cannabis sativa	Wistar rats	Oral ethanolic extract	Prevented oxidative damage; androgen receptor activation	Antioxidant; androgenic modulation	Modulates sperm quality via receptor pathways
Capparis spinosa	Human (*in vitro*)	24 h incubation	Preserved DNA integrity and motility	Reduced oxidative stress	Supports human sperm preservation
Cranberry extract	Wistar rats	Phenobarbital-induced toxicity	Improved sperm and testicular parameters	Anti-apoptotic; antioxidative	Protective against drug-induced reproductive damage
White mulberry *(Morus alba)*	Wistar rats	Carmustine toxicity	Prevented spermatological damage	Antioxidant-mediated protection	Effective chemotoxic protective agent
Eruca sativa	Wistar rats	BPA-induced toxicity	Improved histological and hormonal parameters	Restored antioxidant balance	Protects against endocrine disruptor damage
Entada abyssinica	Ram (*in vitro*)	Cryopreservation extender	Improved post-thaw sperm resistance	Prevented lipid peroxidation	Useful semen extender antioxidant
Echinacea	Ram (*in vitro*)	Cryopreservation extender	Improved frozen-thawed sperm quality	Antioxidant effect	Enhances semen preservation
Ferulago angulata	Mice	Lead & diazinon toxicity	Improved sperm cryotolerance	Antioxidant protection	Counters environmental toxicant damage
Ficus carica	Mice	Formaldehyde toxicity	Improved sperm count and GSI	Reduced oxidative damage	Partial reproductive restoration
Hygrophila spinosa	Wistar rats	Oral alkaloidal fraction	Increased testosterone; stimulated Leydig cells	Androgenic stimulation	Spermatogenic enhancer
Lycium barbarum	Mice; Human clinical	Diabetes; Ethanol toxicity; Clinical trial	Improved spermatogenesis; reduced oxidative stress	Anti-apoptotic; antioxidant; reduced collagen deposition	Strong translational evidence
Lepidium sativum	SD rats	Oral supplementation	Stimulated spermatogenesis	Antioxidant action	Fertility-enhancing

Table 2. Continued.

Plant extract	Model type	Experimental condition	Reproductive outcomes	Oxidative/mechanistic findings	Overall interpretation
Lavender (Lavandula)	Ram (*in vitro*)	Cryopreservation	Improved post-thaw sperm quality	Antioxidant membrane stabilization	Beneficial semen additive
Mucuna pruriens	Wistar rats	High-fat diet model	Improved spermatogenesis and hormones	Antioxidant; metabolic modulation	Reverses obesity-induced infertility
Momordica charantia	Wistar rats	Chronic stress	Restored reproductive function	Antioxidant; modulated protein phosphorylation	Anti-stress reproductive protection
Moringa oleifera	Roosters; Leydig cells	Dietary supplementation; *in vitro*	Increased fertility and androgenic activity	Antioxidant enzyme activation	Androgenic and antioxidant effects
Olea europaea (Olive leaf)	Wistar rats	Rotenone toxicity	Improved sperm quality; ↓ MDA	Increased TAC	Strong testicular antioxidant
Origanum majorana	SD rats	Oral supplementation	Enhanced fertility	Antioxidant effect	Spermatogenic stimulation
Opuntia sp.	*In vitro*	Testicular injury	↑ Sperm quality	Anti-inflammatory & antioxidant	Tissue protective
Opuntia ficus-indica	Rats; Human (*in vitro*)	MTX toxicity; Cryopreservation	Improved sperm quality	Antioxidant; fertility boosting	Protective against chemotoxicity
Origanum vulgare	Ram (*in vitro*); Mice	Capacitation; Finasteride toxicity	Improved sperm characteristics; protected testis	Anti-apoptotic; antioxidant	Protects against drug-induced damage
Panax ginseng	SD rats	Doxorubicin toxicity	Prevented testicular injury	Modulated NF-κB/COX2/AR pathways	Strong anti-inflammatory antioxidant
Petroselinum crispum	Rats	Acrylamide-induced toxicity	Improved reproductive impairment	Inhibited NF-κB; modulated steroidogenesis	Anti-inflammatory and antioxidant protective effect
Portulaca oleracea	Wistar rats	Acrylamide toxicity	Restored steroidogenesis	Antioxidant; anti-apoptotic	Protective against toxicant-induced dysfunction
Palm Pollen + Pomegranate Peel	Rabbits	90-day supplementation	Improved sperm development	Antioxidant	Reproductive disorder effectively treated
Rumex hastatus	SD rats	Triclosan toxicity	Improved fertility	Reduced oxidative stress	Mitigates endocrine toxicant damage
Rubus apetalus	Wistar rats	Cryptorchidism	Improved fertility potential	Increased antioxidant enzymes	Potential infertility therapy
Rhus tripartite	Wistar rats	Propylparaben toxicity	Reduced testicular injury	Anti-inflammatory; enhanced 5-α reductase	Protects against endocrine disruptors
Thymus vulgaris	Rats	Cadmium toxicity	Mild amelioration	Antioxidant activity	Limited but protective
Tribulus terrestris	Human (*in vitro*)	Sperm incubation	Improved sperm parameters	Antioxidant-mediated	Direct sperm quality enhancement
Turnera diffusa	SD rats	Type 2 diabetes	Restored steroidogenesis	Antioxidant; endocrine modulation	Improves diabetic reproductive impairment
Withania frutescens	Albino rats	Lead toxicity	Prevented testicular damage	Antioxidant bioactives	Protective against heavy metal toxicity
Zingiber officinale (Ginger)	Human; Roosters; Ram (*in vitro*)	Clinical trial; Dietary supplementation; Cryopreservation	Reduced SDF; Improved motility & fertility	Enhanced seminal antioxidant status	Clinically relevant antioxidant

2.39 *Thymus vulgaris*

Onoja et al. [112] investigated the protective effects of *Thymus vulgaris* extract against cadmium-induced testicular toxicity in male rats. Cadmium exposure resulted in marked histopathological alterations, increased oxidative stress, reduced sperm count, and disrupted sex hormone levels.

Although *T. vulgaris* extract exhibited partial protective effects, it did not completely reverse cadmium-induced reproductive damage. These findings indicate limited but measurable antioxidant and cytoprotective activity of *T. vulgaris* in heavy metal–induced testicular injury.

2.40 *Withania frutescens*

Bentaiba et al. [113] evaluated the protective effect of *Withania frutescens* root extract against lead-induced reproductive toxicity in rats. Lead exposure caused marked histopathological alterations in testicular tissue, reduced serum testosterone levels, decreased sperm count, and lowered the tubular differentiation index (TDI) and spermiogenesis index (SPI).

In contrast, rats treated with *W. frutescens* alone, as well as those co-treated with lead and the extract, showed significant mitigation of these adverse effects. The extract improved testosterone levels, increased sperm count, and restored TDI and SPI values, while attenuating lead-induced histological damage. *W. frutescens* root extract demonstrates substantial protective and restorative effects against heavy metal–induced testicular dysfunction, likely mediated through its antioxidant properties.

2.41 *Zingiber officinale*

Ginger root is rich in bioactive phenolic compounds such as gingerols, shogaols, and gingerdiol, which exert potent antioxidant activity and may enhance semen quality. Hosseini et al. [114] evaluated the effect of *Zingiber officinale* on sperm DNA fragmentation (SDF) in infertile men. Participants were randomized into ginger and placebo groups; the treatment group received 500 mg/day of ginger powder (two 250 mg capsules) orally for three months. Semen parameters were assessed before and after intervention, and ginger supplementation significantly reduced SDF levels compared to placebo.

In an avian model, Nemati et al. [115] examined the impact of dietary ginger supplementation on aging broiler breeder roosters. Ginger administration improved the testicular spermiation index, seminal antioxidant capacity, and sperm motility, indicating enhanced reproductive performance.

Similarly, Merati and Farshad [116] investigated the addition of ginger and echinacea extracts to semen freezing extenders for ram epididymal spermatozoa. Supplementation enhanced mitochondrial activity, acrosomal integrity, and overall post-thaw sperm quality. The findings suggest that ginger, alone or in combination with other natural antioxidants, improves sperm functional parameters and fertility potential across species.

Plant-derived antioxidants demonstrate substantial potential in mitigating oxidative stress–mediated male reproductive dysfunction. By attenuating reactive oxygen species (ROS) and enhancing endogenous antioxidant defense systems, plant-derived compounds appear to protect germinal epithelium integrity and preserve sperm functional capacity. Their primary mechanism appears to involve restoration of redox homeostasis, leading to improvements in spermatogenesis, steroidogenesis, and sperm quality parameters. Notably, extracts rich in polyphenols and flavonoids demonstrated broader antioxidant enzyme modulation compared to extracts with less characterized phytochemical composition. Table 2 shows the comparative summary of various plant-derived antioxidants functions in male reproduction highlighting their reproductive outcomes and oxidative/mechanistic findings of respective plant extracts. The majority of investigated plant extracts exert beneficial effects on male reproductive function primarily through attenuation of oxidative stress, restoration of steroidogenesis, and preservation of spermatogenic integrity.

However, efficacy is context-dependent, dose-sensitive, and heterogeneous across plant types and experimental models. While promising, plant antioxidants should not be considered universal fertility enhancers but rather targeted modulators within oxidative stress–associated infertility paradigms.

3. Discussion

Oxidative stress (OS) is a central pathophysiological mechanism in male infertility, contributing to lipid peroxidation, mitochondrial dysfunction, sperm DNA fragmentation (SDF), and impaired spermatogenesis. Multiple antioxidants have therefore been investigated as therapeutic strategies for targeting redox imbalance. The antioxidant compounds investigated in these studies and their reported effects are summarized in Tables 1,2, whereas detailed information on the treatment protocols, doses, routes of administration, and experimental conditions is provided in **Supplementary Tables 1,2**. It is found that therapeutic antioxidants significantly improve spermatogenesis, sperm function, mitochondrial integrity, and steroidogenesis while protecting against oxidative and toxicant-induced testicular injury by reducing lipid peroxidation and enhancing total antioxidant capacity. Deficiencies in key antioxidants-such as vitamins C, E, folate, zinc, selenium, and carnitine have been associated with impaired spermatogenesis and elevated sperm DNA fragmentation, supporting the biological plausibility of antioxidant therapy in male infertility. Accumulating experimental and clinical evidence suggests that plant-derived antioxidants, vitamins, minerals, and micronutrients can ameliorate oxidative stress–mediated testicular dysfunction and improve conventional

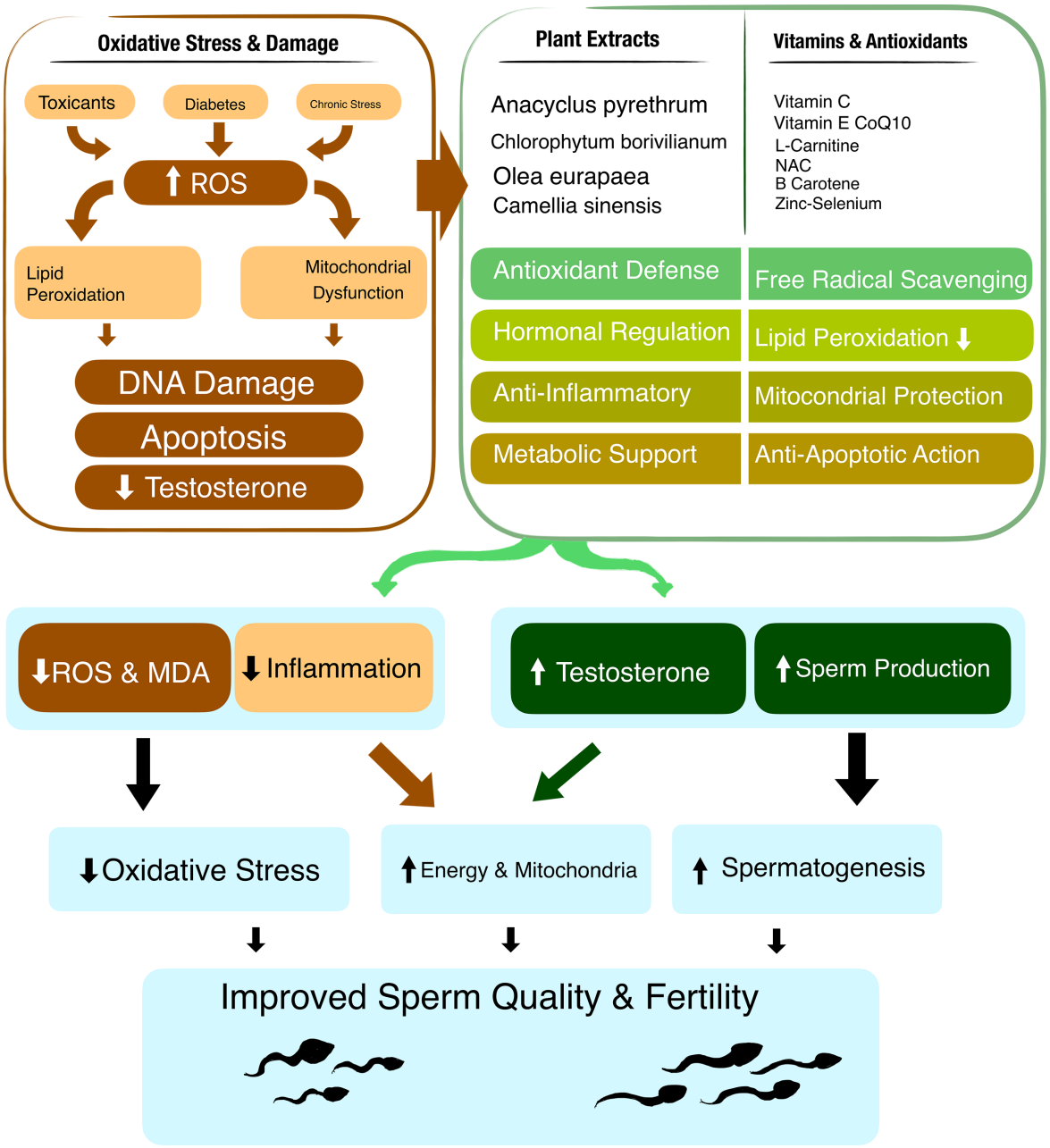

Fig. 4. Shows the summary of proposed mechanisms underlying antioxidant-mediated improvement of male fertility. ROS, Reactive Oxygen Species; MDA, Malondialdehyde. up arrow = increase, down arrow = decrease (created using Adobe Fresco and Sketchbook).

semen parameters. Mechanistically, these agents are proposed to reduce reactive oxygen species (ROS), attenuate lipid peroxidation, enhance mitochondrial bioenergetics, stabilize sperm DNA integrity, and support steroidogenesis. Across rodent toxicological, stress-induced and metabolic infertility models, consistent improvements were observed in sperm concentration, motility, viability, and testosterone levels. Overall, evidence suggests that antioxidant supplementation primarily improves functional sperm parameters (motility, morphology, concentration). Moreover, it reduces sperm DNA fragmentation and can even improve pregnancy and live birth rates, particularly in ART settings. Antioxidant therapy represents a promising pharmacological strategy for preserving male fertility and mitigating reproductive toxicity.

However, high-quality randomized controlled trials (RCTs) have produced inconsistent clinical outcomes. In a large multicenter RCT, Steiner et al. [117] reported that daily supplementation for three months with a combined antioxidant formulation (zinc, vitamin C, selenium, folic acid, L-carnitine, vitamin E, and lycopene) did not improve semen parameters, *in vivo* pregnancy rates, or live-birth rates

compared with placebo in couples with documented ovulatory and tubal patency. Similarly, Schisterman et al. [118] found no significant benefit of folic acid plus zinc supplementation on live birth rates or semen quality. In a more targeted clinical context, Chayachinda et al. [119] observed no additive improvement in total sperm motility when coenzyme Q10 was administered alongside doxycycline in men with pyospermia. Also, despite the antioxidant role in improving fertility, evidence showed an inconsistent sperm concentration and the dose dependent toxicity is possible in some antioxidant therapy.

4. Conclusion and Future Avenues

The effect of various antioxidants from diverse source including plant extracts, vitamins, minerals and or through diet might have a positive impact on the male fertility (Fig. 4). From all the studies, it can be concluded that oxidative stress is an important contributing factor in male infertility, with elevated seminal ROS reported in a substantial proportion of infertile men. However further research and study need to conclude its effect as well as its interference in fertility. Overall, while mechanistic and preclinical data support a role for antioxidants in restoring redox homeostasis and testicular function, robust clinical evidence remains heterogeneous. The therapeutic benefit appears context-dependent, influenced by baseline oxidative status, etiology of infertility, dosage, formulation, and treatment duration. Future precision-based approaches incorporating oxidative stress biomarkers and individualized supplementation strategies may clarify which subgroups derive genuine reproductive benefit. Thus, antioxidant therapies, which consist of dietary supplementation therapy with one or more antioxidant compounds, may represent a potential adjunctive approach in appropriately selected patients with oxidative-stress-associated infertility. It may also be important to have more studies on the effects of formulation, which may consist of antioxidant from plant sources, vitamin and other nutraceuticals in humans as well as in experimental animals. These findings would further pave the way for better management of male infertility by utilizing these antioxidant compounds.

Author Contributions

VN, GG, RKK, VKR: conceived the idea for study. VN: wrote the first draft. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/IJP50143.

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