

Supplement Table 3. Inclusion and exclusion criteria of the patients enrolled in the studies included in this meta-analysis

Reference	Year	Study design	Inclusion criteria	Exclusion criteria
Eslamian et al [51]	2020	RCT	Healthy, voluntary, idiopathic asthenozoospermic men, aged 20–45 years, unwanted childlessness for ≥ 1 years with the same female partner, normal endocrine function, and with the total number (or concentration) of spermatozoa, and percentage of morphologically normal spermatozoa, equal to or above the lower WHO reference limits.	1) To have abnormal testis, cryptorchidism, varicocele, had genital surgery, abnormal karyotypes, or endocrine hypogonadism detected via physical examination and paraclinical testing; 2) A history of the use of antioxidant and ω-3 supplements within the previous 3 months; 3) A history of receiving radiation and/or chemotherapy, testosterone, and antiandrogens; 4) Genital tract infection or use of medication for this condition within the previous 3 months; 5) Being a candidate for ICSI owing to severe sperm motility failure; 6) Exposure to extreme heat and/or pollutants such as pesticides, chemical solvents, heavy metals, and/or radioactive agents; and 7) Enrollment or planned enrollment in other research that might conflict with full participation in the current study or confound the observation or interpretation of the study findings.
Kopets et al [38]	2020	RCT	Age 21–50 years, idiopathic male infertility (absence of conception in a couple having regular unprotected intercourse for 12 months with a woman without evident pathology), OAT.	Genetic, anatomical, inflammatory, trauma, testicular cause of male infertility, cause of female infertility, STIs, inflammatory bowel disease, alcohol or drug addiction.
Steiner et al [42]	2020	RCT	Couples with at least 12 months of infertility were included in the study. Male partners were 18 years of age or older with at least one abnormal semen parameter in the preceding 6 months: sperm concentration ≤ 15 million/mL (oligospermia), total motility ≤ 40% (asthenospermia), normal morphology ≤ 4% (teratospermia), or DNA fragmentation ≥ 25%. Female partners were between 18 and 40 years of age with regular menstrual cycles, defined as 25–35 days in duration, and evidence of ovulation by biphasic basal body temperature, ovulation predictor kits, or luteal serum progesterone level ≥ 3 ng/mL; and a normal uterine cavity with at least one patent Fallopian tube. Women over the age of 35 had normal ovarian reserve, defined as an early follicular phase FSH ≤ 10 IU/L, AMH ≥ 1.0 ng/mL, or antral follicle count > 10.	Male partners were excluded if they had a sperm concentration less than 5 million/mL or if they were taking fertility medication or testosterone. Men were required to be off all vitamins for 4 weeks prior to randomization.
Ardestani Zadeh et al [27]	2019	RCT	Infertile patients with varicocele who underwent sub-inguinal varicocelectomy.	Usage of supplements, vitamins or alcohol, tobacco smoking, addiction to opium or using the opium during the follow-up period, diabetes mellitus, peptic ulcer history, hormonal disorders (based on clinical history and medical examination), chronic or active genitourinary infection (according to the history, medical examination, urine and semen analysis) and previous reaction to folic acid, selenium or vitamin E. As well, patients with missed follow-up, incorrect usage of drugs, presenting side effects, and delayed complications of varicocelectomy including recurrent varicocele, hydrocele or testicular atrophy were excluded from the study.
Kizilay et al [28]	2019	RCT	Infertile (> 12 mo) patients with OAT with grade I–III varicocele, spouses < 35 years, no female infertility.	Genitourinary system and/or varicocele surgery, idiopathic infertility, disease affecting fertility, medical treatment affecting fertility, undescended testis, testicular cancer, testicular trauma, post-pubertal mumps, endocrine disorder, obstructive urogenital disease, HIV, acute infection, fertility-specific diet, alcohol, drugs, cigarettes, opioids and hallucinogens.

Supplement Table 3. Continued 1

Reference	Year	Study design	Inclusion criteria	Exclusion criteria
Nouri et al [60]	2019	RCT	Infertile men aged between 25–45 years, a sperm count of less than 20 million per milliliters, normal sperm of <65% and sperm volume of <3.0 mL, and average motility of <60% while receiving no treatments.	History of disorders (urinary tract infection, testicular atrophy, testicular torsion, azoospermia, asthezoospermia, inguinal and genital surgery, genital trauma, and other genital diseases, such as current genital inflammation and cryptorchidism), anatomical disorders, endocrinopathy, previous hormonal therapy, use of androgens, antiandrogens, anticoagulants, cytotoxic drugs, or immunosuppressants. Patients with physiological and psychiatric disorders that could affect sperm and sexual performance, alcohol and drug abuse, and BMI of ≥ 30 kg/m ² were also excluded.
Blomberg Jensen et al [69]	2018	RCT	Impaired semen quality (determined by WHO criteria) and vitamin D insufficiency (25-OHD level <50 nmol/L).	Serious comorbidities.
Busetto et al [36]	2018	RCT	Age 18–50 years, oligo-, astheno- and/or teratozoospermia, with or without varicocele, having a history of infertility for more than 12 months. Varicocele patients were not surgically treated before and during the treatment, patients without varicocele were suffering from idiopathic male infertility, no other previous history of diseases affecting fertility. Fertile female partners were required with regular menstrual cycles, age <40 years and couples not looking for fertility-related procedures (IVF/ICSI/IUI) for the next 90 days.	Known hypersensitivity to any of the treatment compounds, history of undescended testes or cancer, endocrine disorders, history of post-pubertal mumps, genitourinary surgery, obstructive azoospermia or obstructive pathology of the urogenital system, autoimmune disease, cystic fibrosis, history of taking any therapy affecting fertility within last 3 months, excessive consumption of alcohol or regular use of illicit or "recreational" drugs, positive serology for HIV, participants following any special diet, any condition which in the opinion of the investigator might put the participant at risk by participating in this study, participants involved in any other clinical trials.
Lu et al [55]	2018	RCT	The patients were diagnosed with a left-sided clinical varicocele in the urology clinic. Fifty-four patients who were mildly oligospermic (sperm count: 5–15 million) and could not have a child for at least 1 year were included.	Not specified.
Stenqvist et al [43]	2018	RCT	Normal reproductive hormone levels and high SDF ($\geq 25\%$).	Smoking, use of anabolic steroids, AOX, anti-hypertensive drugs, statins, obesity and hypogonadism.
Busetto et al [35]	2017	RCT	Infertile patients with oligo- and/or astheno- and/or teratozoospermia, history of infertility for more than 12 months.	Subjects with known hypersensitivity to any of the treatment compounds, history of undescended testes or cancer, endocrine disorders, history of post-pubertal mumps, genitourinary surgery, obstructive azoospermia or obstructive pathology of the urogenital system, autoimmune disease, cystic fibrosis, history of taking any therapy affecting fertility within last 3 months, excessive consumption of alcohol or regular use of illicit or "recreational" drugs, positive serology for HIV, subjects following any special diet, any condition which in the opinion of the investigator might put the subject at risk by participating in this study and subjects involved in any other clinical trials. Female factor excluded.

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Reference	Year	Study design	Inclusion criteria	Exclusion criteria
Barekat et al [29]	2016	RCT	Age <45 years, primary infertility, left-sided varicocele (grade 2–3) diagnosed by palpation and Doppler duplex ultrasound. Female partner with age <35 years, normal ovulatory cycles and patent tubes (confirmed by hysterosalpingography or laparoscopy)	Varicocele grade I, azoospermia, recurrent varicocele, leukocytospermia, urogenital infections, testicular size discrepancy, abnormal hormonal profile, anatomical disorders, Klinefelter's syndrome, cancer, fever in the 90 days prior to surgery, seminal sperm antibodies, excessive alcohol and drug consumption, previous history of scrotal trauma or surgery and occupational exposure. Female partner with endometriosis, cycle irregularity, or gross anatomical abnormalities was also excluded.
Ener et al [30]	2016	RCT	Males diagnosed with a left-sided clinical varicocele in the urology outpatient clinic, and for whom subinguinal varicocelectomy was planned.	The use of alcohol, tobacco or any drugs including vitamins.
Boonyarangkul et al [46]	2015	RCT	Abnormal semen analysis of at least one parameter according to WHO criteria 2010 (concentration <15 million/mL, motility <40%, or morphology <4%), failure of the female partner to conceive after one year of regular unprotected sexual intercourse, no history of tamoxifen and folate allergy.	Use of tamoxifen and folate within three months before recruitment, use of other medicines or vitamin during the study period.
Cyrus et al [31]	2015	RCT	A palpable varicocele in physical examination and accompanying abnormalities in count, motility, or morphology of sperm in two separate semen analyses (according WHO criteria 1999), age range between 18 and 50 years, weight between 50 and 100 kg and being married.	Missed follow-up, incorrect usage of the capsules, demonstrating side effects due to vitamin C, commencement of smoking or opium addiction during the follow-up period, delayed complications of varicocelectomy such as: hydrocele, recurrence of varicocele, and testicular atrophy. Azoospermia, diabetes mellitus, hormonal disorders (according to medical history and clinical examination), tobacco smoking, opium or recreational drugs addiction, regular usage of vitamins or nutritional supplements, acute or chronic genitourinary infection (based on medical history, physical examination, semen and urine analysis), history of peptic ulcer and previous reaction or intolerance to vitamin C.
Haghighian et al [53]	2015	RCT	Unwilling childlessness at least 24 months in duration with a female partner, no medical condition that could account for infertility, normal fertile female partner according to investigations, all patients were needed to have stopped all medical therapy 12 weeks before the study initiation.	History of epididymo-orchitis, prostatitis, genital trauma, testicular torsion, inguinal or genital surgery, urinary tract infection, or previous hormonal therapy, another genital disease (cryptorchidism, current genital inflammation or varicocele), severe general or central nervous system disease and endocrinopathy, use of cytotoxic drugs, immunosuppressants, anti-convulsants, androgens, or antiandrogens, recent history of STI, psychologic or physiologic abnormalities that would impair sexual performance or the ability to provide semen samples, drug or alcohol abuse, hepatobiliary disease, significant renal insufficiency, occupational and environmental substances to possible reproductive toxins, BMI of >30 kg/m ² , participation in another investigational study, unlikely availability for follow-up.
Moslemi Mehni et al [57]	2014	RCT	Age 25–40 years, infertile men with OAT, healthy fertile wives.	Existence of genital abnormalities (undescended testes, varicocele, atrophy of testes), occupational chemical exposure history, systemic diseases, abnormal semen volume, pH, agglutination or viscosity, serum hormonal abnormalities (FSH, LH, testosterone, estradiol, PRL), wives with known fertility risk factors confirmed by gynecologist.

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Reference	Year	Study design	Inclusion criteria	Exclusion criteria
Azizollahi et al [32]	2013	RCT	The presence of grade III varicocele assessed by clinical parameters and was confirmed by Doppler ultrasound scanning.	Evidence of leukocytospermia, low testicular volume <15 mL, congenital urogenital abnormalities and urogenital infections.
da Silva et al [49]	2013	RCT	Subfertile male patients who did not take any additional supplement and/or vitamin other than the supplement provided, and who did not change eating habits during the follow-up period.	All the men were required to be between the ages of 20 and 55 years at the time of enrollment. Patients with high FSH serum levels, azoospermia and patients treated with clomiphene citrate were excluded.
Gopinath et al [37]	2013	RCT	Age 21–50 years, infertility >1 year, sperm count less than 15 million/mL, sperm total motility <40%, no history of taking therapy for infertility, no history of OAT, regular sexual intercourse with a potentially normal fertile female, willing to sign informed consent and likely to be available for all visits during follow-up period.	Primary testicular disease, any organic cause for infertility including varicocele, prostate-vesiculo-epididymitis, genital infectious disease, planning for any other ART during study period, serum FSH >15 mIU/mL, abnormal serum levels of LH, testosterone, estradiol and PRL, presence of antispermatozoa antibodies, severe oligospermia (<2 million sperm/mL), azoospermia, seminal WBCs more than 10 ⁶ /mL, major hepatic and renal disease, myopathy, history of allergy to any ingredient of the formulation, not likely to be available for follow-up, have participated in another clinical trial in the past 3 months, female partners with anatomic or physiological alterations causing subfertility.
Safarinejad et al [64]	2012	RCT	History of primary infertility of more than 2 years, abnormal sperm count and motility according to WHO criteria, wife's age between 20 and 40 years, documentation of fertile female partner, no known medical or surgical condition which can result in infertility.	History of cancer chemotherapy or radiotherapy, history of genital disease such as cryptorchidism and varicocele, history of genital surgery, BMI 30 kg/m ² or greater, any endocrinopathy, Y chromosome microdeletion or karyotype abnormalities, leukocytospermia (more than 10 ⁶ WBC per mL), drug, alcohol or substance abuse, tobacco use, use of anticonvulsants, androgens or antiandrogens, significant liver (serum bilirubin greater than 2.0 mg/dL) or renal dysfunction (serum creatinine greater than 2.0 mg/dL), occupational and environmental exposure to reproductive toxins, severe oligozoospermia (less than 5×10 ⁶ /mL), azoospermia and testicular volume less than 12 mL.
Nadjarzadeh et al [59]	2011	RCT	OAT, infertility (having been trying for pregnancy for >1 year unprotected intercourse).	Seminal WBC >1,000,000 /mL, presence of anatomical abnormalities of the genital tract, presence of infectious genital diseases or systemic diseases, presence of treatment with other drugs and dietary supplement during the 3 months before enrolling in the study, currently smoking, using drug, or alcohol use or occupational chemical exposure.
Safarinejad [65]	2011	RCT	Unwanted childlessness of at least 24 months.	Female infertility, abnormal testis, cryptorchidism, varicocele, genital surgery, Y chromosome microdeletion, abnormal karyotype, azoospermia, hormonal abnormality, history of cancer chemotherapy, thymidine/thymidine, anti-androgens and AOX usage, smoking, medical problems associated with decreased fertility, hepatobiliary disease, renal insufficiency, BMI ≥30 kg/m ² , occupational and environmental exposure.
Dimitriadis et al [50]	2010	RCT	Unclear	Unclear

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Reference	Year	Study design	Inclusion criteria	Exclusion criteria
Martinez-Soto et al [56]	2010	RCT	Men suffering from male factor infertility, according to the WHO guidelines (WHO 1999), and who were undergoing infertility evaluation during the period 2009 to 2011.	Oncological patients, those suffering from metabolic disease, chromosomal or genetic alterations, and patients on anticoagulant treatment.
Morgante [58]	2010	RCT	Age 28–45 years, sperm concentration $<20 \times 10^6$ spermatozoa/mL, sperm progressive motility $<30\%$, normal morphology $<30\%$, leucocyte $<1 \times 10^6$ /mL, no infections.	Men younger than 28 and over 45, sperm concentration $>20 \times 10^6$ spermatozoa/mL, sperm progressive motility $>30\%$, normal morphology $>30\%$, leucocyte $>1 \times 10^6$ /mL, current infections, history of testicular pathology: cryptorchidism, varicocele, surgical operations, radiotherapy or chemotherapy, use of anabolic steroids, deficiency of hypothalamic-pituitary-gonadal axis, genital tract infections.
Peivandi et al [62]	2010	RCT	At least two abnormal sperm analyses based on WHO criteria with a two-week interval during four weeks, normal range of gonadotropins, testosterone and PRL concentrations.	Varicocele, testicular atrophy, ejaculatory disorders, use of medications, azoospermia, endocrinological disorders, ICSI candidacy or other causes of infertility.
Balercia et al [34]	2009	RCT	Age 20 to 40 years, infertility >2 years, regular sexual intercourse with a potentially fertile female, normal rheologic characteristics (appearance, consistency and liquefaction) of semen and volume and pH in normal range, sperm count $>20 \times 10^6$ /mL, sperm motility $<50\%$ (WHO 1999), normal morphology $>30\%$, seminal WBC $<1 \times 10^6$ /mL and a negative sperm culture, normal levels of gonadotropins.	Genital disease and anatomical abnormalities of the genital tract including varicocele, systemic disease, treatment with other drugs within 3 months of being enrolled in the study. Smoking, alcohol and drug addiction and exposure to occupational chemicals.
Ciftci et al [47]	2009	RCT	Patients with idiopathic infertility with normal sperm parameters.	Infertile patients with well-known pathologic features such as varicocele, leukospermia, hormonal abnormalities, and/or obstruction were excluded from the study. The additional exclusion criteria included the presence of cryptorchidism, vasectomy, abnormal liver function, cigarette smoking, and alcohol consumption.
Safarinejad and Safarinejad [66]	2009	RCT	Sperm count $>5 \times 10^6$ /mL, over 2 years of failed conception, no female fertility problems, no history of possible cause for male infertility.	Abnormal testes, history of cancer or chemotherapy, testosterone or antiandrogen usage, usage of selenium or N-acetylcysteine supplements, abnormal hormone levels, genital disease, genital inflammation or varicocele, history of genital surgery, major surgery, central nervous system injury, a known sperm defect or retrograde ejaculation. Y chromosome abnormalities, sexually transmitted disease, genitourinary infection, leukocytospermia, smoking, any environmental exposures to reproductive toxins. Medical, neurological or psychological problems. A history of drug or alcohol abuse, hepatobiliary disease or significant renal insufficiency. Any endocrine abnormality, BMI of 30 kg/m^2 or over, participation in another investigational study and a likelihood of being unavailable for follow-up.

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Reference	Year	Study design	Inclusion criteria	Exclusion criteria
Safarinejad [67]	2009	RCT	Minimum 2 years unprotected intercourse with 2 years unwilling childlessness. Male infertility diagnosed if 1 or more standard semen parameters were below cutoff levels accepted by WHO. A fertile female partner. No known medical condition that could account for infertility, testicular volume 12 mL or greater. No medical therapy for at least 12 weeks before the study begins. Only patients seeking medical attention for infertility were included.	Azoospermia or severe oligozoospermia (sperm count less than 5 million/mL). A history of epididymal-orchitis, prostatitis, genital trauma, testicular torsion, inguinal or genital surgery. Any genital or central nervous system disease, endocrinopathy, usage of cytotoxic drugs, immunosuppressants, anticonvulsives, androgens, antiandrogens, a recent history of sexually transmitted disease. Psychological or physiological abnormalities that would impair sexual functioning or ability to produce sperm samples. Drug, alcohol or substance abuse. Liver disease, renal insufficiency or chromosome abnormalities. Occupational and environmental exposures to reproductive toxins. A BMI of 30 kg/m ² or over, participation in another investigational study and a likelihood of being unavailable for follow-up.
Stanislavov et al [68]	2009	RCT	The patients were aged between 30 and 50 years. They had been in a stable sexual partnership for the past 6 months persisting over the whole period. The duration of infertility was more than 2 years and had different deviations in sperm concentration, motility and morphology in terms of semi-logical nomenclature: oligo-, astheno, teratozoospermia or a combination of these deviations, according WHO Laboratory Manual (WHO, 1999).	Testicular maldescent, varicocele, orchitis, globozoospermia, infections, disturbances of semen deposition (hypospadias), severe cardiovascular disease, severe hypertension ≥ 90 mmHg; ≥ 150 mmHg, renal failure, hepatic insufficiency, endocrine hypogonadism abnormality, psychiatric disorders, testicular tumors; treatment of ED with any drugs during the past 4 weeks.
Ornu et al [61]	2008	RCT	Asthenozoospermia with normal sperm concentration (20 to 250 million/mL) but with 40% or more immotile sperm.	Sperm concentration of <20 million/mL.
Paradiso Galatioto et al [40]	2008	RCT	Having performed a retrograde embolization with concomitant oligospermia, persistent oligospermia and infertility >12 months.	Smoking, alcohol consumption, taking any fertility drugs within 3 months prior to the study, serious medical or psychiatric condition, abnormal hormonal profile, sperm infection.
Sigman et al [71]	2006	RCT	Males 18 to 65 years with infertility of at least six months duration, sperm concentration of at least 5 million sperm/mL, motility of 10% to 50%, absence of pyospermia and normal FSH and testosterone levels.	History of post-pubertal mumps, cryptorchism, vasal or epididymal surgery, history of medication or chemotherapy. Alcohol and chronic marijuana usage. Usage of testosterone or steroids. Exposure to environmental toxins. Recent history of fever. Having a history of diabetes, liver failure, renal failure, endocrine disorder, untreated varicocele, urogenital infection, or prior vasectomy reversal.
Balercia et al [33]	2005	RCT	Primary infertility ≥ 2 years after regular intercourse with a fertile woman, 20 to 40 years of age, normal rheologic characteristics, sperm count $>20 \times 10^6$ /mL, sperm motility $<50\%$, normal sperm morphological features $>30\%$, seminal WBC $<1 \times 10^6$ /mL, negative sperm culture and Chlamydia trachomatis and Ureaplasma urealyticum infection, normal serum gonadotropins, testosterone, E2 and PRL.	Infectious or genital disease, anatomic abnormalities of the genital tract, systemic diseases or treatment with other drugs within the 3 months before enrollment in the study, smoking, alcohol or recreational drug use or occupational chemical exposure.
Greco et al [52]	2005	RCT	Men consulting for infertility in whom previously performed TUNEL assay showed the presence of fragmented DNA in more than or equal to 15% of ejaculated spermatozoa.	Varicocele, genitourinary inflammation, or infection, and smokers.

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Reference	Year	Study design	Inclusion criteria	Exclusion criteria
Lenzi et al [54]	2003	RCT	OAT, age between 20 to 40 years, infertility >2 years with regular intercourse, without a history of endocrine disease, cryptorchidism, genital infections or obstructions, varicocele or testicular hypertrophy and anti-sperm antibodies.	None
Závczki et al [45]	2003	RCT	Unsuccessful pregnancy attempts for over one year. A healthy female partner examined by a gynecologist. Sperm volume <2 mL and/or sperm concentration <20 million/mL and/or morphology ratio <30% and/or motility <50%. No genital tract infection, no bacteria or fungi in urine or semen. Hormones are within physiological range. Intact renal function. No excessive magnesium intake.	Unclear
Conquer et al [48]	2000	RCT	Asthenozoospermic, sperm motility <50% of total sperm.	Unclear
Rolf et al [63]	1999	RCT	Asthenozoospermia (<50% motile) diagnosed after 2 examinations, normal or reduced sperm concentration ($>20 \times 10^6$ per ejaculate) and without infection of accessory glands.	Unclear
Omu et al [39]	1998	RCT	Asthenozoospermia with normal sperm concentration (20 to 250 million/mL) but with 40% or more immotile sperm.	Sperm concentration of < 20 million/mL.
Scott et al [41]	1998	RCT	Low sperm motility.	Not specified
Suleiman et al [44]	1996	RCT	Asthenospermia ($\geq 20 \times 10^6$ /mL). Sperm motility $\leq 40\%$, normal sperm count, leucocyte concentration <5%, normal fructose concentration, normal female.	Unclear
Dawson et al [70]	1990	RCT	Sperm agglutination over 25%, negative sperm antibodies, physically normal, no inflammatory disease.	Unclear

AMH: anti-Müllerian hormone, AOX: antioxidant, ART: assisted reproductive technique, BMI: body mass index, E2: 17 β -estradiol, ED: erectile dysfunction, FSH: follicle-stimulating hormone, HIV: human immunodeficiency virus, ICSI: intracytoplasmic sperm injection, ILU: intrauterine insemination, IVF: *in vitro* fertilization, LH: luteinizing hormone, OAT: oligo-astheno-teratozoospermia, PRL: prolactin, RCT: randomized controlled trial, SDF: sperm DNA fragmentation, STI: sexually transmitted infection, TT: thymidine/thymidine, TUNEL: terminal deoxynucleotidyl transferase dUTP nick-end labeling, WBC: white blood count, WHO: World Health organization, 25-OHD: 25-hydroxy vitamin D.