



Effects of Withania Somnifera (Ashwagandha) Supplementation on Oxidative Stress Response: A Systematic Review of Human and Animal Studies in Various Exercise and Non-Exercise Models

REVIEWS

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ABSTRACT

This study aimed to determine how ashwagandha supplementation affects oxidative stress. For our systematic review, we searched several literature databases, including Science Direct and PubMed. Articles on physical activity, ashwagandha, and oxidative stress published between 2011 and 2025 were found. A total of 480 published articles were found using PubMed and Science Direct. Ten papers that met the inclusion criteria were selected and reviewed for this systematic review. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were used in this study to assess standard operating procedures. According to the reviewed literature, ashwagandha supplementation may reduce certain biomarkers of oxidative stress. Withania somnifera supplements have the ability to reduce certain oxidative stress levels due to their bioactive phytochemical constituents, according to the reviewed studies. Ashwagandha may enhance the antioxidant defense system and help control the ratio of endogenous antioxidants such as SOD, GSH, and GPX to reactive oxygen species, according to human and animal studies. These results suggest that ashwagandha supplementation may be a viable natural method for reducing oxidative stress, such as MDA, in both exercise-induced and non-exercise-induced conditions. However, further research is needed to elucidate the ideal dosage, mechanism of action, and long-term therapeutic efficacy.

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Exercise, or planned physical activity, and physical activity, which is defined as any movement that increases energy expenditure over resting levels, is known to improve fitness and health in a variety of age groups and medical problems (Montoye et al., 2022) (Qiu & Fern, 2023). Strength, endurance, balance, flexibility, and coordination training are examples of regular moderate-intensity physical exercise that improves all facets of human health and is widely recognized as a therapeutic and preventive approach for a number of diseases, including lung diseases, neurological conditions such as Parkinson's disease and multiple sclerosis, metabolic diseases such as hyperlipidemia, metabolic syndrome, and type 2 diabetes, and cardiovascular diseases such as cardiomyopathy, cardiac ischemia/reperfusion injury, and heart failure (Rueggesser & Booth, 2018) (Pedersen & Saltin, 2015). However, no appreciable alterations in body homeostasis are anticipated if exercise falls short of the required intensity level (Qiu et al., 2023). Prolonged hard exercise can increase the risk of myocardial infarction, and abrupt high-intensity exercise can result in negative cardiovascular events in untrained persons (Franklin et al., 2020). Therefore, in order to have a favorable impact on health, the type and intensity of exercise are crucial.

Exercise is a typical stressor that results in an oxygen supply that is insufficient to meet the body's rapidly increasing oxygen demand. As a result, many tissues and organs release a number of highly reactive molecules, including reactive oxygen species (ROS) and reactive nitrogen species (RNS). Oxidative stress (OS) would occur when the oxygen metabolism by-products were produced and accumulated and eventually beyond oxidation-resist ability (Lu et al., 2021). ROS, such as superoxide anion ($O_2^{\cdot-}$), hydroxyl radical ($OH^{\cdot-}$), and hydrogen peroxide (H_2O_2), are important in stress responses (Powers et al., 2020). An oxidative stress reaction occurs when the generation of ROS surpasses its ability to be scavenged (Wibawa et al., 2025). ROS are involved in many cellular processes under normal physiological conditions, such as signal transduction, cellular energy metabolism, and gene expression regulation. However, elevated ROS levels can also harm biomacromolecules in cells, including lipids, proteins, and nucleic acids, which can cause cellular aging and even death (F. Wang et al., 2021). Numerous studies have demonstrated that while excessive endogenous free radical production during exercise can affect the physiological function of various tissues, including skeletal muscle, regular or normal exercise produces modest amounts of ROS (Koyama, 2014).

Excessive ROS results in contraction dysfunction and muscle weakness. Skeletal muscle is a dynamic component of the sports system, and physiological level ROS is a crucial substance for maintaining its function, which is involved in muscle force production, muscle content maintenance, intracellular signal transduction, gene expression, and other related activities (Thirupathi et al., 2020). It is well known that ROS produced by skeletal muscle contraction during exercise can strengthen the antioxidant defense system and raise oxidative stress levels. High amounts of ROS can lead to contractile dysfunction even though exercise-induced ROS are required for skeletal muscle to produce force normally (Magherini et al., 2019). Because the sarcoplasmic reticulum Ca^{2+} release channel is more susceptible to ROS, myofibrils will be less responsive to Ca^{2+} , which will impact muscle contraction (Magherini et al., 2019) (Cheng et al., 2016).

Additionally, the type, intensity, and duration of exercise all affect how much ROS accumulates in the body. Proteins, lipids, and nucleic acids are among the important macromolecules that can be oxidized by unchecked ROS activity (Gandouzi et al., 2023) (Irato, 2021) (Martemucci et al., 2022). Malondialdehyde (MDA), which is produced by lipid peroxidation, and 8-hydroxy-2'-deoxyguanosine (8-OHdG), a marker of DNA damage, are common biochemical markers of oxidative damage. Other markers of oxidative stress include S-glutathionylation and protein carbonylation (Garcia-gim & Irene, 2024). Exercise-Induced Muscle Injury (EIMD) can also be brought on by excessive or unfamiliar exercise (Pincheira et al., 2023). Overuse of a muscle results in EIMD, which is characterized by physical stress, microtears in the muscle fibers, and Delayed-Onset Muscle Soreness (DOMS) (Anugrah, 2023). In order to promote the regeneration of damaged muscle tissue, this injury sets off the body's inflammatory response. Alternative approaches are therefore required to avoid and reduce this.

Ashwagandha, or *Withania somnifera*, is one herb that has garnered a lot of scientific and medical interest. The little plant known as ashwagandha is indigenous to regions of Africa, the Middle East, and the Indian subcontinent. The Sanskrit term "ashwagandha" means "smell

of a horse,” alluding to its distinct scent and purported capacity to provide horse-like power and vitality. Ashwagandha has been used for more than 3,000 years in Ayurvedic medicine. It is regarded as a revitalizing herbal rasayana that enhances general health, stress tolerance, and longevity (Singh et al., 2011). Ashwagandha has long been used to treat stress-related illnesses, boost endurance, replenish energy, and reduce weariness (Lee et al., 2020) (Smith et al., 2023). Ashwagandha’s medicinal actions are mediated by a number of physiologically active phytochemical components. Withanolides, a class of steroidal lactones having anti-inflammatory, antioxidant, immunomodulatory, and neuroprotective qualities, are the most researched substances (Sun et al., 2016). Alkaloids (including omniferin and tropin), cytoindosides, and acylsterylglucosides are other significant constituents, many of which have been suggested to regulate the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis (Fajkiel-madajczyk et al., 2023). Ashwagandha’s capacity to act as an adaptogen, assisting the body in lowering and adjusting to psychological and physical stress, is facilitated by these biochemical effects (Mikulska et al., 2023).

There are few comprehensive summaries of research on the benefits of ashwagandha supplementation as an antioxidant that combine data from human and animal trials, both in exercise and non-exercise contexts. Furthermore, there is a lack of comprehensive explanations of its molecular mechanisms in various physiological and pathological conditions, particularly in terms of how it modulates oxidative stress. Exercise is considered a significant physiological context among others, and this review seeks to provide an integrative narrative synthesis of experimental and clinical information on the effects of ashwagandha supplementation on oxidative stress across various models. Therefore, the scientific question in this study is: What are the effects of ashwagandha on oxidative stress in various models?

MATERIALS AND METHODS

STUDY DESIGN

To comprehensively evaluate the evidence on how ashwagandha supplementation reduces oxidative stress in both exercise and non-exercise contexts, a systematic review methodology was employed. To provide an integrated understanding of the antioxidant mechanisms associated with ashwagandha supplementation in humans, a clear, reproducible, and structured synthesis of findings from human and animal studies was enabled using a systematic review approach. To ensure transparency, reproducibility, and methodological rigor, the review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria. The aim of this review was to compile the most recent data on how ashwagandha affects oxidative stress in both exercise and non-exercise experimental settings. International scientific databases, such as PubMed and ScienceDirect, were selected for their extensive coverage of biological, clinical, and experimental research to obtain peer-reviewed literature. To ensure inclusion of the most up-to-date and relevant material, studies published between 2011 and 2025 were considered (Table 1). This review did not undergo a formal risk of bias assessment. Therefore, the methodological and potential sources of bias of the included studies were not systematically evaluated.

WEB SEARCH ENGINES	PUBMED, SCIENCE DIRECT, SCOPUS, AND WEB OF SCIENCE
Publishing period	2011–2025
Keyword	Physical exercise, ashwagandha, and oxidative stress
Language	English
Type of article	Original research article
Full Text	Articles matched the purpose and/or topic of the research.

Table 1 Inclusion criteria.

SEARCH STRATEGY

To identify relevant studies on the effects of ashwagandha supplementation on oxidative stress and exercise-related physiological responses, a comprehensive and organized literature search was conducted. To ensure comprehensive coverage of the biomedical and transdisciplinary literature, electronic databases such as PubMed and ScienceDirect were searched. Due to its

comprehensive indexing of the biological literature, PubMed was included; full-text scientific articles can be accessed through ScienceDirect.

Only peer-reviewed, English-language publications were included. To identify additional studies, the reference lists of relevant review papers and eligible publications were manually reviewed. Importantly, inclusion was not limited to post-exercise recovery settings or randomized controlled trials. Mechanistic syntheses were considered if supported by both exercise-related and non-exercise-related experimental models.

Predefined keywords and Boolean operators (AND, OR) were used to build the search strategy. “ashwagandha” OR “Withania somnifera” was the primary search term utilized in PubMed.

AND (“oxidative stress” OR “ROS” OR “antioxidant”)
AND (“exercise” OR “physical activity”)
AND (“no exercise” OR “without exercise” OR “sedentary” OR “resting state” OR “rest”
OR “inactive” OR “physical inactivity”) as well as through manual screening of
reference...lists from relevant articles.

To capture mechanistic and molecular studies, additional keywords were entered using the OR operator: (“withanolides” OR “steroid lactone” OR “alkaloid” OR “anti- antioxidant enzyme” OR “sitoinoside” OR “Withaferin A”).

Medical Subject Headings (MeSH) terms were applied in PubMed where appropriate, including: “ashwagandha,” “Oxidative Stress,” “Antioxidant,” and “Exercise.” Equivalent indexing terms were adapted for other databases.

While maintaining conceptual consistency, the search string was modified to suit the indexing system and search interface of each database. To identify further relevant studies, the reference lists of relevant publications and review papers were also manually reviewed. Only English-language publications published in peer-reviewed journals were included in the search. A total of 480 records were retrieved by the search (PubMed = 345; ScienceDirect = 135). However, in Scopus and Web of Science, we found no manuscripts meeting our inclusion criteria and none related to the keywords we used.

STUDY SELECTION

Figure 1 shows the selection procedure, which aligns with PRISMA recommendations. The database search yielded a total of 480 records (345 in PubMed and 135 in ScienceDirect). Beyond those found through PubMed and ScienceDirect, searches in Web of Science and Scopus did not yield any relevant documents meeting our inclusion criteria. After removing duplicates and other factors (n = 288), 192 distinct records remained for screening. Eighty-eight records were eliminated during the title and abstract screening process due to missing or irrelevant biomarkers. Finally, the eligibility of 104 full-text articles was evaluated. Ninety-four of these were eliminated due to missing oxidative stress outcomes, having an unoriginal design, or having insufficient data. Ultimately, ten papers were included in this evaluation because they met all inclusion requirements. To eliminate inconsistencies, each numerical value was carefully checked and matched with the PRISMA flowchart.

PROCEDURE

To find, assess, and compile pertinent research on oxidative stress and inflammation, a thorough assessment of the literature was carried out. To guarantee openness and methodological rigor, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards were implemented. Finding relevant terms, such as “oxidative stress,” “free radicals,” “antioxidants,” and “reactive oxygen species (ROS),” was the first step in the process.” To increase the accuracy of the search results, these terms were used both separately and in combination using Boolean operators like OR.

The remaining records were screened for irrelevant studies using abstracts and titles. The full-text publications were then assessed using pre-established inclusion criteria:

1. Innovative clinical or experimental studies
2. Interventions based on ashwagandha
3. Oxidative stress and/or antioxidant biomarker measurements
4. Sufficient methodological reporting

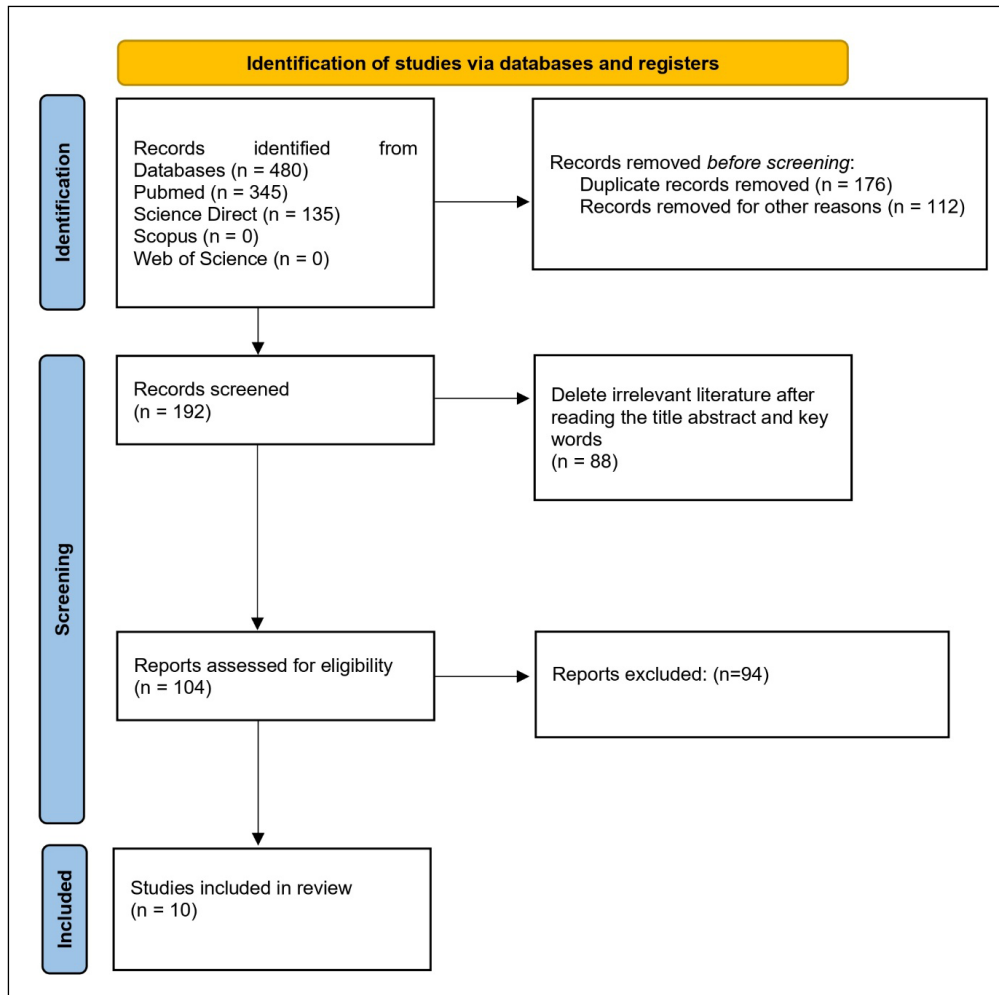


Figure 1 PRISMA flowchart of the article selection process.

RESULTS

The results of this study involved 10 included studies, 8 in animals and 2 in humans (Table 2). Regular consumption of ashwagandha (*Withania somnifera*) supplements has been shown to have potent antioxidant and anti-stress effects, according to numerous experimental studies in animals and humans. Ashwagandha can lower levels of malondialdehyde (MDA), a marker of oxidative stress, and increase the activity of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase (CAT), glutathione reductase (GR), and glutathione S-transferase (GST), according to studies in rats, mice, horses, dogs, and humans. Ashwagandha's capacity to reduce physiological stress and strengthen the body's antioxidant defenses has also been demonstrated by several studies showing lower cortisol levels and higher total antioxidant status. Ashwagandha administration has also been associated with increased muscle strength and reduced exercise-induced muscle damage in human studies involving healthy individuals and strength training participants. Overall, the results of this study suggest that ashwagandha may be a natural antioxidant that is beneficial for reducing oxidative stress and increasing the body's antioxidant capacity.

ANTIOXIDANT EFFECT

In all included studies, ashwagandha consistently demonstrated antioxidant activity through direct free radical scavenging and modulation of the endogenous antioxidant system. We grouped animal studies and human studies. Ashwagandha supplementation at doses of 60 mg/kg body weight and 100 mg/kg body weight significantly reduced MDA levels in mice ($p < 0.05$) (Babu et al., 2025). Physical stress intervention given to horses and supplemented with ashwagandha extract for 21 days showed positive results in increasing endogenous antioxidant SOD and reducing cortisol levels as a marker of stress levels $p < 0.05$ (Priyanka et al., 2020). Previous research also showed a positive effect of 25 mg/kg bw ashwagandha supplementation given to mice, which showed a significant increase in total antioxidants $p < 0.05$ (Sajid et al., 2025). Previous data conducted on mice given ashwagandha supplementation showed that

ashwagandha supplementation with several doses such as 100 mg/kg body weight, 150 mg/kg body weight, and 200 mg/kg body weight had a significant effect on increasing endogenous antioxidants such as SOD and significantly reducing MDA levels $p < 0.05$ (Hashem et al., 2023). Overall, all included studies demonstrated that ashwagandha supplementation has consistent antioxidant effects through reductions in oxidative stress biomarkers and enhancement of the endogenous antioxidant system. In animal studies, ashwagandha supplementation at various doses (25–200 mg/kg bw) significantly reduced malondialdehyde (MDA) levels and increased the activities of antioxidant enzymes such as SOD, GPx, GR, GST, and CAT. Furthermore, ashwagandha administration has also been shown to reduce cortisol and inflammatory cytokine levels in physical and metabolic stress models. These protective effects appear to be stronger at higher doses, particularly under stress-induced exercise, as evidenced by decreases in biomarkers of muscle damage such as creatine kinase, myoglobin, and lactic acid.

Further experiments provided evidence that the comparison between physical exercise and non-physical exercise and ashwagandha supplementation showed significant results. The results showed that serum and muscle concentrations of lactate dehydrogenase, MDA, myoglobin, creatine kinase, and lactic acid in the ashwagandha-supplemented group experienced significant decreases in mice, especially at the high ashwagandha dose (200 mg/kg). Compared with the exercise group, ashwagandha administration also increased antioxidant enzyme activity and significantly reduced inflammatory cytokine formation ($p < 0.05$) (Tuzcu et al., 2024). Previous data from ashwagandha interventions in dogs showed a significant decrease in MDA levels, SOD levels, an antioxidant, increased significantly, and cortisol levels also decreased significantly after supplementation ($p < 0.05$) (Bharani et al., 2024). MDA levels also decreased significantly in mice that had been given ashwagandha supplementation of 200 mg/kg bw $p < 0.05$ (Bhargavan et al., 2015). The positive effects of ashwagandha supplementation were also shown in the results of another study on albino mice that showed a significant increase in total antioxidants such as GPx, GR, SOD, and CAT levels ($p < 0.05$) (Anwer et al., 2012).

The results of other studies showed that in people who were given 500 mg ashwagandha intervention for 6 months, it had a significant impact on increasing SOD antioxidant levels and reducing MDA levels $p < 0.05$ (Kuchewar et al., 2014). This means that ashwagandha supplementation provides benefits in increasing antioxidant levels which are important in warding off free radicals. Research on 58 participants who were given ashwagandha intervention twice a day and a placebo given for 8 weeks showed a positive effect of the impact of ashwagandha in significantly reducing muscle damage after weight training $p < 0.05$ (Wankhede et al., 2015). It can be concluded that oxidative stress during weight training, which is identical to muscle damage due to exercise, can be reduced by ashwagandha supplementation. Thus, several studies have demonstrated the positive effects of ashwagandha on oxidative stress and antioxidant activity in both exercise and non-exercise settings. We would like to further explore the underlying mechanisms.

DISCUSSION

OXIDATIVE STRESS INDUCED BY EXERCISE AND NON-EXERCISE

An imbalance of pro-oxidative and antioxidant molecules in a system is the definition of oxidative stress, which was first proposed several decades ago (Sies et al., 1985). Although the exact role of antioxidants and free radicals is still unknown, it is known that free radicals play a number of inflammatory and signaling roles in the body (Sharifi-Rad et al., 2020) (Ji et al., 2021). The natural antioxidant defense systems that control the amounts and activity of many radicals are frequently overwhelmed during pathology and aging, becoming ineffective and causing tissue damage. In this context, free radicals can generally also be viewed as useful mediators (Kamati et al., 2025). Therefore, it is believed that oxidative stress plays a role in the genesis and pathophysiology of a number of disorders (Sharifi-Rad et al., 2020).

While everyone agrees that oxidative stress is important for human health, it is also commonly acknowledged that there is still much to learn about this phenomenon before it can be effectively used in clinical settings (Ji et al., 2021). The significant biological variation seen in these mediators both within and across species may be one of the primary causes of the lack of understanding surrounding oxidative stress and the natural role of radicals and antioxidants (Kamati et al., 2025). The antioxidant defense system is impacted by environmental factors,

AUTHOR	DESIGN	PARTICIPANTS	INTERVENTION	OUTCOME
(Babu et al., 2025)	Experimental	24 rats	- Group I: As the negative control, normal rats were fed water (2 ml/kg bw) orally for three weeks. - Group II: As the positive control, rats received an oral gavage of ashwagandha (60 mg/kg bw diluted in distilled water) for three weeks. - Group III: For three weeks, rats were given an oral gavage of aluminum (100 mg/kg bw dissolved in distilled water). - Group IV: Rats given oral gavages of aluminum (100 mg/kg bw) and ashwagandha (60 mg/kg bw) for three weeks.	MDA levels significantly decreased $p < 0.05$.
(Kuchewar et al., 2014)	Experimental	30 healthy volunteers	- They were divided into three groups at random. - For six months, each group received three differently colored capsules containing 500 mg of ashwagandha, guduchi, and a placebo. Each capsule was given twice a day.	Higher SOD levels and lower MDA levels.
(Priyanka et al., 2020)	Experimental	24 healthy horses	- Four groups of six horses each were created from the horses. - In addition to a regular diet, treatment groups 2, 3, and 4 received ashwagandha root extract combined with brown sugar at different doses for 21 days. - A physical stress intervention was also administered to the horses.	SOD levels increased and cortisol levels decreased following ashwagandha administration.
(Sajid et al., 2025)	Experimental	14 mice	From the day of the nerve lesion until the study's conclusion, mice in the treatment group received an oral dose of ashwagandha at a rate of 25 mg/kg body weight.	Total antioxidant status significantly increased and total oxidant status significantly decreased.
(Wankhede et al., 2015)	Experimental	participants	- While the control group took a starch placebo, the subjects in the treatment group took 300 mg of ashwagandha root extract twice a day. - Following baseline measurements, both groups trained with weights for eight weeks. At the conclusion of the eighth week, measurements were taken again.	As evidenced by the stabilization of blood creatine kinase, ashwagandha also significantly decreased exercise-induced muscle damage.
(Hashem et al., 2023)	Experimental	Thirty-six mature male Wistar albino rats in good health	Multiple dosages of supplementation were administered to the male Wistar albino rats, including 100 mg/kg body weight, 150 mg/kg body weight, and 200 mg/kg body weight.	All dosages of ashwagandha administration raised SOD and total antioxidant levels while lowering MDA levels.
(Tuzcu et al., 2024)	Experimental	Twenty-eight rats were divided into four groups	- Sedentary control group: Rats were given physiological saline orally and did not exercise during the trial. - Exercise group: Rats were given physiological saline orally and worked out on a rodent treadmill. - E + JHF 100 group: Rats were given JHF 100 mg/kg (BDMC-enriched curcumin + Ashwagandha + BSE) orally while exercising on a rodent treadmill. - E + JHF 200 group: Rats were given JHF 200 mg/kg (BDMC-enriched curcumin + Ashwagandha + BSE) orally while exercising on a rodent treadmill.	The combined formulation containing curcumin, ashwagandha, and BSE increased antioxidant enzyme activity.

(Contd.)

AUTHOR	DESIGN	PARTICIPANTS	INTERVENTION	OUTCOME
(Bharani et al., 2024)	Experimental	Twenty apparently healthy dogs	1. Starch that was identical to the research product in terms of appearance, color, odor, and taste was given to the placebo group. 2. The chosen dogs were given 15 mg/kg body weight of ashwagandha powder or a placebo orally once a day, mixed into their medi. 3. Owners of dogs were advised to mix the powder evenly into their usual diet based on the animal's body weight.	MDA levels significantly decreased following ashwagandha administration. In addition, antioxidant markers such as SOD and glutathione increased markedly, accompanied by a significant reduction in serum cortisol levels.
(Bhargavan et al., 2015)	Experimental	Adult male Wistar	1. Group A: The control was distilled water. 2. Group B: Ashwagandha 200 mg/kg. 3. Group C: 4 g/kg of alcohol. 4. Group D: 4 g/kg of alcohol and 200 mg/kg of ashwagandha after four hours. 5. For 28 days, which is the amount of time needed for mice to complete the spermatogenesis cycle, all animals in the group were given alcohol and ashwagandha orally.	MDA levels significantly decreased following the administration of ashwagandha supplements.
(Anwer et al., 2012)	Experimental	Wistar albino rat	1. Group I: Citrate control, given a pH 4.5 citrate buffer solution 2. Group II: Controlling type 2 diabetes with a single intraperitoneal dosage of STZ (100 mg/kg) 3. Group III: Ashwagandha (200 mg/kg, p.o.) was used to treat type 2 diabetes. 4. Group IV: Ashwagandha (400 mg/kg, p.o.) was used to treat type 2 diabetes.	Ashwagandha administration significantly increased antioxidant enzyme activities (GPx, GR, GST, SOD, and CAT) compared with type 2 diabetic control mice.

Table 2 Summary of the design and intervention of the studies.

such as exposure to endogenous (natural) and exogenous (environmental and synthetic) harmful substances, which also promote the production of free radicals (Phaniendra & Babu, 2015). Individuals frequently have antioxidant deficiencies as a result of increased antioxidant consumption, decreased antioxidant intake, or decreased endogenous antioxidant system effectiveness brought on by illness or aging (Kurutas, 2016). Humans and other living things are never exposed to free radicals since they are byproducts of regular cellular metabolism. However, the type of targeted macromolecule, its concentration and location, and the occurrence of subsequent harmful processes like chain reactions all affect how much damage is caused by the generation and/or buildup of free radicals (Davies, 2016).

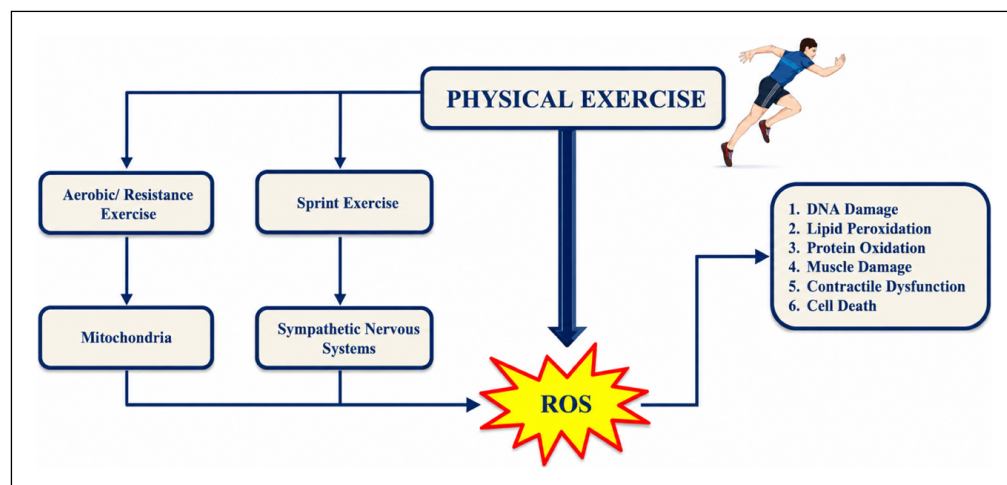


Figure 2 Physical Exercise Increases ROS and Triggers Oxidative Stress (Wibawa et al., 2025).

Mitochondria are organelles that act as energy stores that increase the formation of ATP in muscles, so that in the mechanism there is also ion leakage which has an impact on increasing oxidative stress (Wibawa et al., 2025) (Figure 2). The control of oxidative stress brought on by elevated ROS (reactive oxygen species) is intimately linked to physical exercise (Toledo, 2023). Excessive physical activity also has negative health impacts, such as discomfort and swelling, muscle cell structural damage, weakened immunity, inflammation, and increased susceptibility to infection, all of which can lead to a number of disorders (Canals-Garzón et al., 2022). The body's incapacity to control excess oxidants results in reactive oxygen species (ROS), which can lead to oxidative stress and have detrimental effects on health (Lushchak & Storey, 2021). An unpaired electron, which is extremely reactive, is the definition of a free radical. Compounds like the hydroxyl radical (OH⁻), peroxy radical (ROO⁻), and superoxide radical (O₂⁻) are the primary free radicals (Yilgor, 2024). Depending on the surroundings, the human body can produce ROS either endogenously or exogenously (Afzal et al., 2023). Free radicals are frequently generated both internally by intracellular metabolism and outside by things like exposure to cigarette smoke and air pollution when an overworked antioxidant system is unable to combat them (Sharifi-Rad et al., 2020). When endogenous sources like NADPH oxidase transfer NADPH electrons to molecular oxygen during cellular respiration, superoxide anion is created (Afzal et al., 2023). By changing the fundamental structure of DNA, ROS constantly jeopardize the integrity, form, function, and structure of genetic material (Obermann et al., 2025). This DNA damage can act as an epigenetic marker to regulate gene expression in addition to interfering with genome function (Gruber et al., 2018). Polyunsaturated fatty acids (PUFA) in the lipid layer of cell membranes interact with ROS to cause lipid peroxidation. Furthermore, as a result of lipid peroxidation, malondialdehyde (MDA) is extremely reactive, and other toxic aldehyde compounds are a serious risk for the development of compromised bodily functions (Badriyya et al., 2024). One important indicator of oxidative stress is MDA. Lipid membranes can be harmed by oxidative stress because it increases their fluidity and permeability (Mukherjee et al., 2024). According to earlier systematic review research, exercise increases MDA levels, which in turn causes oxidative stress (Ayubi et al., 2024).

THE ROLE OF ASHWAGANDHA PHYTOCHEMICAL COMPOUNDS IN REDUCING OXIDATIVE STRESS DURING PHYSICAL EXERCISE

Ashwagandha high phytochemical concentration sets it apart (Garkal et al., 2025) (Figure 3). The raw materials chemical makeup changes according to its location (Mikulska et al., 2023).

The roots of *Withania somnifera* contain 48 major and minor phytoconstituents, compared to 75 in the leaves. At least 29 components are present in both (Garkal et al., 2025). More than 12 alkaloids, over 40 withanolides, and numerous cytoindosides have been discovered in the aerial parts, roots, and berries of *W. somnifera* (Lerose et al., 2024). Withanolides, which are mostly found in the roots and leaves of ashwagandha, are its primary active ingredients (Ahirrao et al., 2024). Alkaloids, steroids, essential oils, and reducing sugars are reportedly found in the plant's roots, while 12 withanolides, condensed tannins, flavonoids, glycosides, and free amino acids are found in the leaves (Abdelwahed et al., 2023). The primary active components include flavonoids, alkaloids, tannins, glycosides, steroidal lactones, saponins, withanolides, withanosides, withanolide glycosides, also known as glyco-withanolides, steroidal saponins with extra acyl groups, cuscohygrine, anahygrine, salts, coagulins, and numerous other substances (Mazurkiewicz et al., 2024). Alkaloids such as somniferin, pseudotropin, choline, pseudowitanin, kuskohigrin, isopeletierin, witanin, tropin, somniferin, somnin, and anaferin are present in the medications under discussion (Al-Eisa, 2026). Flavonoids are a wide range of secondary plant metabolites that serve different biological purposes. The phenylpropanoid pathway in *W. somnifera* converts phenylalanine or tyrosine into flavonoids (Shinde et al., 2023). Among the antioxidant phytochemicals included in *W. somnifera* are polyphenols, cytoindosides VII-X, withaferin A, and glycowithanolide (A. Singh et al., 2010) (Singh, 2024). Extraction techniques have a major role in determining the biological effects of *W. somnifera* and other plants in the genus *Withania*, especially their phytochemical content and antioxidant capability (Dhanani et al., 2013).

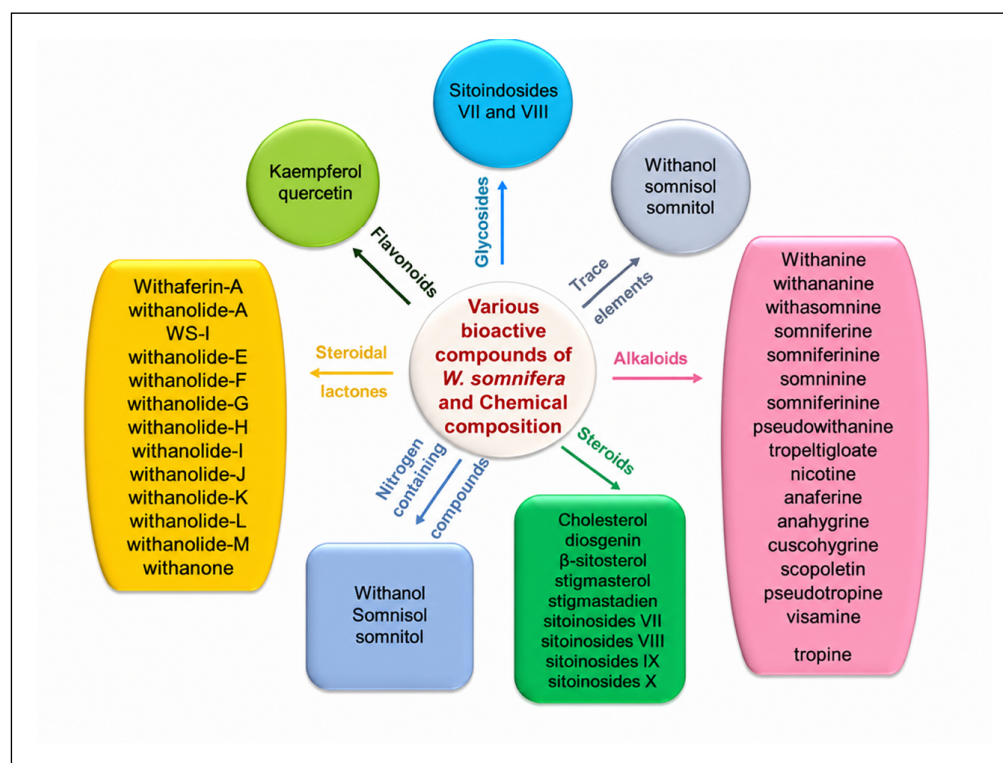


Figure 3 Various phytochemicals present in *Withania somnifera* (Garkal et al., 2025).

About 20% of the organism's oxygen supply is used by the brain, and damage from free radicals to the nervous system results in considerable neuronal death (Bhattacharya et al., 2001). Prior research concentrated on assessing how these elements affect the function of important free radical scavenging enzymes, such as glutathione peroxidase (GPX), catalase (CAT), and superoxide dismutase (SOD). Groups of six rats were given active *W. somnifera* glycowithanolide (10 or 20 mg/kg intraperitoneally) once daily for 21 days. The dose-dependent rise in all enzymes administration was comparable to that seen with intraperitoneal of deprenyl, a recognized antioxidant, at a rate of 2 g/kg/day. This implies that *W. somnifera* possesses antioxidant properties. Rats exposed to lead nitrate have been shown to have higher levels of antioxidant enzymes, including glutathione (GSH), glutathione S-transferase (GST), superoxide dismutase, and chloramphenicol acetyltransferase (CAT), after being given *W. somnifera* root extract (Sharma et al., 2011). Supplementing with ashwagandha has been demonstrated in experiments to boost the activity of antioxidant enzymes such as glutathione (GSH), catalase,

and superoxide dismutase (SOD). Increased enzyme activity lowers the intensity of lipid peroxidation and MDA production following exercise by speeding up the detoxification of ROS produced during muscle contraction. As a result, it effectively scavenges free radicals by boosting endogenous antioxidants.

The decrease in malondialdehyde (MDA) levels and the increase in the activity of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT) in several models likely indicate an improvement in redox balance through reduced lipid peroxidation and an increase in endogenous antioxidant defense systems. The general mechanism underlying these changes is thought to be related to the ability of bioactive compounds in ashwagandha, particularly withanolides, to reduce the formation of reactive oxygen species (ROS) and increase cellular antioxidant activity.

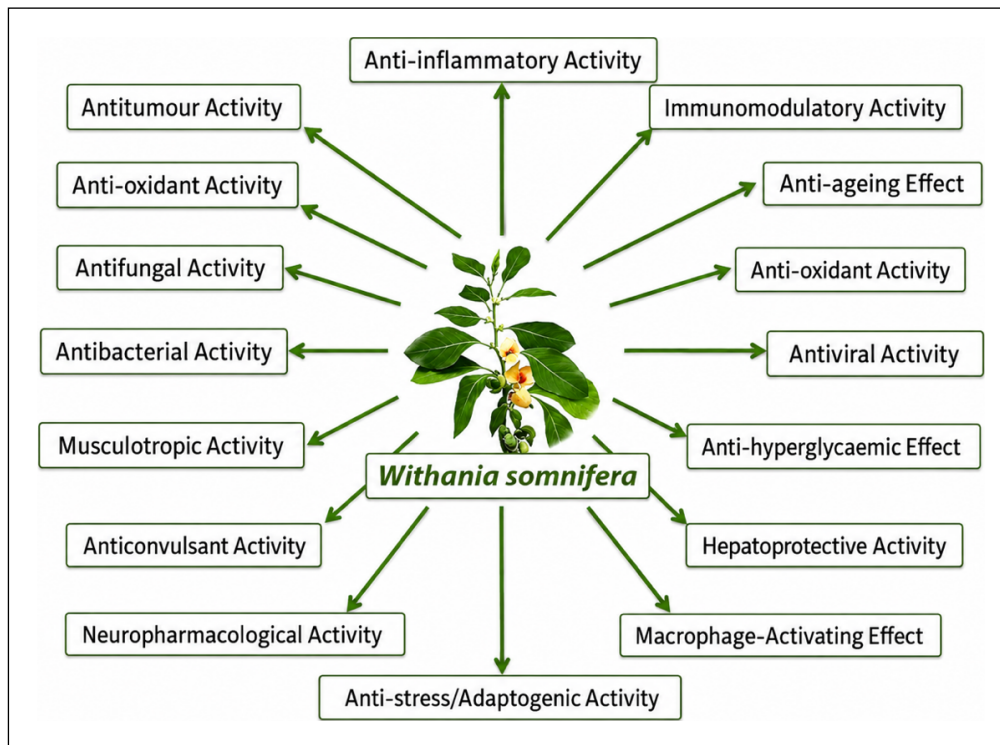


Figure 4 Pharmacological effects of ashwagandha (Garkal et al., 2025).

The research has emphasized ashwagandha's importance in enhancing physical supplement performance in healthy individuals, in addition to its use in health and wellbeing. In a randomized clinical trial (RCT) lasting eight weeks (Choudhary et al., 2015), In addition to a significant increase in arm muscle size, those who took 300 mg of ashwagandha root extract twice daily reported a significant increase in bench press muscle strength (ashwagandha group: 46.0 kg, placebo: 26.4 kg; $p = 0.001$). A different study found that over the course of a 12-week supplementation period, a 500 mg dose of ashwagandha extract in water significantly improved upper and lower body strength, encouraged a favorable body composition, and benefited healthy, active men (Wankhede et al., 2022).

Ashwagandha is notable for its special adaptogenic qualities, which can enhance general health, recuperation, and physical performance (Jayawardena & Weeras, 2025). It is noteworthy that ashwagandha's active compounds, help to improve muscle deterioration, indicating that it may be used for muscle restoration (Lopresti et al., 2019). Additionally, the plant's antioxidant qualities, which aid in preventing cell damage brought on by free radicals, may contribute to the beneficial effects of ashwagandha aqueous root extract on physical performance (Jayawardena & Weeras, 2025). Physiological adaptation mechanisms during sports exercise may be linked to the supplement's ability to maintain optimal physiological levels of reactive oxygen species (J. Wang et al., 2021).

Overall, we speculate that ashwagandha's antioxidant qualities, which lessen oxidative damage to muscle cells during exercise, and its capacity to boost cellular energy production and utilization through adenosine triphosphate (ATP) formation and enhanced mitochondrial

function are the reasons behind its benefits on oxidative stress. Additionally, these benefits seem to help muscles absorb and supply more oxygen, which increases aerobic capacity and muscular endurance. Additionally, it has been demonstrated that ashwagandha administration is superior to a placebo in terms of enhancing muscle strength-related variables as well as other aspects such as weariness, exhaustion, and recuperation (Petro et al., 2021). The antioxidant qualities of the plant's roots can account for this effect. The body's ability to adapt to exercise is known to depend on physiological levels of reactive oxygen species (ROS). However, circumstances such as overtraining, inadequate energy intake, or poor sleep hygiene can raise ROS levels, which can prevent physiological adaptations brought on by exercise (Bonilla et al., 2021). Myofibrillar proteins may undergo structural alterations as a result of elevated ROS levels, impairing their ability to perform certain functions, such as decreasing their sensitivity to intracellular calcium (Ca²⁺). Antioxidant supplements can help postpone muscular exhaustion over extended periods of physical activity, according to several studies (Medved et al., 2026).

Ashwagandha administration has been linked to increases in hematological indicators including hemoglobin (Hb), which may enhance oxygen transport and lead to better aerobic performance in terms of cardiorespiratory fitness and endurance (VO₂Max). However, this distinction must be taken into account because cardiorespiratory fitness is impacted by other variables outside of hematological changes, such as lung function and cardiovascular efficiency (Mehta et al., 2013). The rise in VO₂Max may be largely explained by these physiological factors. Long-term use of this supplement improves specific physical abilities in young, healthy people (Sandhu et al., 2010). Ashwagandha delivers a wider range of benefits by simultaneously influencing hormonal balance, stress response, inflammation, and neuromuscular coordination, even if it may not be as effective in standalone processes as some of these drugs (Garkal et al., 2025) (Figure 4). Because of this special mix, it might be especially helpful when there is both psychological and physical stress. To ensure its relative effectiveness in various athletic scenarios, more comparative research is necessary. Ashwagandha affects the regulatory pathways of cellular stress and inflammation linked to exercise-induced oxidative damage in addition to strengthening the antioxidant system. Additionally, during the post-exercise recovery period, its antioxidant actions can reduce the amplification of ROS generation. Therefore, a combination of direct antioxidant actions, augmentation of the endogenous antioxidant system, and regulation of molecular signaling pathways that regulate oxidative stress and inflammation can explain the mechanism of MDA reduction caused by ashwagandha supplementation. These systems work together to lower the amounts of lipid peroxidation in muscle tissue following physical activity, which may improve recovery and physiological adaptation to exercise.

STRENGTH AND LIMITATIONS

This systematic review has the advantage of focusing only on randomized controlled trials, the most reliable form of scientific evidence, and eliminating the potential for ambiguous cause-and-effect relationships. The supplementation focused on analyzing the effects of ashwagandha and not other supplements. One limitation we identified was the lack of information on how ashwagandha affects exercise and the oxidative stress induced during exercise. The limited number of studies on this topic indicates a paucity of research. Therefore, this study is crucial to provide information on the positive impact of ashwagandha supplementation on oxidative stress. Future research is strongly recommended to focus on the effects of ashwagandha supplementation during exercise on antioxidant levels, free radicals, and inflammation.

This study has several limitations that should be considered when interpreting the results. First, the number of studies meeting the inclusion criteria was limited, with animal studies predominating over human studies. Therefore, generalization of the findings to the human population requires caution. Second, there was considerable heterogeneity between studies, particularly regarding the dosage of ashwagandha supplementation, intervention duration, subject characteristics, and exercise patterns or stress models used, which may affect the consistency of the results and the reliability of the conclusions. Third, this review did not conduct a stratified analysis between animal and human studies due to the limited number of available studies, particularly in human populations. Furthermore, a comprehensive assessment of the methodological quality and risk of bias of the included studies was not conducted, resulting in limited certainty in the evidence obtained. Therefore, further research is needed, particularly

human clinical trials with standardized designs and better methodological quality, to confirm the effectiveness of ashwagandha supplementation on oxidative stress and physiological recovery.

CONCLUSIONS

Current limited evidence suggests that ashwagandha supplementation may improve certain biomarkers of oxidative stress, particularly in animal models. Further well-designed human studies are needed to confirm its efficacy, mechanisms, and optimal dosage.

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COMPETING INTERESTS

The authors have no competing interests to declare.

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