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Systematic Review

Impact of Ashwagandha in Stress, Depression, and Sports; A Systematic Review

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Abstract

Ashwagandha is a well-known traditional medicine and is a part of many formulations in the Ayurveda medicine system. Besides its many medicinal and nutritional uses, the drug has been prescribed to treat stress and depression. The objective of the study is to comprehensively review the use of Ashwagandha in stress, depression, and sports. Due to the presence of multiple nutrients, it has been employed by sportsmen for stamina and strength. The literature was searched by electronic databases including PubMed, Scopus, Google Scholar, and Web of Science. The published data from 1987 till date was included. Based on needs, traditional reports were also reported beside scientific literature. This review included many scientific studies focusing on the use of Ashwagandha in stress, depression, and sports. It was found in the studies that Ashwagandha has proved its logical use in conditions related to stress, anxiety, depression, stamina, and fatigue. In many cases, Ashwagandha was equipotent to the conventional anxiolytic agents. The most important compounds isolated from Ashwagandha for use in stress and depression were withanolides. In sports-related activities, it was found that Ashwagandha increases the oxygen consumption. It is well established from the scientific literature that Ashwagandha has potent regenerative tonic properties, it has anti-stress, and anxiolytic properties. It increases the stamina of sportsmen and improves their physical performance. Thus, the mentioned results clearly showed that the traditional use of Ashwagandha has a logical and scientific basis.

Keywords: Ashwagandha, Withania, Withanolides, stress, depression, sports

1. Background

Indian Ayurvedic medicine system is very rich and the Withania genus of plants has an especially important contribution to this system. The genus is well known for its pharmaceutical and nutraceutical properties. The genus comprises small herbs that are found in the Canary Islands, North Africa, and the Southwest of Asia (Bhandari, 1990; Hepper, 1991) . About twenty-three species of Withania are known but *Withania somnifera* commonly called Ashwagandha is the most significant economically (Negi et al., 2006). Ashwagandha is the most dominant species of the Solanaceae family (Hemalatha et al., 2008). Ashwagandha has a widespread use in Ayurvedic medicine. Arthritis and rheumatism are the main conditions for which Ashwagandha has been prescribed as a general tonic, for overall health beings. It has proved to improve athlete's health. It also has positive health effects in pregnant women and in elderly patients. A lot of biological and pharmacological experiments have been carried out to investigate its use in various health and disease conditions including anti-inflammatory and anti-stress studies (Mishra et al., 2000).

Ashwagandha is also included among the group of herbs known as 'adaptogens.' The herbs containing phytonutrients have a role in metabolism in case there is internal or external stress in the body and are called as adaptogens. It normalize the body functions as well as develop resistance against any future stress by increasing the body's performance to a higher level

(Wankhede et al., 2015). Ashwagandha is a Sanskrit word that means 'horse smell.' This name is given to the drug due to its root's odor which is similar to a sweaty horse. The species name 'somnifera' is from Latin which means 'sleep-inducing' and it is due to its property of causing sedation (Verma and Kumar, 2011). Its properties are similar to Chinese drug 'ginseng' which is also used to promote physical and mental health (Lopresti et al., 2019). In Ayurvedic the drug Ashwagandha is mentioned as *Rasayana* and is attributed to the belongings of *balya* and *mamsavivardhan.* In Ayurvedic clinical practices preparations of root powder are commonly given to enhance the general body strength (Raut et al., 2012). Sometimes, *Withania somnifera*, is also regarded as Indian ginseng. Other names included are Winter Cherry in English, Ajagandha, and Kanaje in Hindi, and Ayamodakam in Malayalam. Its extract may be commercially obtained from various sources. In Ayurveda, Ashwagandha has been prescribed for longevity, youthfulness, and improve intelligence. The roots are used for to diuretic, aphrodisiac, and germicidal activities. The roots are bitter in taste, hot in action, and alleviate 'vata' and 'kapha.' It is known to treat ulcers, cough, and fever. It is useful in respiratory conditions, in dropsy, impotence, and in leucoderma. Due to the presence of multiple nutrients, it is given as a tonic to improve physical health. It is also reported to have anti-cancer effects. Its anxiolytic activity is also significant. Some of well marketed drug preparations in Ayurvedic are Asvagandharishtam, chavanaprasam, Valiya Narayana tailam etc. (Pratibha et al., 2013).

It is also reported to combat infectious diseases due to the presence of withanolides which are present as steroidal lactones. Withanolides are also reported to have immunomodulation, anti-inflammatory, and analgesic properties. The primary withanolides are withaferin A and withanolide D which have been studied in the areas of oncology, immunology, neuroregeneration, and neurodegeneration. Withanolides act upon hormones as a regulator (Gardner and Level, 2015). A glycoprotein identified from Ashwagandha has antimicrobial properties. The drug is usually used in combination with milk and has been stated to maximize the protein level and increase body weight. This drug has been regarded as a treasure of nature because of its benefits in the heart, sex, and nervous systems (Tiwari et al., 2014). In Ayurveda, the dugout roots are at times boiled in milk, before drying, this is done to remove the undesirable constituents. The fruits are employed as an alternative for rennet, for coagulation of milk in cheese making. Notably, it has already been reported to be used in headaches and fevers (Barbieri).

Ashwagandha may have anti-anxiety effects, help manage fatigue, reduce levels of cortisol, and maybe even improve athletic performance (English). One more study reported that Ashwagandha helps our bodies adapt to stress, reduces inflammation, and improves both muscle strength and mass. All these salient health applications of this herb in medicine are discussed in this review focusing on its potential role in maintaining good health, in sports, stress, and depression.

2. Material and Methods

2.1. Data Extraction Methods

The current review is according to the PRISMA guidelines (Liberati et al., 2009). The literature was searched by electronic databases including PubMed, Scopus, Google Scholar, and Web of Science. The published data from 1987 till date was included.

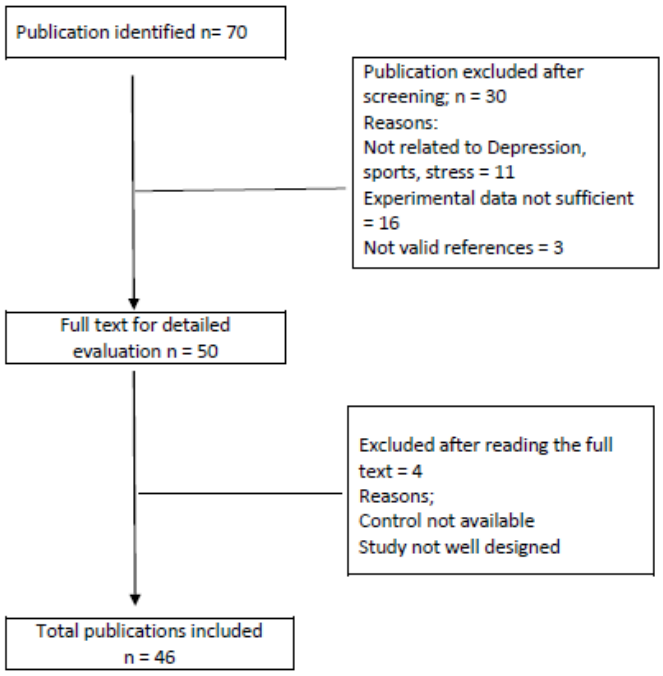
2.1. Types of Studies

Types of studies included were traditional uses, reports, and animal, and human trials. All included studies were written in English.

2.2. Types of Participants

This review may include observation studies based on traditional systems of medicine and experimental studies.

Figure 1: Flow char for selection of publication.



2.3. Types of Outcomes Measures

Interventions evaluating the effect of Ashwagandha on sports, stress, and depression were included.

2.4. Search

The applied search keywords were: Ashwagandha, *Withania somnifera*, and Indian ginseng in combination with stress, depression, sports, athlete etc.

2.5. Inclusion/Exclusion Criteria

The result of the search was presented briefly, and duplications were removed. Only those publications were included in which the controls were used in the study, were experimental, followed the guidelines of international standards of human study, etc. The exclusion criteria included substandard publications, and observational studies, and only used the qualitative methodology. The authors unanimously agreed to the inclusion of the selected data.

3. Use of Ashwagandha in Sports

Physical appearance is the top concern these days in society. In developed nations, people (about 24%) do exercises for a healthy performance. The use of drugs and other substances by the sports-men is quite common. Among such substances are dietary supplements. There are cases of irrational use of such drugs and substances which leads to untoward effects (Zovko Koncic and Tomczyk, 2013). One such substance comes from a medicinal plant known commonly as Ashwagandha. It is used in traditional Ayurvedic supplements to improve muscle strength and to recover any muscle damage due to hard training. One study suggested that using Ashwagandha after exercise may reduce the perception of pain in muscles, so, the athlete can train with more intensity and harder. The study revealed that Ashwagandha at a dose of around 200-400 mg per day increases the testosterone level to about 17% and enhances the muscles building ability (Morgado et al., 2023).

One of the studies was carried out on commercially available supplements. The supplement was produced for use in sports. The product is traded as ShroomTechSport™ and it is available as a blend of Ashwagandha root along with green tea extract, *Cordyceps sinesis*, and *Rhodiola rosea*. The study was conducted to investigate the effect of products on muscular strength and endurance. The study was carried out on 10 healthy adults with an average age of 24. The participants received 3-4 capsules of ShroomTechSport™ or 2.5 g of cellulose for the placebo effect. Maximal oxygen consumption was measured during the treadmill test. Additionally, a rating of perceived exertion was noted during the test. It was found that there was an improvement in Subjective Fatigue at the treadmill test in the group using the product. This study showed not much satisfactory results of the product tested and suggested a more detailed study on ShroomTechSport™.(Munoz, 2015).

A particularly good study was carried out to test the effect of Ashwagandha on body mass. Two groups were compared in the study one with a placebo effect and the other taking Ashwagandha. Both groups were engaged in resistance training. It was found that there was a significant increase in muscle strength in the Ashwagandha group (46.05 kg, 95 % CI 36.56, 55.54; $p = 0.001$) compared with the placebo group (Placebo: 26.42 kg, 95 % CI, 19.52, 33.32) for the upper body. Similarly, for the lower body Ashwagandha (14.50 kg, 95 % 10.76, 18.23; $p = 0.04$) and Placebo (9.77 kg, 95 % CI, 7.18, 12.35; $p = 0.04$). Another parameter studied was to check the level of recovery from exercise-induced muscle damage. It was assessed at the end of the resistance training session by evaluating the serum creatine kinase from hours 24 to 48 hours. The author was surprised to observe that recovery was dramatic after resistance training of 8 weeks. In the Ashwagandha group, the recovery was substantial compared with the placebo group (Placebo: 1307.48 U/L, 95 % CI, -1202.82, 1412.14 vs. Ashwagandha: 1462.68 U/L, 95 % CI, 1366.27, 1559.09; $p = 0.03$) (Wankhede et al., 2015).

It was also noted that Ashwagandha also enhanced the stamina in experimental groups. It improved all the parameters studied like oxygen consumption, namely, VO_2 max ($\boldsymbol{t}$ = 5.356; $\boldsymbol{P} < 0.001$), METS ($\boldsymbol{t}$ = 4.483; $\boldsymbol{P} < 0.001$), and period for tiredness on the treadmill ($\boldsymbol{t}$ = 4.813; $\boldsymbol{P} < 0.001$) in link to the placebo group showing no change with respect to their baseline parameters (Shenoy et al., 2012). A similar study was conducted in 2013 to evaluate the effect of supplementation of Ashwagandha on the $VO_{2\ max}$ and Hemoglobin in Hockey Players. 32 male hockey players (17.4±1.7 years and BMI 20.9±2.9 kg/m^2) volunteered for the study. Players were grouped into two. Group 1 (n=16): Ashwagandha group and Group 2 (n=16): Placebo group. The experimental group received 500 mg capsules of Ashwagandha twice daily for 8 weeks. The placebo group was given starch capsules. $VO_{2\ max.}$ with Cooper 12 minutes run test and hemoglobin (Hb) of both experimental and control groups were determined. A significant improvement in the $VO_{2\ max}$ ($t=2.98$, $p<0.01$) and hemoglobin ($t=2.78$, $p<0.01$) in the Ashwagandha group was found as compared with the placebo group. It was concluded that Ashwagandha improves $VO_{2\ max}$ and hemoglobin concentration in young hockey players (Arvind et al., 2013).

In another experiment, oxygen consumption was noted, and found that there was an increase from baseline ($\boldsymbol{P} < 0.0001$) in the mean VO_2 max with KSM-66 Ashwagandha ($\boldsymbol{n}$ = 24) equated to placebo ($\boldsymbol{n}$ = 25) at 8 weeks (4.91 and 1.42, respectively) and 12 weeks (5.67 and 1.86 respectively). The QOL scores for all subdomains were significantly enhanced to a greater degree in the ***Ashwagandha*** group at 12 weeks compared to placebo ($\boldsymbol{P} < 0.05$)(Choudhary et al., 2015). Another useful study about the use of ***Withania somnifera*** in stamina, balance, and blood pressure was conducted. It was 8-week study, and it was found that the oxygen consumption increase was significant from 13.54 ±2.46 to 14.47±2.28 ($\boldsymbol{P}$=0.005). Similarly, the maximum velocity increased from 5.37±0.75 to 5.53±0.70 ($\boldsymbol{P}$=0.005), the

average absolute power from 711.90 ±221.62 to 774.79 ±247.42 (***P***=0.002) and average relative power from 11.10 ±3.17 to 12.22 ±3.40 (***P***=0.007). However, the balance and blood pressure parameters remained almost unchanged (Sandhu et al., 2010).

One of the impediments to the use of herbal supplements is false claims by the manufacturer and this is taking away the trust of end users like athletes. Such claims are often without any scientific evidence. Therefore, in one study some herbs including Ashwagandha, based on their traditional use were assessed for their effects on performance and exercise recovery. Other than Ashwagandha the effect was mild and there were no significant findings. The study suggested to evaluate such herbs in specific sports and on selected exercises (Končić, 2017). An excellent study was conducted on Hockey players. In this study, a supplement of Ashwagandha was assessed on center muscle quality and steadiness in players. Young hockey players were selected (n = 32 age = 17.3 ± 1.8 , BMI 20.7 ± 2.8 kg/m^2). One group was given Ashwagandha 500 mg capsules twice a day for 8 weeks. The placebo group was treated with the starch capsules. A remarkable change within the Center Muscle Quality & Solidness after 4 weeks (t = 2.99 , p< 0.021 , on tail rest) and 8 weeks (t = 9.05 , p < 0.02 , one tail test) in this test(Sachin et al.; Ziegenfuss et al., 2018). It is also known that Ashwagandha can be used for muscle strength and stability. To assess this, another useful study included male subjects with a wider age range were experimented. A total of 57 young males with the age range of 18-50 years were selected. All the participants had some previous experience of resistant training. All the subjects were given 300 mg of Ashwagandha root extract two times a day for 8 weeks. The results were compared to the placebo group. It was observed that subjects on the bench-press exercise, almost 20 kg over placebo, had a significant increase in muscle strength. In the leg-extension exercise, the improvement was 5 kg over the placebo group. Other parameters studied were serum testosterone, muscle size, and muscle recovery. The improvement was significant in all cases.

In 2014 a remarkably interesting study was designed to test the muscle strength and stability of 32 male hockey players. A supplement of Ashwagandha (500 mg capsules, twice daily, 4-8 weeks) was used as testing material. The capsules contained the aqueous root extract. This was found that muscle strength was increased to a significant level. This study supported the usefulness of Ashwagandha in sports. An experimental study assessing the activity of Ashwagandha for 30 days (750 mg/day x 10 days , 1.000 mg/day x 10 days , 1.250 mg/day x 10 days) in healthy individuals stated a significant increase in muscle strength. The strength was determined by hand grip strength, quadriceps strength, and back extensor force. The water extract of 500 mg/day for eight weeks also reported to improve physical performance (Gaspari). The herbal supplements have caught the attention of sprinter athletes to a greater extent compared to other sports. In one study male sprinters were put under trial for various fitness variables. The testing supplement was Ashwagandha. Twenty male sprinters were divided into two groups. Ashwagandha was given with milk. The study period was 12 weeks. It was found that the Ashwagandha taking group showed improvements in various variables studied, like standing broad jump, fifty meters dash, pull-ups, sit-ups, shuttle run, and 12 minutes run/walk (Yadav, 2014). Ashwagandha is also used as an anti-aging in Ayurveda. To explore this effect a study was conducted on elderly individuals. The target was sarcopenia in old-age subjects. Ashwagandha was given to the elderly for 3 months. It was found that this herb improved the muscle strength and durability of aged individuals. It was measured by assessing creatinine level in blood, a rise in level suggested that muscle metabolism might have increased in the group using Ashwagandha (Aphale et al., 1998).

Detailed in an examination led on rodents, admission of ginseng and Ashwagandha for 90 days, specialists discovered a critical increment in body weight, nourishment utilization, liver weight, and improved hematopoiesis. They did not show any lethality of the cerebrum, heart, lung, liver, spleen, kidneys, stomach, testis, and ovaries. Further, the reactions of WS were not essentially the same as those accomplished by placebo-treated people. The duration of the study was sixty days. The subjects used were sixty healthy children between 8-12 years of age. It was noted that there was a slight increase in hemoglobin level, packed cell volume, serum iron, hand grip, and body weight. There was a significant change in mean corpuscular hemoglobin level (Sachin et al.).

4. Role of Ashwagandha in Stress and Depression

Due to multi nutrient contents, this drug has been employed for conditions related to stress and depression. The drug Ashwagandha has already been employed in such conditions. Here are a few experimental examples of why this drug has been used in stress conditions.

Somnifera has been researched in adult Swiss albi no rats with stress. Experimental rats underwent 14 h immobilization stress and were treated with an extract of Ashwagandha root powder. Was used as capsules of Stresscom (Dabur India Ltd). Control rats were kept in environments that were totally unstressed. Thionin-stained serial coronal parts (7 μm) of the brain pa ssing through the rat hippocampal area (E1 grou) showed 85 percent of the subareas CA2 and CA3 degenerating cells (dark cells and pyknotic cells). There was a significant reduction of regenerating cells which was about 80%. The study suggested that Ashwagandha has anti-stress and neuroprotective activity (Jain et al., 2001).

Ashwagandha has been included in the group of herbs known as adaptogens. A standard extract from its roots was evaluated in an animal model using rats. Chronic stress was induced in adult male Wistar rats in a gentle way. It was repeated for 21 days study period. Chronic stress complications like hyperglycemia, increased corticosterone, gastric ulcer, immunosuppression, and mental confusion were studied. It was noted that Ashwagandha at a dose of 25-50 mg/kg po relieved the complications produced due to stress. The results indicated that Ashwagandha has significant anti-stress adaptogen activity, confirming the clinical use of the plant in Ayurveda (Bhattacharya and Muruganandam, 2003).

There is another study that probed the anxiolytic and antidepressant activity of the bioactive glycowithanolides (WSG), separated from *Withania somnifera* (WS) roots, in rats. WSG (20 and 50 mg/kg/day) was given by oral route for 5 days and the results were matched by those produced by the benzodiazepine lorazepam (0.5 mg/kg, i.p.) for anxiolytic studies, and by the tricyclic anti-depressant, imipramine (10 mg/kg, i.p.), for the antidepressant studies. The standard drugs were given once, 30 min earlier to the tests. Surprisingly, the effect of WS was equal potent to the effect exhibited by the standard drugs. Additionally, WS and lorazepam, lower brain levels of tribulin, an endocoid marker of clinical anxiety in rats. The levels were previously increased by administering an anxiogenic agent, pentylenetetrazole. WS also showed an antidepressant result compared with that induced by imipramine. The different tests applied were forced swim and 'learned helplessness' tests. The studies support the use of WS as a mood stabilizer in clinical conditions of anxiety and depression in Ayurveda (Bhattacharya et al., 2000). The first test of isolated compounds against stress was carried out in 1987 where the two new acylsterylglucosides, sitoindoside VII and sitoindoside VIII, from the roots of *Withania somnifera* Dun., were tested for supposed anti-stress action. A series of tests were conducted to describe the activity of the samples. The total MeOH-H_2O (1:1) extractives of the roots of *W. somnifera* (SG-1) and equimolecular combination

of sitoindosides VII, VIII, and withaferin-A, a withanolide, (SG-2), showed significant anti-stress activity. The two sitoindosides also showed *per se* anti-stress activity, which was potentiated by withaferin-A. A preliminary acute toxicity study showed that the compounds have a low order of acute toxicity. The anti-stress activity of SG-1 and SG-2 is consonant with the therapeutic use of *W. somnifera* in Ayurveda, the Indian system of medicine (Bhattacharya et al., 1987).

In one study antioxidant activity of compounds from *Withania somnifera* (WS) was related to its anti-stress activity. The antioxidant potential of *Withania somnifera* (WS) glycowithanolides was evaluated in chronic foot's hock stress-induced changes in rat brain frontal cortex and striatum. The stress method, given for 21 days, caused an increase in superoxide dismutase (SOD) and lipid peroxidation (LPO) activity, with a simultaneous decline in catalase (CAT) and glutathione peroxidase (GPX) activities in both the brain regions. Glycowithanolides (WSG), given orally 1 h prior to the stress method for 21 days, in the doses of 10, 20, and 50 mg/kg, inducted reversal of the stress effects in a dose-dependent manner. Thus, WSG normalize the SOD and LPO activities and improved the activities of CAT and GPX. The results showed that a part of chronic stress-induced pathology may be due to oxidative stress, which was alleviated by WSG, providing support to the clinical use of the plant as an anti-stress (Bhattacharya et al., 2001). Various fractions of *W. somnifera* root extracts and a constituent called compound X were evaluated for adaptogen activity using rats as an experimental model. The animals were inducted with stress by cold, hypoxia, and restraint (C-H-R). The result *W. somnifera* water suspension (360 mg/Kg b.w) and compound X (20mg/Kg b.w) on the fall and recovery of colonic temperature was noted. There was an increase of ≈38% and ≈54% in the time taken to attain Trec 23°C by rats given a single dose of freshwater suspension and Compound X respectively, whereas a decrease in the recovery time to reach Trec 37°C is ≈13% and ≈33% respectively when compared with control group. It was concluded that Ashwagandha-treated group withstood the C-H-R stress in a much better way compared to the control (Kaur et al., 2001).

Withania somnifera (WS) Dunal is categorized in Ayurveda, the ancient Hindu system of medicine, as a rasayana, and is known to revitalize the body in weakened situations and increase longevity. The effects are considered similar to ginseng in contemporary medicine. The adaptogen activity of Ashwagandha root extract was evaluated in rats. The chronic stress-induced complications were reduced by WS (25 and 50 mg/kg po) and by PG (100 mg/kg po), administered 1 h before feet hock for 21 days. The results indicate that WS, like PG, has significant antistress adaptogenic activity, confirming the clinical use of the plant in Ayurveda (Bhattacharya and Muruganandam, 2003). Ashwagandha is known to induce immune modulation and has been proved to be as anti-stress agent. Research work conducted in India showed that this drug contains antioxidant constituents. Ashwagandha has been indicated for the treatment of cerebral disorders for many years. This is especially indicated for the elderly with memory loss. A scholar from the University of Leipzig experimented with the effects of Ashwagandha on the neurotransmitters of the brain. In the experiment, it was found that the drug led to an increase in acetylcholine receptor activity. This was concluded that such activities are responsible for enhancing cognitive and memory ability. Another scholar at the University of Texas conducted a similar experiment. It was found that the activity of Ashwagandha was similar to GABA in the tested doses. This research supports the use of this drug in stress, anxiety, and depression (Kumari et al., 2011).

To investigate the antistress activity of *Withania somnifera*, an alcoholic extract from roots & seeds in normal saline was administered (100mg/kg intraperitoneal as a single dose) to 20-25 g mice in a swim performance trial in water at 28'-30' C. It was observed that with the use of drugs, the swim times increased 100%. It was submitted that

Withania somnifera increased the resistance during stress. The total glycoside fraction of *Withania somnifera* showed significant anti-stress activity in the forced swim test in mice (Mishra et al., 2000). One more study revealed that the antioxidant action of Ashwagandha was due to the presence of withanolides in root extract. The other possible constituents that can exert antioxidant effects were expected to be polyphenols, flavonoids, and vitamin C. In an experiment, goat blood was exposed to 1, 4-dioxane to produce oxidative stress, and the reversal was noted with the addition of Ashwagandha. There is another evidence of the use of Ashwagandha in stress. The volunteers were selected at the workplace (not mentioned) and the perceived stress scale was evaluated employing the standard parameters. All the subjects revealed a significant improvement in the workplace stress scale (Ashok and Shende, 2015).

Ashwagandha contains numerous constituents which can exert their pharmacological effect. One such constituent isolated is withanolide as mentioned earlier. These compounds can serve as precursors of important hormones found in the human body. Withanolides have similar properties of exerting their anti-stress effect by occupying the cell membrane receptors and showing its effect analogy to serum cortisol. That is why even in the modern era herbalists include Ashwagandha in the adaptogen class. Over the past many years plethora of studies carried out indicate that Ashwagandha has anti-stress as well as rejuvenating effects (Supe et al., 2011). A similar study carried out showed that Withaferin-A is an active constituent of *Withania somnifera* and has shown experimentally to possess anti-stress, antioxidant, and immunomodulation properties (Modi et al., 2012). Another study revealed the curing effect of Ashwagandha in chronic stress in 64 patients. The study included clinical and laboratory tests before and after the study. Two random groups were made, a drug treated and a placebo control. All the patients were advised to take one 300 mg capsule twice daily for 60 days. The patients were inquired about any compliance on a 15-day interval. Any reported adverse effects were noted. After 60 days the final assessment was made. It was noted that patients receiving 300 mg of Ashwagandha extract showed a significant decrease ($P<0.0001$) in all the stress measuring scales as compared with the placebo group. The blood cortisol was markedly reduced ($P=0.0006$) in the Ashwagandha group. The side effects were gentle in nature and were similar in both groups. No serious adverse reactions were informed (Chandrasekhar et al., 2012).

The anxiolytic drug diazepam is one of the most used drugs in allopathy today. The effect of this drug was compared with the Ashwagandha in one animal study. The anxiety and depression were observed in groups of rats by inducing these social isolation protocols. Two tests named elevated plus maze (EPM) and forced swim test (FST) were performed. The rats were separated for 6 weeks and changes in behavior were assessed. Isolation-reared rats spent less time in the open arms on EPM and significantly augmented immobility time in FST related to group-housed rats. WS (100, 200, or 500 mg/kg, oral) and diazepam (1 or 2 mg/kg, ip) increased the time spent and entries into the open arms on the EPM test and exhibited the anxiolytic property in a dose-dependent manner. WS (100, 200, or 500 mg/kg, oral) also reduced the immobility time in FST, consequently presenting antidepressant action in both groups. The studies support the use of WS as a mood stabilizer in socially isolated behavior in Ayurveda (Kaur et al., 2001). In one study two sitoindosides were isolated from Ashwagandha and reported to possess anti-stress action, which was potentiated by withaferin-A. An initial acute toxicity study showed that the compounds have a low order of acute toxicity. The anti-stress properties of SG-1 and SG-2 are consonant with the therapeutic use of *W. somnifera* in Ayurveda (Chandrasekhar et al., 2012). The roots of Ashwagandha have been evaluated in individuals with behavioral disturbances. The bioactive compound withanolides isolated from

Ashwagandha in doses of (20 and 50 mg/kg/day) for 5 days reduced the anxiety. The results were equipotent to the standard drug used. The standard drug used to compare the withanolides effect were lorazepam (0.5 mg/kg, i.p.) for anxiety and imipramine (10 mg/kg, i.p.) for depression. The standard drugs were given thirty minutes before the tests. The different tests selected for the said study were elevated plus-maze, social interaction, and feeding latency tests in an unfamiliar environment. Clinical findings showed that withanolides and lorazepam tend to reduce the level of tribulin in the brain. Withanolides also presented an antidepressant activity, similar to imipramine, in the forced swim-induced 'behavioral despair' and 'learned helplessness' tests. The studies support the use of Ashwagandha as a mood stabilizer in anxiety and depression in Ayurveda (Bhattacharya et al., 1987).

Water extract from Ashwagandha roots was investigated for anti-stress properties by assessing lipid peroxidation in rabbits and mice. In this study lipopolysaccharide isolated from Klebsiella pneumonia and peptidoglycan were administered in doses of 0.2 μg/kg and 100 μg/kg, respectively to induce lipid peroxidation. The elevated level of lipid peroxidation is considered to have connections with stress and anxiety. Ashwagandha in a dose of 100 mg/kg reduced the lipid peroxidation level in rabbits and mice (Bhattacharya et al., 2001). Research conducted in the Institute of Basic Medical Sciences at Calcutta University studied the activity of Ashwagandha on chronic stress in rats. The stress was induced by a gentle electric shock in the feet. The experiment continues for 21 days. This stress resulted in complications of hyperglycemia, high corticosterone levels, gastric ulcer, cognitive deficit, and depression. All these parameters were improved after the researchers administered Ashwagandha. This research confirms the theory that Ashwagandha has a significant anti-stress effect (Dhuley, 1998; Singh et al., 2010). Another study in humans was conducted using ethanol extract of Ashwagandha root. It was a double-blind placebo study. A total of 39 individuals were selected with anxiety disorder. 20 were given Ashwagandha extract and 19 were selected as a placebo group for 6 weeks. At the end of the study, it was revealed that the Ashwagandha treated group showed anxiolytic potential which was far superior to the placebo-treated group. The authors concluded that Ashwagandha tends to reduce anxiety and needs further investigation (Andrade et al., 2000; Verma and Kumar, 2011).

A scholastic study carried out in India showed that *Withania somnifera* extract (125mg QD, 125mg BID, or 250mg BID) or placebo groups showed anxiolytic activity. The participants were divided randomly, and observations were carried out for 60 days. The modified Hamilton Anxiety Scale was used to study the results of the experiment. The extract (125 mg QD) treated group significantly reduced anxiety by lowering the serum cortisol, serum C-reactive protein, pulse rate, and blood pressure. Conversely, it enhances the hemoglobin level. It was also clinically observed that extract in all doses also improves the blood sugar and lipid level. Moreover, this study also revealed that there were no notable side effects observed. Therefore, it was evident that the use of *Withania somnifera* extract significantly reduces experiential & biochemical indicators of stress (Abedon and Ghosal, 2008).

Ashwagandha has enjoyed a path of upward sales on the US market for the last many years. Sales data collected by HerbalGram, which compiles annual sales assessments of botanical products, disclosed a rise for Ashwagandha in the natural retail channel of 25 percent year-over-year. This is boosted by the increase in adaptogenic consumer products with overall health claims, from additives to tonics to functional drinks (Ziegenfuss et al., 2018).

5. Conclusion

It is well established from the scientific literature that Ashwagandha has potent regenerative tonic properties because of its various pharmacological activities like antistress and neuroprotective. It is

beneficial for diverse types of conditions like Parkinson's, dementia, memory loss, and stress-induced diseases. It has a useful effect on sports activity, increases physical performance, muscle tonicity, and stamina and it also increases muscle mass. Thus, the mentioned results clearly showed that the traditional use of Ashwagandha has a logical and scientific basis. Large-scale clinical studies are desirable to verify the clinical efficacy of this herb, especially in stress-related diseases and neuronal disorders.

Conflict of Interest

The authors declare no competing interest.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article. Data can be available on demand.

Ethics approval and consent to participate.

Not applicable

Authors' contributions

FA designed the study and carried out most of the data-acquiring parts. AR, SM, and HW, data acquiring and search. All authors read and approved the final manuscript.

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