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REVIEW ARTICLE

Medicinal and Therapeutic Potential of *Withania somnifera* (Indian Ginseng)

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METADATA

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ABSTRACT

Background: The Solanaceae family includes the woody evergreen shrub, *Withania somnifera*, which is notable for its various medicinal properties and is used in folk, conventional, and natural therapies in India. It has been a part of traditional Indian medicine for around 3,000 years.
Objective: To critically highlight the therapeutic relevance of *W. somnifera* by evaluating its antioxidant, anti-inflammatory, antimicrobial, antidiabetic, and anticancer properties.
Methodology: Relevant literature from scientific databases like PubMed, Google Scholar, ScienceDirect, Web of Science, and ResearchGate was reviewed to evaluate the pharmacological potential of *W. somnifera*.
Results: *W. somnifera* exhibits significant antioxidant potential by neutralizing free radicals and reducing oxidative stress. It shows marked anti-inflammatory activity through inhibition of pro-inflammatory cytokines. It possesses considerable antimicrobial effects against multiple bacterial and fungal strains. *W. somnifera* effectively lowers blood glucose levels, demonstrating its antidiabetic properties. Moreover, it displays strong anticancer activity by inducing apoptosis and inhibiting proliferation in cancerous cells. It can limit the onset of particular diseases like insomnia, diabetes, Parkinson's and Alzheimer's diseases, epilepsy, hyperlipidemia, and heart attack etc.
Conclusion: *W. somnifera* is a medicinal herb known for its diverse therapeutic properties, including antioxidant, antidiabetic, antimicrobial, anti-inflammatory, and anticancer activities. Its bioactive compounds, particularly withanolides, contribute to the modulation of oxidative stress, immune function, and metabolic balance, making it a promising candidate for managing chronic diseases.

INTRODUCTION

The use of plants for therapeutics and medicinal purposes to treat illnesses and enhance human health is known as herbal therapy or phytomedicine (Singirala *et al*. 2025). Medicinal plant parts that can be employed include leaves, seeds, roots, flowers, fruits, and even the entire plant. Phytochemicals are active compounds used as therapeutic agents. These active ingredients, such as secondary metabolites, phenols, vitamins of various types, essential lipids, flavonoids, alkaloids, and reducing sugars etc., are found in the majority of medicinal plants. Compounds originating from medicinal plants can significantly treat diseases like cancers of various types, such as breast cancer, colon cancer, lung cancer, leukaemia, pancreatic cancer, and prostate cancer, etc., which are difficult to treat.

Medicinal plants can limit the onset of particular diseases like insomnia, diabetes, Parkinson's and Alzheimer's diseases, epilepsy, hyperlipidemia, and heart attack etc. (Jayakumari *et al*. 2020). Now-a-days, there is a growing demand and acceptance of medicinal herbs. The World Health Organization (WHO) estimated that the primary source of medical care for 3.5 billion people in poor nations is herbal remedies. There are more than 120 important polyphenols that come from plants, and about 90% of labelled plant medications come from natural resources.

Natural products make up around half of the medications being used in clinical settings (Singh *et al*. 2021). These herbs are very beneficial to human health, especially in areas where access to treatment is limited. Even while herbal therapy has gained popularity, concerns about its efficacy, safety, and quality still exist. Herbal therapy integrates emotional, spiritual, and mental aspects of health. Despite their widespread use and general assumption of safety, medicinal herbs have the potential to be poisonous (Aftab and Hakeem 2021). *Withania somnifera* L. is an evergreen, small, delicate, perennial shrub that reaches a height of roughly 2 meters and a width of approximately 1 meter. The stems are upright and have a brownish colour. It is grown as a medicinal crop in India because of its fleshy roots, which are rich in bioactive chemicals (Paul *et al*. 2021). It has been used for centuries by herbal healers. The plant is called "winter cherry" and is utilized in supplements and blends that are intended to provide a variety of effects. It has numerous medicinal applications in both conventional and contemporary medicine (Mahendran *et al*. 2024), such as Withanolide A, Withanolide D, Withasomnillide, Withanone, Withasomniferanolide, Somniferwithanolide, and Somniwithanolide. Ashwagandha that are used to treat thyroid problems, improve reproductive health, increase vitality, fight weariness, boost energy levels, and enhance general well-being, boost memory, lessen the ageing-related debility, rheumatism management, constipation relief; to treat goiter, carbuncles, ulcers, uncomfortable swellings, colds, and coughs. Its trunk cortex contains somniferanolide, Withasomnilide, somniferawithanolide, somniwithanolid, phenols, vitamins, essential lipids, flavonoids, alkaloids, and reducing sugars, etc. (Buchanan *et al.* 2021; Singirala *et al*. 2025). Major phytochemicals are shown in Fig. 1.

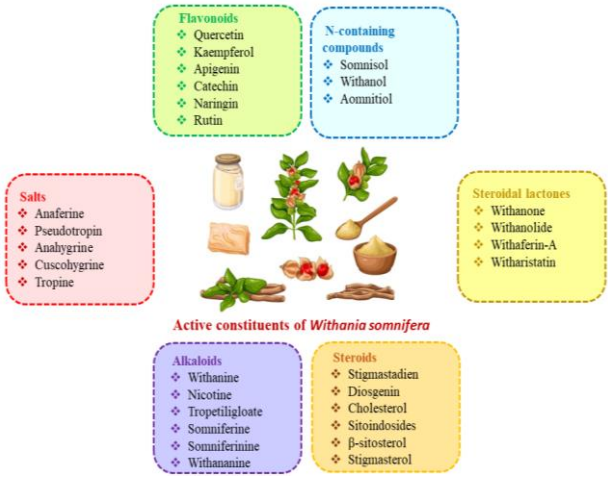

Fig. 1: Role of AI in SMEs and challenges in its implementation

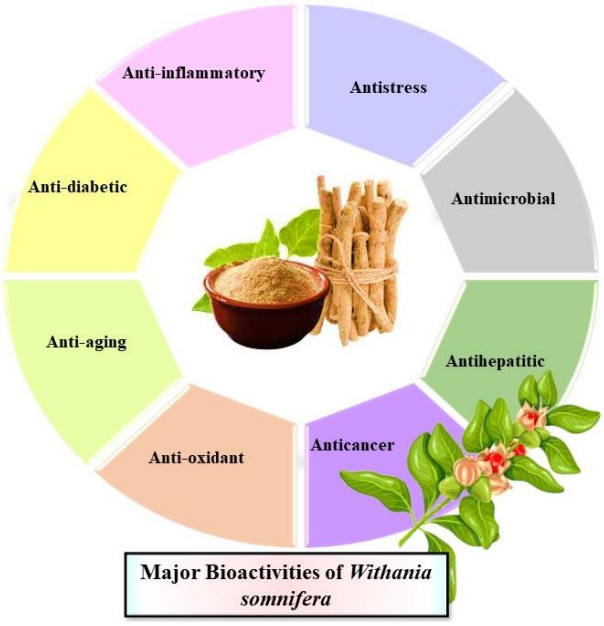

Fig. 2: Bioactivities of *W. somnifera*

MEDICINAL IMPORTANCE

A versatile therapeutic plant known as a member of the *Solanaceae* family. Folk medicine practitioners cure various ailments such as pyrexia, neoplastic conditions, hyperglycemia-related illness, metabolic disease, chronic airway inflammation, lesions, hepatic infection, vision-related problems, rheumatic conditions, piles, and swollen anal veins by using bioactive plant compounds such as natural steroidal lactones, psychotropic agents, hepatic safeguarding, inflammatory response modulator, fungal growth suppressor, free radical scavenger, heart-protecting, and physique-supporting agents (Saleem *et al*. 2020) (Fig. 2). *W. somnifera* protects several organs, regulates inflammation, suppresses pro-inflammatory cytokines, maintains immunological balance, and has antiviral, anti-stress, and antihypertensive qualities (Singh *et al*. 2022). Thyroid hormones thyroxin, thyroid-stimulating hormone, and T3 respond to stimulation from iodine. Withaferin A (WA) is the chemical that primarily increases thyroid function as well as cytotoxic properties. So, *W. somnifera* is used to treat hypothyroidism, diabetes, COVID-19, and many other ailments. Witanoside V and somniferin may have the ability to block the main SARS-CoV-2M protease (Abdel-Wahhab *et al*. 2019).

ANTIOXIDANTS ACTIVITY

The antioxidants restrict the oxidation of proteins, lipids, DNA, and other materials by stopping the progression steps of an oxidative chain reaction. Due to their higher iron and lipid content, which are thought to be significant contributors to the production of ROS, the brain and nervous system are comparatively more vulnerable to ROS damage than other tissues. The brain used 20% of the oxygen supply.

Neurological disorders like Alzheimer's, epilepsy, Parkinson's, schizophrenia, and others, as well as age-related cognitive decline, have been linked to ROS-impaired neurons. Antioxidants help neutralize ROS, thereby having the potential to protect the body from these diseases. The alkaloid content of the *W. somnifera* is shown to be primarily responsible for its total antioxidant and reducing activities, with flavonoids and withanolides ranking second and third, respectively. The fresh, dried leaves and tubers of this plant were reported to have more antioxidant compounds than the delicate roots and stems. Moreover, catechin is the primary flavonoid present at the highest concentrations in this plant (Chidambaram *et al*. 2024).

The effect of root aqueous extract was investigated in a study on endotoxin-induced stress in hares and rodents. Oxidative stress markers concentration in the blood increased upon endotoxin administration. A concurrent oral dose of 100 mg/kg of *W. somnifera* extract stopped the rise in lipid peroxidation. It reduced the elevated activity of cholinesterase and sodium, potassium, and adenylphosphatase in the brain, striatum, and limbic structure, as well as a significant increase in the production of TNF-alpha. It also prevented the inhibition of nicotinic function through sustaining an appropriate acetylcholine effect. *W. somnifera* helps to improve memory because one of its compounds, WA, was found to increase the activity of a certain enzyme (ROS prostaglandin-endoperoxide synthase-2) in rabbit joint cells, which then promoted the production of type-2 collagen, depending on the dose and duration of use. The biological effect of *Withania* genus, especially their antioxidant properties, depends on how the plant is extracted. When compared to extracts made with water, acetone, or a mix of water and methanol (1:1), the extract made with methanol, chloroform, and water (1:1:1) showed stronger antioxidant and reduced activity. This was true for all tested plant compounds, except tannins (Balkrishna *et al*. 2022).

Lab-grown roots (in vitro sprouted) had higher levels of antioxidant activity than roots collected from the field. Methanol extracts of *W. somnife*ra shoots, leaves, and roots contained high amounts of natural antioxidants like flavones and phenolic acids such as gallic, *p*-coumaric, syringic, and benzoic acids. These compounds are known for their ability to neutralize free radicals. Lighter plant compounds were best extracted using ethyl alcohol and *n*-hexane. The antioxidant capacity of *W. somnifera* extracts was measured using the phosphomolybdenum (PMo) method and expressed in vitamin C equivalents per gram. Among the different types of extracts tested, the one made with chloroform showed the strongest ability to scavenge free radicals. The total flavonoid content in each extract was measured using the aluminum chloride assay. Because of its antioxidant power, *W. somnifera* has been used to support brain health and manage neurological problems related to oxidative stress. It may also help in the recovery from neurodegenerative diseases (Paul *et al*. 2021).

ANTI-DIABETIC ACTIVITY

Diabetes is an endocrine and metabolic condition in which the body does not use glucose properly. One aspect of pathophysiology is increased oxidative stress, which damages beta cells and alters the histology of the pancreas. Diabetes has several different complications, including organ infections, obesity, and both microvascular and macrovascular problems (Vesa *et al*. 2021). WA may cause changes in lipid profiles and glucose metabolism. It promoted weight loss and reduced inflammation in diabetic patients, which raised insulin sensitivity (Khalilpourfarshbafi *et al*. 2019). The WA reduced rat hepatic steatosis. Expression of genes for insulin signaling is downregulated in diabetes. WA therapy enhanced mRNA transcriptional activity that comprises the insulin receptor substrate-1, phosphatidylinositol 3-kinase. According to the investigations, WA lessens the effect of type-1 diabetes (Eguchi *et al*. 2021).

Additionally, diabetic patients' blood glucose levels were considerably reduced when *W. somnifera* root powder was taken orally. Lactonic steroids are responsible for their antidiabetic effects. Numerous withanolides that had been extracted from *W. coagulans* fruits had shown anti-diabetic activity, and many of their biological functions had been documented. Extracts from leaves and roots both enhanced the absorption of glucose in rat adipocytes (3T3-L1) and myotubes (L6) (Makhlouf *et al*. 2024). Furthermore, insulin production in insulin-producing cells was enhanced by more than fifty percent by leaf extract, despite root extract. It also stimulated cells that did not experience this effect. In patients with type 2 diabetes, raising basal insulin levels has been linked to decreased hepatic glucose synthesis, fasting glucose, and free fatty acid levels. Selected withanolides that had been extracted from *W. somnifera* were evaluated for their hyperglycemic properties. In diabetic mice, flavonols and polyphenols found in different plant parts effectively lowered blood glucose levels. While substantially greater levels of Alpha-lipoprotein were observed in diabetic rats, the phenolic content of root and leaf extracts helped lower blood sugar levels. The preclinical experimental outcomes were encouraging. Studies on animals have demonstrated their capacity to reduce blood glucose levels. Additionally, it was demonstrated that WA had great therapeutic promise since it can effectively regulate type-1 diabetes in rats that had been produced by modulating Nrf2/NFκB signaling. Using molecular docking, in silico studies have also validated the potential of steroidal lactone. It has a positive impact on the lipidemic profile. Both the antioxidant effect and the decrease in cholesterol levels are benefits of this plant observed in a white albino rat that had elevated cholesterol levels. Interesting outcomes were obtained in changing the lipidemic profile in the diabetic clinical trials, even though there was no effect on blood sugar level. There was a decrease in the patient's lipidemic profile evaluation using the DDS17 measure to gauge the patient's level of distress. A

standardized extract from *W. somnifera* under the brand name SENSORIL enhanced the lipidemic profile and antioxidant parameters while also proving the raw material's safety and tolerability. A change in the reflection index [RI] of 3.8% was shown and an impact on the lipidemic profile despite being safe and tolerable (Mikulska *et al*. 2023).

ANTIMICROBIAL ACTIVITY

Drug resistance in microorganisms poses a significant and expanding problem. Hence, *W. somnifera* is a beneficial medicinal supplement in the management of various infections caused by bacteria. Even though most of the medications applied to treat infections induced by bacteria were effective, toxicity results in severe, harmful side effects. While *W. somnifera* has very few adverse effects. Research had demonstrated that it was an efficient source of suppressing, proliferation of methicillin resistant. *Enterococcus* species and *Staphylococcus aureus*, *Salmonella typhi*, *Citrobacter freundii*, *Proteus mirabilis*, *Pseudomonas aeruginosa,* and *E. coli*. Many of its characteristics were thought to represent the mechanism of its antimicrobial action. Studies related to animal models demonstrated that *W. somnifera* effectively reduced the progression of infection after contracting salmonellosis, indicating its efficacy as a treatment for the disease. It inhibited oral cavity bacterial growth, including *Streptococcus sobrinus* and *Streptococcus mutans*. Additionally, it prevented bacteria from producing acid, becoming acid-tolerant, and growing biofilms (Khanchandani *et al*. 2019).

It was especially effective in combating *S. typhi*. The withanolides that were extracted from *W. somnifera* cause *Leishmania donovani* promastigotes to die by triggering apoptosis. It causes reactive oxygen species to be released from mitochondria by altering mitochondrial membrane potential. According to studies, it also has important antifungal properties against a few different types of fungi, including *Candida albicans*. Glycoprotein has been isolated from its root tubers and has antibacterial and antifungal characteristics against *Clavibacter michiganensis* subsp. *Aspergillus flavus*, *Fusarium verticillioides* and *Fusarium oxysporum.* Root extract exhibited increased antibacterial activity against *P. aeruginosa*. Research on the action of root extract's antibacterial activity, utilizing membrane stabilization and morphological analysis revealed that it worked by rupturing the *P. aeruginosa* cell membrane. *W. somnifera* extracts, particularly in large quantities, in animal studies, were useful to treat malaria by considerably lowering parasitaemia. Flavonoids have demonstrated outstanding antibacterial properties against *E. coli, P. mirabilis, C. albicans,* and *S. aureus*, but are inefficient against Aspergillus oryzae var flavus. However, *W. somnifera* methanolic extract was found to have a minimum inhibitory concentration (MIC) against both *C. albicans* and *Neisseria gonorrhoeae*, but the aqueous extract was found to have MIC against *N. gonorrhoeae*. Its glycoconjugates exhibited fungicidal activity for *Fusarium verticillioides* and *A. flavus*, as well as bactericidal potential for *Corynebacterium michiganense* (Mikulska *et al*. 2023). *W. somnifera* performed best against *B. thuringiensis* and *C. diphtheria*. Antibacterial agents such as steroids, anthroquinone, alkaloids, and Flavonols had all been detected in the plant leaves. The chloroform extract from *Withania* leaves had anti-*B Therogenesis* and anti-*C Diphtheria* properties. *W.* and *Calotropis procera* both possessed antibacterial qualities against pathogenic strains. The antibacterial properties were evaluated by phytochemical components in alcoholic and chloroform extracts of *W. somnifera* stems, leaves, and roots (Sandhiya *et al*. 2022). Human immunodeficiency virus (HIV) has claimed 40.1 million deaths, and there is no known cure, making it one of the most historically significant diseases. Alzheimer's disease (AD) patients have been linked to one of these HIV-related causes. Interestingly, WA demonstrated its effectiveness in treatment for HIV indirectly. Additionally, the study revealed that WA causes a higher means of CD4 cell count. Additionally, it was shown that WA inhibited the HIV strain by preventing the microbes' replication as well as transcription. *W. somnifera* lowered the progression of disease markers, on CD8+T lymphocytes and CD38, suggesting that it has anti-HIV properties (Ozeer *et al*. 2024).

It suppressed and controlled the coronavirus main protease and Membrane Receptor protein serine protease-10 and prevented severe acute respiratory syndrome coronavirus (SARS)-associated coronavirus entry by reducing the electrochemical element in the angiotensin-converting enzyme 2 (ACE2) complex and SARS-CoV-2 receptor binding domain. It is a powerful medicinal plant that fights COVID-19. It also helped to prevent infections. According to *in silico* research, *W. somnifera* suppressed the COVID-19 virus's ability to replicate via modifying T-cell separation and NK-cell cytotoxicity. Several withanolides downregulated nucleoplasmic sequences (N-gene) and viral envelope (E-gene) expression. It was discovered that withanolide P, mesoanaferine, withanolide O, bsitosterol, withanolide D, and somniwithanolide limited the coronavirus protease of SARS-CoV-2. At the same time, 3CLpro and PLpro were suppressed by tropine, choline, and withanisomniferol C. Apart from these, several potent substances might be effective in treating the sickness (Willett *et al*. 2022). In conclusion, WA exhibits protective effects against both bacterial and viral infections.

ANTI-INFLAMMATORY ACTIVITIES

Because of above mentioned characteristics, *W. somnifera* was being studied to treat a wide range of inflammatory diseases, including diabetes, cancer, neurological disorders, and autoimmune, pulmonary, and cardiovascular conditions. Through the inhibition of inflammatory markers such as cytokines, nitric oxide, and reactive oxygen species, it can regulate mitochondrial activity, apoptosis and reduce

inflammation. Meanwhile, a possible inhibitory impact of powdered *W. somnifera* root was shown in a lupus-ridden mouse model in circumstances including nephritis and proteinuria. The effect of *W. somnifera* for rheumatic illnesses was also being studied. Rats were given powdered *W. somnifera* root orally for three days. Rats were fed phenylbutazone as part of the control group (positive control). A marked decrease in inflammation and altered quantities of several serum proteins, including pre-albumin, acute phase protein α1 and α2 glycoprotein, were observed after the use of *W. somnifera*. To find out how an aqueous extract from *W. somnifera* root inhibited the expression of pro-inflammatory cytokines like interleukin (IL)-8 and IL-6, a study was conducted using the human keratinocyte cell line (HaCaT). Ashwagandha aqueous extract (ASH-WEX) was found to have anti-neuroinflammatory effects against lipopolysaccharide-induced systemic neuroinflammation (Kanjilal *et al*. 2021).

In a preclinical study, ASH-WEX showed reduced expression of nitro-oxidative stress enzymes and inhibition of reactive gliosis in treated animals. The underlying molecular processes behind ASH-WEX's anti-inflammatory properties seem to entail blocking the P38, JNK/SAPK, MAPK, and NFκB pathways that were triggered by lipopolysaccharide (LPS). *W. somnifera* might be used to reduce nervous system inflammation linked to a variety of neurological conditions. It was demonstrated that treating patients' arthritic symptoms with *W. somnifera* extract administered for eight to twelve weeks could be helpful (Mikulska *et al*. 2023). ECM dysregulation and lung inflammation is caused by a variety of mechanisms, including loss of proteostasis, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, genomic instability, epigenetic alteration, telomere attrition, incorrect intercellular communication, cellular senescence and unregulated nutrient-sensing. Ashwagandha showed a decrease in TNF-α and NF-KB and an increase in IL-10, which might be contributing factors to the development of lung inflammation. Because it made it easier to reduce skeletal muscle inflammation, decreased levels of IL-10 are intimately linked to lung inflammation (Kashyap *et al*. 2022).

CARDIOPROTECTIVE ACTIVITY

Myocardial infarction (MI) is a leading cause of mortality globally, also an essential medical problem. Withanolid A 1 mg/kg stimulated the mitochondrial antiapoptotic pathway by reducing apoptotic cell death and upregulating the protein Bcl-2. According to the in vivo investigation, rats administered a modest quantity of WA showed protection against MI injury. WA demonstrated beneficial cardiac activity by inducing adenosine monophosphate kinase activation and inhibiting the intrinsic apoptotic pathway. WA can therefore be used therapeutically for cancer patients who also have cardiovascular system problems (Li *et al*. 2018).

W. somnifera treats heart diseases by reducing oxidative stress, improving antioxidant enzyme activity, and reducing inflammation. Several heart conditions, including heart attack, hypertensive cardiomyopathy, chronic ventricular coronary artery disease, hypertrophic cardiomyopathy, and uncontrolled cardiomyopathy, were associated with cardiac collagen depositions and could be treated with *W. somnifera*. WA inhibited ferric chloride-induced platelet aggregation as well as thrombin-catalyzed fibrin polymerization, prolonged hemostasis, and suppressed tumour necrosis factor-alpha-induced inhibitor of plasminogen activator formation. These findings collectively demonstrated the cardioprotective potential of WA; however, given its safety and effectiveness, further clinical trials are required to substantiate its therapeutic function in heart disorders (Behl *et al*. 2020).

OSTEOPOROSIS

An imbalance in bone growth and resorption was the hallmark of osteoporosis, a condition of the skeletal bones (Tit *et al*. 2018). *W. somnifera* promotes osteogenic cells' development and proliferation by regulating osteoblast-specific transcription factors' expression. WA prevented the synthesis of cytokines that cause inflammation. Moreover, WA inhibits the production of osteoclast acid phosphatase and osteoclast differentiation factor, receptor WA reduces the number of osteoclasts, also referred to as bone-resorbing cells (Saleem *et al*. 2020).

ANTI-HEPATITIS ACTIVITY

W. somnifera shows strong potential against hepatitis-related liver damage, particularly in advanced conditions like NAFLD with hepatitis and nano-ALD, which increase the risk of chronic liver disease and cancer (Taylor *et al*. 2020). Excessive lipids lead to harmful fat accumulation, oxidative stress, inflammation, and ER stress – mainly due to ceramides. WA, a key compound in *W. somnifera,* reduces liver damage by lowering oxidative stress through oxygenase activity and activation of the NRF2 pathway, highlighting its role as a natural hepatoprotective agent (Kalluri *et al*. 2023).

ANTISTRESS EFFECT

Stress is defined as a state of worry or mental tension that is brought on by a challenging situation. Antistress activity lowered the risk of most diseases. A widespread improvement in stress resilience was observed after using *W. somnifera*. Sitoindosides VII and VIII, two of its glycosides, had strong anti-stress effects in models including forced-swim immobility, stomach ulcers, auto-analgesia generated stress, altered thermic response to morphine, and morphine-induced toxicity in mice. *W. somnifera* exhibited noteworthy antistress efficacy, which was determined by swimming endurance tests (Speers *et al*. 2021).

ANTICANCER/ CYTOTOXIC ACTIVITY

Unchecked cell division was a characteristic of a disease called cancer. Cancer was caused by modifications to proteins that encode genes that were part of the cellular division cycle, including prototypes of cancerous genes and non-cancerous genes. According to the diagnoses in the US alone in 2022, heart disease was the world's biggest cause of death, with cancer coming in second. Although *W. somnifera* did not affect healthy human cells, it was cytotoxic to a wide range of tumour cells, suggesting that it only affected cancer cells. It had been demonstrated that *W. somnifera* upregulated the expression of several conjugating enzymes, indicating that the phytochemicals worked either directly or through indirect means by regulating additional cell protective routes, including NFE2L2 (Kashyap *et al*. 2022). Researchers used a variety of molecular techniques, including global gene-expression sequencing, antibody-based protein detection assays (western blot), fluorescent immune-staining, real-time cDNA amplification, and siRNA-mediated gene silencing, to identify signalling cascades. It caused intrinsic apoptosis in Glioblastoma Multiforme (GBM) cells and markedly reduced GBM growth both in vivo and in vitro. Thr161 CDK1 was dephosphorylated, causing GBM cells to be stopped in the cell cycle's G2/M phase. This discovery holds significance for enhancing WA-based regimens intended for the multifactorial aggressive brain cancer reduction. Previous research identified that the extract reduced inflammation and damage from oxidative stress in the hepatic and splenic tissues, defending against the deleterious consequences of radiation exposure. These results indicate that *W. somnifera* root extract might have therapeutic uses in preventing damage to the liver and spleen, otherwise two important organs damaged by radiation (Mikulska *et al*. 2023).

Prostate cancer

Prostate cancer is the 2nd leading type of cancer in men and accounts for 3.8% of men who die from cancer globally (Bray *et al*. 2018). Additionally, WA caused a weal to accumulate at the mitotic transition, which caused a dose-dependent decrease in cell survival. Through PAWR-mediated extrinsic signalling, downregulation of matrix gelatinase a by azido-modified WA limited cellular invasion. Furthermore, *in vivo* research showed that mice's angiogenesis was prevented, and p-ERK and p-Akt expression were reduced. By inducing ER stress and affecting the transition of prostate cancer cells from autophagy to apoptosis, 3-azido WA also demonstrated anticancer potential against prostate cancer. Metabolic reprogramming of lipids in cancer cells and an emerging method of triggering prostate cancer cell death might be revealed by recent reports (Hassannia *et al*. 2020).

Colon cancer

Among all malignancies, colon cancer ranked second in terms of mortality cases and third in terms of incidence worldwide. Ethanolic extracts of *W. somnifera* were found to exhibit azoxymethane-triggered immunomodulatory effects in Swiss strain mice with colorectal cancer (Mukherjee *et al*. 2021). Ashwagandha-derived steroidal lactone shows cytotoxic potential against anti-colorectal malignancy (Gharaibeh *et al*. 2020). Additionally, Balb/c nude mice with HCT116 xenograft tumours showed a significant decrease in tumour weight and volume after receiving steroidal lactone treatment. Mice treated with withanolids exhibited a significant reduction in tumour growth, volume, polyp size, and adenomas when compared to controls (Alnuqaydan *et al*. 2020).

Ovarian cancer

W. somnifera treated ovarian cancer in several ways. WA stopped the G2/M phase cell cycle in human ovarian cancer cell lines (SKOV3 and CaOV3) (Davis *et al*. 2024). By suppressing the cell signalling and apoptosis regulation, WA triggers apoptotic protease activation, which results in cell death. At suboptimal doses, withanolids, cisplatin, and doxorubicin produce ROS and kill cells (Atteeq *et al*. 2022). In xenografted tumors, WA lowered the levels of phospho-p65 cytokines linked to NF-kB both in the cytosol and the nucleus (Kelm *et al*. 2020).

Leukemia

W. somnifera is a potent medicinal herb fighting against leukaemia. When *W. somnifera* was applied to solid tumours, withaferin-A (an essential phytochemical of *W. somnifera*) showed strong anticancer properties. Its effectiveness in preventing haematological malignancies has shown significant results, WA inducing apoptosis through the p38/MAPK signalling pathway, inhibiting cell growth in several leukemic lymphocytes as well as cancerous blood cells, and cytotoxicity. Additionally, *W. somnifera* shows many anti-leukemic properties, including the capacity of phytochemical extracts to enhance superoxide production, trigger cell cycle arrest, deliver Ca+2 ions homeostasis, also weaken the T-lymphoblastoid cell lines and DNA structure (Dutta *et al*. 2019).

Lung cancer

The leading cause of cancer-related deaths worldwide is lung cancer (Siegel *et al*. 2021). Swiss albino mice with benzopyrene-induced lung carcinogenesis were protected against oxidative impairment by the antioxidant activity of *W. somnifera* (Singh *et al*. 2021). Its withanolides also reduced the attachment of human leukemia monocytes to lung adenocarcinoma cells by blocking Akt phosphorylation, inhibiting NF-κB activity, and lowering the expression of VCAM-1 and ICAM-1 (Mandlik *et al*. 2021). Moreover, in lung adenocarcinoma cells, withanolides counteracted

cachexin-induced changes, disrupted cytokine signaling, and promoted cancer cell death (Dutta *et al*. 2019). These results supported the investigation of *W. somnifera*'s effectiveness in treating pulmonary malignancy (Kumar *et al*. 2023).

Breast cancer

The most common type of cancer among women is breast cancer (Siegel *et al*. 2021). Aggressiveness and the spontaneous metastasis of breast cancers were strongly affected by their structural distinctions (Al-Mahmood *et al*. 2018). Research employing fluorescence microscopy demonstrated that WA was useful in phosphorylating the H3 histone at the Ser10 position and inducing a mitotic stop in MDA-MB-2 and MCF-7 cell lines in breast cancer cells (Kumar *et al*. 2023). The same cells also underwent FOXO3a-induced apoptosis. WA demonstrated a unique mechanism for inducing apoptosis. It had been demonstrated that WA inhibited oxidative phosphorylation in breast cancers and triggered ROS to cause cell death and improved anti-metastatic and anti-invasive behaviors (Paul *et al*. 2021). WA methylates or demethylates a large number of genes linked to basal-like breast carcinoma, blocks the unique characteristics of slightly vigorous luminal breast cancer, and improves healing efficacy (Vel Szic *et al*. 2019).

CONCLUSION

W. somnifera exhibits a wide spectrum of pharmacological effects, including antioxidant, antidiabetic, antimicrobial, anti-inflammatory and anticancer activities. These effects are largely attributed to its diverse phytoconstituents, particularly withanolides. Extensive *in vitro* and *in vivo* studies have confirmed its ability to scavenge free radicals, modulate immune responses, inhibit microbial growth, regulate blood glucose levels and induce apoptosis in cancer cells without harming normal tissues. Furthermore, emerging clinical investigations support its therapeutic potential in managing chronic diseases, highlighting its role as a promising natural candidate for integrative medicine. Continued exploration through advanced research and clinical trials is essential to validate its efficacy, safety and mechanistic pathways in human health. These multifaceted benefits underscore the plant's therapeutic versatility and justify further exploration in clinical settings. Yet, extensive research is still needed to validate its medicinal claims and understand its active compounds. Advances in biotechnology and sustainable cultivation can further support clinical and pharmaceutical applications.

AUTHOR CONTRIBUTIONS

NH: Conceptualized and drafted the manuscript; IS: Conducted literature review and editing; FH: Critically revised the manuscript. All authors approved the final manuscript.

CONFLICT OF INTEREST

The authors affirm that they possess no conflicts of interest.

DATA AVAILABILITY

Not applicable

ETHICS APPROVAL

Not applicable

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