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# Effectiveness of Withania somnifera (Ashwagandha) in prevention of Cancer: A Systematic Review

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Withania somnifera (Ashwagandha) helps prevent cancer through its strong antioxidant and anti-inflammatory properties. It boosts immune function by enhancing natural killer cells and macrophages. Withaferin A in ashwagandha promotes apoptosis in cancer cells without harming normal cells. It inhibits tumour growth by blocking angiogenesis and supports hormonal balance. Ashwagandha also aids DNA protection and repair, reducing cancer risk. The Objective of the study is to systematically evaluate the effectiveness of W. Somnifera in the prevention of cancer, based on evidence from clinical studies. A systematic review was conducted following PRISMA guidelines. Databases searched included PubMed, ScienceDirect, Wiley Online Library, and SpringerLink. Studies from 2001 to 2023 were screened using specific inclusion/exclusion criteria, focusing on W. somnifera effect on cancer-related outcomes. The risk of bias used tool is the Cochrane's revised tool for randomized trials (RoB 2). The systematic review identified six eligible studies that demonstrated various anticancer effects of W. somnifera. This included inhibition of tumor growth, suppression of metastasis, enhancement of chemotherapy tolerance, and improved quality of life. The studies used different preparations of the herb, and the active compounds—particularly Withaferin A and withanone were shown to induce apoptosis, regulate immune responses, and target cancer pathways effectively. Withania somnifera shows promising anticancer potential, acting through multiple pathways including antioxidant defense, hormonal regulation, and tumor suppression. While preclinical and early clinical findings are encouraging, more large-scale human trials are needed to establish its safety, efficacy, and clinical utility in cancer prevention and therapy.

**Keywords:** Withania somnifera, Ashwagandha, Cancer prevention, Withanolides, Withaferin A, Anticancer activity

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## Introduction

Cancer is a broad term that refers to a wide range of diseases capable of affecting any part of the body. A major hallmark of Cancer is the rapid growth of abnormal cells that exceed their usual boundaries, potentially invading nearby tissues and spreading to distant organs.**[1]** Cancer is hyperproliferative disorder that involves transformation, dysregulation of apoptosis, proliferation, invasion, angiogenesis and metastasis. **[2]** These aberrant cells typically upset the balance between cell proliferation and cell death, resulting in benign tumors that develop invasive characteristics and manifest symptoms ranging from benign to metastatic.**[3]** Various approaches to cancer treatment across medical systems are explored in recent literature, including conventional allopathy, Ayurveda, homeopathy, Traditional Chinese Medicine [TCM], and naturopathy.**[4]** Various parts of the plant are widely used in Ayurvedic and Unani medicine [Indigenous systems of medicine in India] for its medicinal properties.**[5]** The Ayurvedic system identifies thousands of plants that help prevent ailments and maintain health, including *Withania somnifera*. L.**[6]**

The leaves and roots of this medicinal plant species have been utilized for more than 3000 years for various health-related purposes in Ayurveda, the Indian traditional medicine. *Ashwagandha* is often called the Queen of Ayurveda or a Rasayana plant because of its exceptional medicinal powers.**[7]** The *Withania* species *W. somnifera* and *W. coagulants in India* are widely used. Even though 23 species of Withania were identified, only W. somnifera, Withania Coagulans (S) Dunal, W. coagulans (Rishyagandha) are thought to have therapeutic properties.**[8]**

Recent scientific studies have highlighted its potential anticancer properties, primarily attributed to its active compounds called withanolides. These bioactive molecules have demonstrated the ability to induce apoptosis (programmed cell death), inhibit angiogenesis (formation of new blood vessels that feed tumors), and suppress metastasis in various cancer cell lines including breast, colon, lung, and prostate cancers. Moreover, *Withania somnifera* has shown potential to enhance the efficacy of conventional chemotherapy while reducing its side effects.

Its immunomodulatory and antioxidant properties further contribute to its anticancer effects by strengthening the body's natural defense mechanisms.**[9]** These withanolides are cytotoxic to cancer cells, immunomodulatory, and neuroprotective in function.**[10]** The alkaloids of *Withania somnifera* bind to the BIR5 protein site, potentially disrupting the mitotic process and demonstrating promising antitumor activity.**[11]**

*Withania somnifera* (*Ashwagandha*) has been found to have anti-epileptic, anti-inflammatory, anti-arthritic, anti-depressant, anti-coagulant, antioxidant, anti-diabetic, and antipyretic efficacies along with palliative effects such as analgesic, rejuvenating, regenerating and growth-promoting impact.**[12]** *Ashwagandha* has been shown to contain high levels of flavonoids, phenolic compounds, and antioxidant compounds.**[13]** There are several other secondary metabolites found in this plant, such as flavonol glycosides, sterols, phenolics, glycosides, starch, reducing sugar, and a variety of amino acids, including aspartic acid, proline, tyrosine, alanine, glycine, glutamic acid, cysteine, tryptophan, and iron.**[14]** Among naturally occurring withanolides present in *W. somnifera*, Withaferin A [WFA) is the most effective anticancer agent.**[15]** *W. somnifera* targets Cancer in a variety of ways by cessation of cancer cell proliferation, induction of apoptosis, and inhibition of tumor-associated inflammation.**[16]** Withanolides found in *Ashwagandha* have been found cytotoxic to cancer cells, immunomodulatory, and neuroprotective in function. Among the most recent therapeutic applications of*W. somnifera*, are the studies in the treatment of various types of cancer like neuroblastomas, prostate cancer. Moreover, the toxicological studies revealed that the reasonable doses of*W. somnifera*are non-toxic and safe.**[17]** This systematic review seeks to evaluate the potential of *Withania somnifera* and its effectiveness in preventing Cancer.

## Materials and Methods

This systematic review was conducted for the effectiveness of Withania *somnifera* in cancer cell growth. The role of *Withania somnifera* in modulating cancer cells Systematic review was conducted following PRISMA guidelines. The literature review was carried out systematically, including the following steps: the research question,

Formulating a strategy for conducting a literature search, searching the literature and retrieving articles, data extraction, interpretation, and evaluation of evidence gathered from the literature.

**Research questions:**

The research question is, "How effective is *Withania somnifera* in the prevention of cancer?"

**Information sources:**

- PubMed
- Elsevier Science Direct,
- Web of science
- Grey literature
- Wiley Online Library, and

**Search strategy**

An electronic search was performed using the above-mentioned databases. The keywords used were a combination of keywords and MeSH terms such as "*Withania somnifera*," "Inflammation," "Effectiveness in cancer," and "Cancer." MeSH terms were used with Boolean operators (*Withania somnifera*) AND (Effectiveness in preventing Cancer) AND (Efficacy); (*Withania somnifera*) AND (Cancer); (*Withania somnifera*) OR (*Ashwagandha*) AND (Cancer).

**Inclusion Criteria**

1. This investigation reviews the randomized control trial conducted from 2001-2024
2. It incorporates complete articles retrieved from search engines such as pub-med
3. The study specifically explores the effectiveness of cancer
4. The study consists of comprehensive articles written exclusively in English.

**Exclusion Criteria**

1. Limit to studies using cancer cell lines as the primary focus or on non-cancer-related pathways.
2. Studies those were deemed redundant or irrelevant.

**Study selection**

Preliminary review of titles & abstracts conducted according to defined inclusion & exclusion criteria. Full-text review of selected articles. Data extraction from eligible studies using standardized form. Methodology Studies which fulfilled eligibility parameters were listed. Data included citation (author/year), place of study, number and type of samples collected, intervention provided, techniques and methods of measurement, and results and inferences drawn from study. Quality assessment was done using Cochrane's revised tool for randomized trials (RoB 2).**[18]**

# Results

This research resulted in 39 articles, of which 9 were full-text articles having accessibility and were eligible for review. Ultimately, 6 articles were chosen for inclusion in this systematic review [Figure 1]. Table 1 shows the Characteristics of the intervention. Table 2 Shows the intervention used in the study included with the outcome. Table 3 shows the risk of bias in all the included studies based on the Cochrane's revised tool for randomized trials (RoB 2). An overview of the steps according to PRISMA guidelines involved in the included studies is shown in the flowchart below.

**Table 1: Characteristics of the intervention of the studies included in the systematic review:**

| SN | Author | Patient Selection | Duration | Preparation Used | Intervention |
|---|---|---|---|---|---|
| 1. | Leemol Davis et al., 2000[19] | 24 healthy Swiss albino mice | 10 weeks | W. somnifera powdered root extract with 70% methanol and resuspended in PBS containing 1% gum acacia. | Twenty-four animals were divided into two groups, with 12 in each group. Group 1 received Withania extract (20 mg/dose/animal, i.p.) for five consecutive days. Group 2 served as the control group. |
| 2. | A.J.M Christina et al.,2004[20] | Male albino Swiss mice (20-30) | 11 days | W. somnifera Dunal root extracted with 70% ethyl alcohol, dried in vacuum and resuspended in water. | Six mice were divided into three groups. Group 1 served as the control group. Group 2 was treated with 200 mg/kg of REWS intraperitoneally. Group 3 received 5-fluorouracil (20 mg/kg), and the treatment continued for the next 10 days. |
| 3. | B.M Biswal et al.,2013[21] | 50 patients with all stages of breast cancer | 6 weeks | W. somnifera root extract in vegetarian capsule form was given at an oral dose of 2 g tds | Fifty patients were recruited into two groups. Group 1 received Withania somnifera along with chemotherapy, which had a positive effect on fatigue and improved the quality of life (QoL) in breast cancer patients. Group 2 served as the control group. |

| | | | | | |
|---|---|---|---|---|---|
| 4. | Eun-Ryeong Hahm et al.,2013[22] | Mice | 7 days | 100 micrograms of W. somnifera administered intraperitoneal for 28 weeks | Sixty animals were initially divided into two groups, with 30 in each group. Group 1 received treatment with Withania somnifera (WA), while Group 2 served as the control group. By the end of the study, Group 1 had 32 mice, and Group 2 had 29 mice. |
| 5. | Prem Kumar Govindappa et al., 2018[23] | Healthy male Wistar rat (8-10 weeks, 180-200g) | 14 days | Test dose of W. Somnifera 2000 mg kg-1, Gentamicin sulphate 40 mg ml-1 injection | Twenty-four rats were divided into four groups. Group 1 received normal saline (1 ml/kg, once daily for 21 days, i.p.). Group 2 was administered gentamicin (GM) (80 mg/kg, once daily for 8 days, i.p.). Group 3, termed the nephroprotective (NP) group, received Withania somnifera (500 mg/kg, once daily for 13 days, p.o.) as a pre-treatment, followed by simultaneous administration of gentamicin (80 mg/kg, i.p.) and W. somnifera (500 mg/kg, p.o.) from day 14 to day 21. Group 4, termed the nephrocurative (NC) group, received gentamicin (80 mg/kg, once daily for 8 days, i.p.) followed by W. somnifera (500 mg/kg, p.o.) from day 9 to day 21. |
| 6. | Adrian L Lopresti et al.,2019[24] | 60 healthy humans | 60 days | 240mg of standardized extract of W. somnifera | Sixty healthy adults were divided into two groups, with 30 in each group. Group 1 received 240 mg of standardized Withania somnifera extract daily for 60 days, while Group 2 served as the control group. |

**Table 2: Characteristics of the primary outcome and results of the studies included in the systematic review.**

| SN | Author | Outcome | Result |
|---|---|---|---|
| 1. | Leemol Davis et al., 2000[19] | Withania administration could significantly inhibit DMBA induced papilloma formation both in terms of incidence of tumour as well as mean number of papillomas/animal. | In the control group, all animals developed tumour on 120th day after tumor induction. Withania treated group, only four animals developed papillomas |
| 2. | A.J.M Christina et al.,2004[20] | PCV in the tumour control mice was found to be high. decrease in tumour weight was noted in the REWS treated mice survived up to 19 days only. | The decrease in the cancer cell number observed in the REWS treated mice of G2 indicates that the test drug is having significant inhibitory effect on the tumour cell proliferation. Treatment with REWS reduced the tumour weight and hence increased the life span. |
| 3. | B.M Biswal et al.,2013[21] | Positive effect on fatigue and improve QoL in patients with breast cancer. | Results suggest that oral dose of 2g ads of w. somnifera root extract in vegetarian capsule form. shows that effectiveness and toxicity of chemotherapy where not altered in patients with breast cancer. |
| 4. | Eun-Ryeong Hahm et al.,2013[22] | W. Somnifera administration shows significant inhibition of mammary cancer burden and pulmonary metastasis incidence and decreased expression of M2-type in the MMTV-neu mouse model. | W. Somnifera administration significantly decreases in macroscopic mammary tumor size, microscopic tumor areas and incidence of pulmonary metastasis. |
| 5. | Prem Kumar Govindappa et al., 2018[23] | W. somnifera effectively reverse renal damage with marked reduction in tubular damage induced gentamycin. Renal injury induced by gentamicin by elevated MDA, total protein, BUN and Cr levels with decreased electrolytes and antioxidant enzymes. W. somnifera with its antioxidant function significantly alleviates adverse effects of GM. | W. somnifera exerts therapeutic efficiency in regulation of lead nitrate induced nephrotoxicity in Swiss albino mice. |
| 6. | Adrian L Lopresti et al., 2019[24] | Primary outcome 1:<br>Hamilton Anxiety Rating Scale (HAM-A) access the severity of patient's anxiety.<br>Primary outcome 2: Depression, Anxiety, Stress Scale-21 (DASS-21) assessing symptoms of stress, anxiety and depression.<br>Secondary outcome 1 to 3: Serum cortisol, DHEA-S, testosterone - Levels of serum and cortisol were measured with the ADVIAO Centaur system using competitive immunoassay direct chemiluminescent technology. | W. somnifera administration significantly decrease stress hormone, cortisol and steroidal hormones, DHEA-S and testosterone. Ashwagandha intake was associated with a reduction in fasting, morning cortisol (0.5% increase and 23% reduction, respectively) and DHEA-S (2.5% increase and 8.2% decrease, respectively). Ashwagandha intake was also associated with a statistically significant increase of 10.6%, in testosterone which compared favorably to the 0.1% increase observed in the placebo group |

**Table 3: Quality assessment of all the included studies:**

| Author | Bias due to randomization | Bias in classification of interventions | Bias due to deviations from intended interventions | Bias due to missing data | Bias in measurement of outcomes | Bias in selection of reported results | Overall Risk of Bias |
|---|---|---|---|---|---|---|---|
| Leemol Davis et al., 2000[19] | | | | | | | |
| A.J.M Christina et al.,2004[20] | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| B.M Biswal et al.,2013[21] | | | | | | | |
| Eun-Ryeong Hahm et al.,2013[22] | | | | | | | |
| Prem Kumar Govindappa et al., 2018[23] | | | | | | | |
| Adrian L Lopresti et al.,2019[24] | | | | | | | |

Low Risk Moderate Risk High Risk

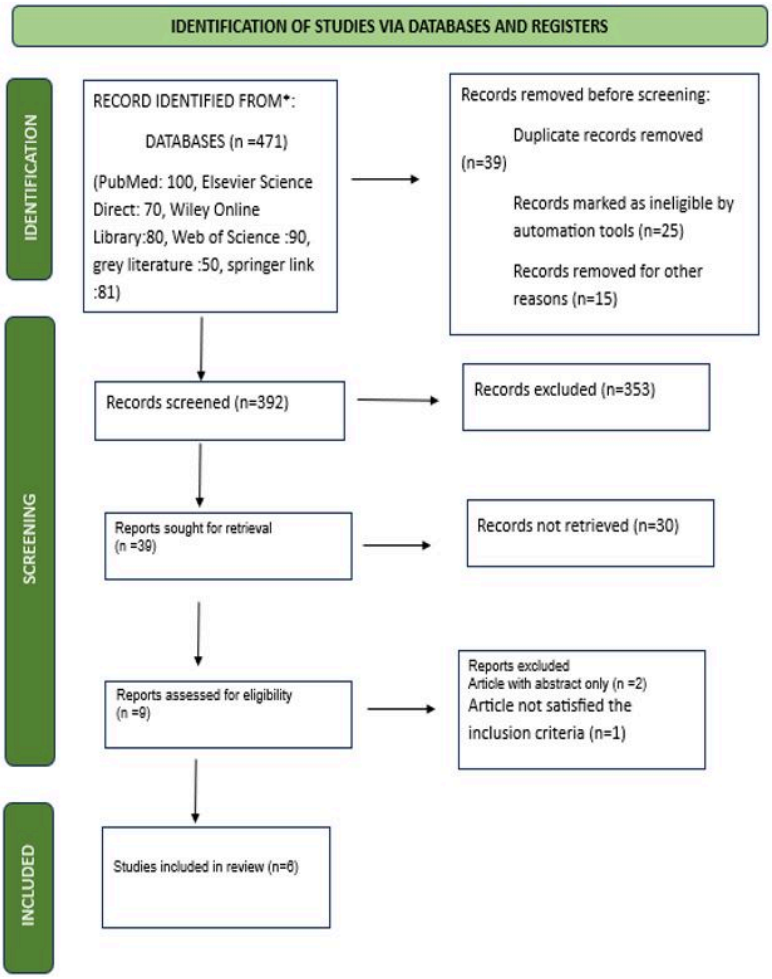


**Figure 1: PRISMA 2020 flow diagram for newly conducted systematic reviews that solely involved database and registration searches.**

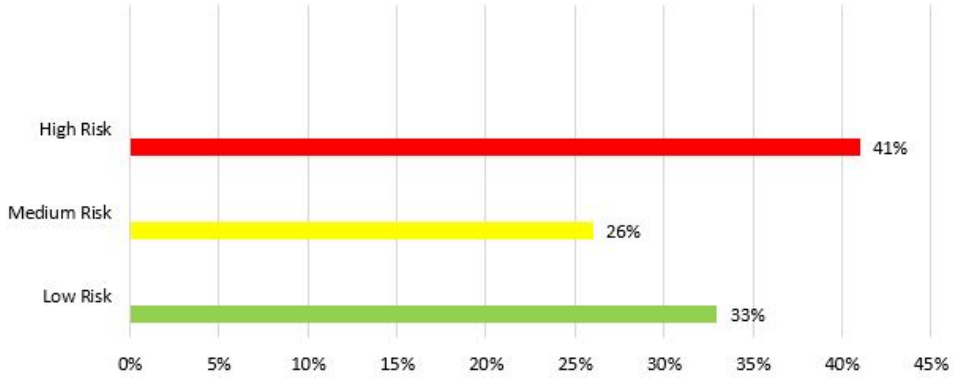


**Figure 2: Overall percentage distribution of bias analysis included in our systematic review.**

## Discussion

*Withania somnifera* gained its anti-inflammatory properties, particularly its effectiveness in preventing Cancer. *W. somnifera* especially inhibits cell proliferation, apoptosis induction, and tumor inhibition. The other benefits of *W. somnifera* are stress management, energy elevation, improved cognitive health, lower inflammation, blood sugar levels, cortisol, anxiety, and depression. *Ashwagandha* extract was investigated in that the main supplement is aerial parts in the form of powder. It has a wide range of medicinal properties such as anti-epileptic, anti-oxidant, anti-inflammatory, anti-arthritic, anti- depressant, anti-coagulant, anti-diabetic, anti-pyretic properties. *W. somnifera* consists of several biochemical levels such as high levels of flavonoid, phonetic compounds and anti- oxidant compounds and amino acids. *W. somnifera* is most effective against cancer. Not only fiber but many other herbal supplements can be converted in potentially anti-cancer metabolites by gut microbiota as American ginseng.

American ginseng has demonstrated that ginseng metabolites (CK, Reg3) can significantly attenuate carcinogenesis through gut cytokine levels reduction, restoration of endogenous metabolites levels and shift of microbiota population. It was also reported that Ginseng administration causes Gram-negative phyla (e.g., Bacteroidales and Verrucomicrobiata), which possibly could promote tumorigenesis, decrease while Gram-positive phyla (e.g. Firmicutes), which possibly could have anti-inflammatory and anti-tumorigenic, increase. Radiation can enhance the efficacy of chemotherapy regimens and serve as the primary treatment option. Radiation treatment is necessary for roughly two-thirds of cancer patients.**[25]** Traditional treatments such as chemotherapy and radiation have significant side effects, driving the search for more targeted and less toxic therapies.**[26]** Herbal medicines have been introduced as an alternate form of treatment to avoid the side effects cause by the drugs.**[27]**

The study conducted Widodo et al.**[28]** demonstrated that *Ashwagandha* leaf extract (i-Extract) selectively kills cancer cells while sparing normal cells. In mouse models, it significantly suppressed tumor growth, and the active component, withanone (i-Factor), was identified. The extract activates or restores p53 tumor-suppressor function in cancer cells, inducing growth arrest or apoptosis. Gene silencing confirmed the involvement of p53 and other targets like CDK5 and BIRC3. These results highlight withanone as a promising, natural, and safe anticancer agent acting through the p53 pathway. The study by Emad M. Elzayat et al.**[29]** evaluated the anticancer potential of *Withania somnifera* (WS) ethanolic extract against MCF7 breast cancer cells and its synergistic effect with doxorubicin (DOX). WS alone showed cytotoxicity with an IC50 of 47.13 µg/ml and selectivity for cancer over normal cells. When combined with DOX, especially at a ½ WS: ¼ DOX ratio (CI = 0.229), the treatment significantly enhanced apoptosis, induced G2/M cell cycle arrest, and modulated apoptotic gene expression (upregulating p53, Bax, Cas3, Cas7 and downregulating Bcl2). The combination also reduced glycolytic enzyme activity and oxidative stress markers. These results suggest WS enhances DOX efficacy and could serve as a natural adjuvant in breast cancer therapy. Though preclinical findings are promising, the study emphasize the need for standardized formulations and clinical trials to establish the safety, efficacy, and therapeutic value of *Ashwagandha* in breast cancer treatment.

## Conclusion

*Withania somnifera (Ashwagandha)* shows promising potential in cancer treatment and prevention due to its bioactive compounds, such as withanolides, which exhibit anti-inflammatory, antioxidant, and anticancer properties. Studies suggest that *Ashwagandha* may help in inhibiting tumor growth, reducing cancer cell proliferation, and enhancing the effectiveness of conventional treatments like chemotherapy and radiation. However, further clinical research and trials are needed to fully understand its mechanisms, optimal dosages, and safety profile in cancer therapy. Its use as a complementary approach alongside traditional treatments holds potential but requires careful consideration.

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