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Review Article

Therapeutic Potential of *Withania somnifera* in Osteoarthritis

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ABSTRACT

In recent years, research on the beneficial effects of winter cherry (Withania somnifera) for health, commonly called ashwagandha, has greatly increased. Studies show its positive effects on various aspects of human health, such as reducing stress, improving sleep, and acting as a natural sedative and adaptogen. It has also been linked to antimicrobial, anti-inflammatory, heart-protective, along with its anti-diabetic qualities, along with potential positive effects for the reproduction process health and hormone regulation. Importantly, growing evidence highlights Ashwagandha's role in osteoarthritis (OA), where it helps reduce joint pain, swelling, and stiffness by lowering inflammation and protecting cartilage. With this expanding research, Ashwagandha is emerging as a promising natural treatment for osteoarthritis as well as several other health issues. This review summarizes the latest evidence, providing an overview of Ashwagandha's possible applications with a special focus on osteoarthritis.

INTRODUCTION

In the conventional medical system, many diseases have been treated utilized plants or plants product. People are interested in using herbal plant because their distinctive therapeutic properties, common causes, cost viability & safe result[1]. Ashwagandha is very popular & widely herb in India. It used in many traditional medicines like Ayurveda, Siddha, Sowa Rigpal, Unani and homeopathy. People use it because it has much health benefits[2]. Ashwagandha (*Withania somnifera*) also called Indian ginseng or winter berry. It is member of solanaceae (night shade plant family)[3]. Ashwagandha's name comes from "Ashwa" means horse and it is thought that eating the root could give an individual strengths & energy like the horse. "Gandha" is the second part that means smell which alludes to this strong scent of the plants raw root[4]. from ancient time, it has been used In Ayurveda to make the neurological system strong. This is because of The adaptogenic properties and therapeutic value, known as

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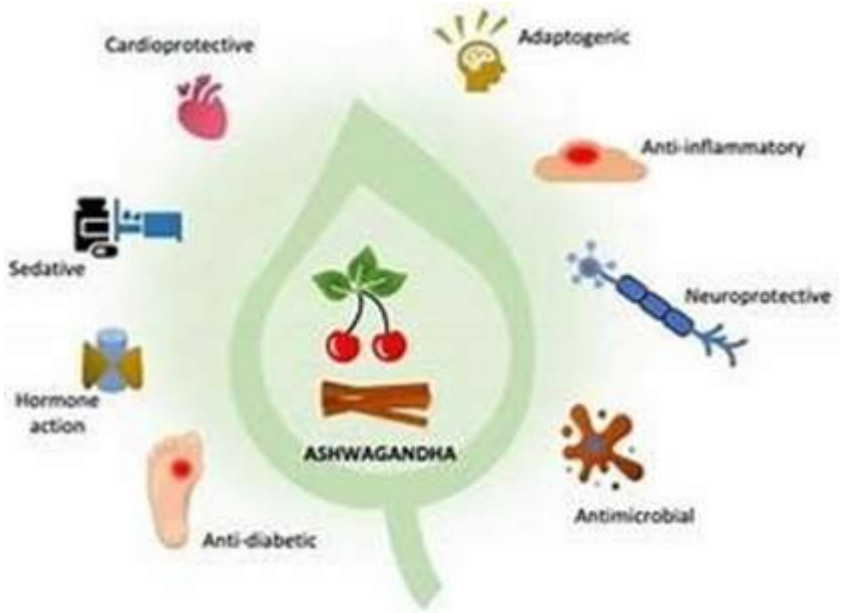
"rasayana"[5]. Its use in Indian medicine is almost 3000 years old. The root has been utilized as a diuretic, tonic, narcotic, and aphrodisiac, deworming medicine together with a stimulant.[6] It grows Naturally in India, but is also grown in the Himalayan areas, Mediterranean nations, the Canary Islands, Africa, the Good Hope Cape and Australia[7]. in ayurveda, this medicine is made by fresh roots boiled with milk. Sometimes, the roots are crushed into a fine powder known as "Churn" and mixed with milk, honey or water. To improve health and increase lifespan, other regions of the plants like Additionally, berries, seeds, shoots, and leaves are used[8]. In ayurveda, it is classified Being a Rasayana, which means it helps in improving physical and mental health, restoring the anatomy, and increasing lifespan. That is well known for its immune modulating activity[9]. This plant has many properties like antioxidant, immunomodulator, anti-diabetic, anti-inflammatory, anti-stress, antimicrobial and cardio protective. It can also improve role of endothelium, lower reactive oxygen species as well as reduce again effects. It is effective in health problem such anxiety, stress, arthritis, epilepsy, fatigue, neurodegenerative disease, thyroid disorder and skin diseases[10]. In recent years, people have shown more interest in ashwagandha's health advantages, especially for managing stress, improving memory and brain function boosting physical strength. Research shows that ashwagandha could protect the brain, help with OCD, and it has anti-inflammatory properties. immune-boosting and antibacterial effect. It may also be useful in treating infertility, cancer, and diabetes. According to certain research, ashwagandha can protect the heart and may help in treating sleep problems.



Health benefits of Ashwagandha

Although Ashwagandha shows many possible health benefits, more investigation is required to fully know how it works and how effective it is in the treatment of different health problems. In this document, we review the available studies on Ashwagandha, mainly focusing on its possible advantages for lowering stress, improving brain function as well as boosting bodily performance[11].

Among its many uses, Ashwagandha is also being studied for its potential role in joint health, including osteoarthritis. Therefore, this project focuses more on its possible applications in osteoarthritis.

ASHWAGANDHA

Synonyms: Roots of Withania, Ashwagandha**,** Indian ginseng, Cherry for winter.

Biological Source: It is made up of *Withania somnifera* Dunal's dried roots and stem bases, which are members of the Solanaceae family.

Drug profile:

Withania somnifera Linn Dunal, or ashwagandha, grows in India's arid and subtropical regions. It is widely distributed throughout northwest India, particularly in Bombay, Gujarat, Rajasthan, Madhya Pradesh, Uttar Pradesh, Punjab, and a few mountainous regions like Himachal Pradesh and Jammu, which reach elevations of 1500 meters. This species is widely spread to numerous other nations, including Poland, Afghanistan, Israel, Egypt, Jordan, Morocco, Spain, the Canary Islands, Eastern Africa, Wingo, South Africa, and Pakistan[12].

Active constituents:

Ashwagandha has many natural plant chemicals. The types of compounds found can change depending on where the plant is grown. The most important compound for its health effects are withanolides & alkaloids.

Sub types:

A) **Withanolides:** these are special compound with a structure similar to steroids. Some examples are withanone, withaferin A & Withanolides A.
B) **Alkaloids:** these include chemical like withanine, somniferine, tropine, choline and anaferine.
C) **Flavonoids:** these are antioxidant compound such as quercetic & rutin[13].

Ashwagandha also has:

- Withanolide glycoside (with added sugar groups) such as sitoindoside 1x & x.
- Steroidal saponins, like sitoindoside vii & viii.
- Other compound like saponins, cocumarins (scopoletin), lipids, carbohydrates, fatty acids, sterols, chlorogenic acid, and resins[14].

Structure of an examples of a withanolide active compound in Ashwagandha[15].

The natural chemicals in *Withania somnifera* (Ashwagandha) are of great interest to research. Scientists have studied this plant and found may tapes of compound, such alkaloids, flavonoids, and steroidal lactones & tannis. From its leaves, roots & berries 138 withanolides, over 13 alkaloids, and a number of sitoindosides (a type of withanolide that has found a glucose molecule that is joined at carbon 27. Changes in the environment can also lead the plant to produce new or different chemical compound[16].

The primary chemical is withanolides found in the plant (mostly in the roots and leaves). There

amount is usually 0.001-0.5% of the dry weight of the plant.

- They are a type of steroidal lactone (special chemical structure).
- In their structure, two carbons atoms (c-22 and c-26) are changed to form 0 ring of six lactones.
- It is known as a withanolide skeleton (scientifically described) as 22 hydroxyergostern-26-oic-acid 122-lactone).
- Changes in carbon skeleton or side chains create different types of withanolides plant naturally make these variations with the help of enzymes that can oxidize (add oxygen) to many parts of the steroid nucleus.
- Withanolides are very similar to another group of compounds called ergesterone type steroids, both having a side chain with a lactone or lactrol ring[17].

Plant part	Bioactive compound	Uses
Leaves 	Alkaloids, Flavonoids	Antipyretic (redce fever) Analgesic (Pain reliver) Antimicrobial (helps wound healing, skin infection when applied as paste)
Fruits 	Withanosides, polphenols	Diuretic (helps in water retention) Laxative (mild) Used in ayurvedic preparation for constipation and hormonal bance
Seeds 	Fatty acids, steroids	Used in treating parasitic infections
Stem 	Triterpenoids, Sitoindosides	General tonic Antioxidant properties Immunity booster

Biological Activity:

1. Anti-Inflamattory & Immunomodulatory Effects:

Many of the disease states of inflammatory origins such as diabetes, cancer, neurological disease, pulmonary disease, cardiac disease, and autoimmune disease are studied in relation to *Withania somnifera* . Before clinical This plant also controls the activity and death of cells and inflammation by suppressing harmful indicators such as cytokines (e.g., IL-6 and TNF-a), nitric oxide, and reactive oxygen species. Meanwhile, experiments on mice with lupus indicated that ashwagandha root powder could have blocking actions in situations such as inflammation of the kidneys and proteinuria[18]. Scientists are also investigating how effective ashwagandha is against rheumatoid arthritis. In an animal study, rats were given *Withania somnifera* root powder by mouth three weeks. Days, an hour before the CFA (complete Freund's adjuvant) injection that provoked inflammation. Phenylbutazone was also given to the rats of the positive control group. There was an evident reduction of inflammation, and there were alterations of certain serum proteins like prealbumin, α2 glycoprotein, and acute phase protein α1[19].

2. Antibacterial & Antimicrobial properties:

Although well known, resistance of germs to drugs is a large and increasing issue. In the past years, there has been a large rise in infections from bacteria that do not respond to drugs. We understand that irresponsible and frequently Overuse of antibiotics has led to the development of drug-resistant bacteria, and at times, these drugs are of no use. So, ashwagandha seems like a beneficial supplement in addition to medicine for the treatment of bacterial infections. Though effective, there are few drugs that are prescribed for bacterial infections that do not have harmful side effects because they are toxic. Ashwagandha hardly ever has adverse effects and is a safe non-toxic plant. In the experiments that have been done, it has has been proved effective in inhibiting the progress of Enterococcus species and methicillin-resistant Staphylococcus aureus[20]. Some of its properties are crucial to how it operates to combat germs. It can be toxic to cells, it can mute genes, and it can alter the workings of the immune system by increasing its activity[21]. found that the W. somnifera extract demonstrated greater antibacterial activity against P. aeruginosa. Experiments on how Ashwagandha extract fights against bacteria were carried out by the use of shape analysis and membrane stability tests. demonstrated that they act by damaging P. aeruginosa's cell membrane. Moreover, mouse experiments confirm that extracts of *Withania somnifera* , at higher concentrations specifically, are effective against malaria because parasites are greatly lowered[22].

3. Huntington’s Diseases Management:

Huntington's disease is not curable. Our drugs today merely give relief from the symptoms but decrease the rate at which the disease advances. Since the disease is inherited as an autosomal dominant disorder, half of the offspring will inherit the allele responsible for the disease. Huntingtin's (htt) protein experiences a conformation shift into its insoluble state because of an IT15 gene mutation on chromosome 4. Rapid neuron death occurs from the aggregation of the mutant huntingtin protein's N-terminal portion that has expanded polyglutamine repeats. As a consequence, dopamine, GABA, serotonin, and cholinergic neurons become imbalanced[23].

A potent neurotoxin is 3-nitroproprionic acid (3-NP). It generates oxidative and nitrosative stress, halts the complex II of the electron transport chain

of mitochondria (which causes an energy-deficient state), and causes biochemical and Behaviors that resembled those of Huntington's disease. An animal model of Huntington's disease symptoms was induced by giving an injection of 3-NP. The plant being studied has antioxidants. It was found that taking ashwagandha extract for a long-time improved health and movement. There was a decrease in lipoperoxidation, a Reduction of lactate and nitrate dehydrogenase levels, elevation of catalase and superoxide dismutase levels, and unbarring of the mitochondrial complex result in the recovery of ATP synthesis. Action of 100 mg/kg and 200 mg/kg was dose dependent[24].

4. Enhancement of muscle strength:

Supplementing with ashwagandha has been found to substantially enhance strength of muscles and enhance recovery of muscles. In a study, we enrolled young men who were otherwise healthy. They received 300 mg of oral *Withania somnifera* root extract two times each day. For eight weeks each day, these men also engaged in physical activity. Participants adhered tightly to a resistance training regimen according to guidelines issued by the National Strength and Conditioning Association (NSCA). Treated individuals experienced a gain of arm and chest muscle size and a definite gain of strength of muscles. The plasma creatine kinase levels stabilized, indicative of significantly lower exercise-inspired muscle damage present in patients who received ashwagandha as compared to those who received a placebo. In addition, the treated group also experienced a large reduction in body fat as well as a visible rise in testosterone[25].

5. Cardioprotective Effect:

Albino rats were used to examine the protective effects of ashwagandha against isoprenaline treatment-induced heart injury. Low levels of glutathione and weaker activity of catalase, creatinine phosphokinase, superoxide dismutase, etc., existed. and lactate dehydrogenase were found in the rats given *Withania somnifera* treatment. Levels of lipid peroxidation also sharply declined. These findings suggest that, in a rat model of isoprenaline-induced necrosis, *Withania somnifera* has a cardioprotective effect[26]. These experiments used rats when cardiac ischemia was induced. Prolonged cardiac necrosis, an oxidative antioxidant disorder, including elevation oflipoperoxidation, followed from this. According to histopathological examinations, revealed ischemia-triggered heart damage is significantly alleviated upon use of *Withania somnifera* . Owing to its anti-apoptotic properties and restoration of the oxidative balance, ashwagandha confers cardioprotection[27].

Therapeutic Potential of New Diseases:

1. Breast cancer (Chemotherapy fatigue):

A clinical study published in 2013 looked at whether A powdered extract of ashwagandha root (from Himalaya Drug Co., New Delhi, India) could reduce Chemotherapy-induced tiredness and improve standard of living in breast cancer patients. Patients receiving chemotherapy for breast cancer were divided alternately separated into two groups: 50 patients in the study group and 50 patients in the control group. The research team took 500mg of ashwagandha dry extract three times a day during all six chemotherapy cycles. The patients who took ashwagandha felt less exhausted and had a improved standard of living compared to the group under control[28].

2. Osteoarthritis:

A clinical trial lasting six weeks conducted in 2012 tested An Ayurvedic formula's safety for treating osteoarthritis in the knees. The formula

(presentation and the maker did not mention) included Zingiber officinale, ginger, and powdered ashwagandha root, Zingiberacea), Guduchi or Indian tinospora (Tinospora, cardifolia, Menispermaceae), Furthermore, Tribulus (Tribulus terrestris, Zygophyllaceous). The study found Not at all serious side effects and none of the individuals involved stopped the trial because of any drug-related problems[29].

3. Hypothyroidism:

Studies in mice showed that ashwagandha can raise thyroxine (T4) levels. Because of this, thyroid function was checked in a clinical trial on 60 patients with bipolar disorder, a condition often linked with thyroid problems.

In this trial, 10 had abnormal thyroid result:

Three individuals taking ashwagandha already had thyroid tests that were abnormal at the beginning (one had high TSH, one had high T3 Lithium caused one to have low T4). By At the study's conclusion, all three had normal Thyroid results, and their T4 levels increased by 7-24%.

Seven patients in the placebo group also had abnormal thyroid tests at the beginning. By the end, six had a drop at T4, with just one displaying an increase[30].

As of 2018, another clinical trial was carried out with Fifty patients having slight hypothyroidism (TSH 4.5-10IU/L). it was A placebo-controlled, double-blind research. For eight weeks, patients received 600 mg of ashwagandha extract every day.

Result showed:

After 4 weeks, TSH, T4 and T3 all improved.

After 8 weeks, the improvements were 17.4% in TSH, 19.6% in T4, and 41.5% in T3.

In the placebo group, there were no meaningful changes[31].

Ashwagandha may improve thyroid function because:

It affects the HPA axis (Stress, system), which is connected to the HPT axis (Thyroid system). high cortisol can reduce thyroid hormones, and ashwagandha helps prevent this. It has dopaminergic and anti-inflammatory effects that influence both systems. Animal studies also show it might directly affect thyroid activity and hormone metabolism So far, no more human trials have been done. But these positive results, along with the link between stress and thyroid problems, suggest that ashwagandha could be useful for people with subclinical hypothyroidism[32].

4. In fertility in men:

In a 2013 clinical trial, infertile men were studied at King George's Medical University's infertility center in Lucknow, India. There were three groups:

- 60 men with similar semen but unexplained infertility,
- 60 men with a low number of sperm but typical sperm shape,
- 60 men with a typical number of sperm and shape but low sperm movement (motility).

A control group included 50 healthy men of the same age who had normal semen and had fathered at least one child.

The patients within the research group were given 5 grams of Powdered ashwagandha root (source from the Central Council for Unani Medicine Research, located in New Delhi: shade- dried up

and finely ground) mixed with milk every day three months.

Semen samples were gathered and tested. The result showed that ashwagandha helped to balance important markers in the seminal plasma and could improve fertility by acting on metabolism, enzymes and hormones[33].

5. Sexual dysfunction (Male & Female):

Ashwagandha is often believed to improve sexual health, but research evidence is limited, in women, one small study showed taking 600 Ashwagandha milligrams extract daily for two months became better sexual function in those who had sexual problems. However, in men, results have not been supportive[34]. A Research on Men who suffer from erectile dysfunction have no benefits from taking 6000 ashwagandha powder milligrams daily for 2 months as contrasted with placebo[35]. An additional study in men aged 40-70 with exhaustion as well showed There is no boost in sexual health, even though testosterone levels increased when they consumed 240 milligrams of ashwagandha extract per day for 2 months[36].

6. Insomnia / Sleep:

Withania somnifera is the Latin name for ashwagandha, shows its connection to go to sleep, as "somnifera" means "promoting sleep." The plant is believed to refresh the neurological system, reduce tension, and improve rest without causing drowsiness[37].

In recent years, five high-quality clinical studies (double-blind, placebo-controlled) have confirmed that ashwagandha helps improve sleep. These studies included healthy adults, stressed adults, people with anxiety and insomnia, those with only insomnia, people with poor-quality sleep, and elderly individuals[38].

Different methods were used to measure sleep, such as actigraphy and sleep surveys ((A gadget worn like a watch to track sleep patterns). Both showed improvements, with sleep quality increasing by 30–72%. The benefits were usually greater in people who already had sleep problems[39].

Most studies gave participants 600 Ashwagandha milligrams root extract per day. One study utilized a mix of root and leaf extract at 120 mg per day, which gave the best results (72% improvement in sleep quality). Treatments lasted 6–12 weeks, and improvements appeared gradually over time[40]. Ashwagandha's stress-relieving effects likely play a major function in enhancing sleep. Animal research also recommend ashwagandha affects the GABA system in the brain, which helps calm the nervous system and supports better sleep[41].

7. Emerging disease (ex-covid 19):

COVID-19, or coronavirus disease 2019, is a virus infection that spread worldwide after December 2019, creating an urgent need for new treatments[42].

Research on *Withania somnifera* (WS, Ashwagandha) shows that some of its natural compounds may help fight COVID-19:[43].

A study predicted that Withanone can attach to the COVID-19 spike protein's receptor-binding domain (RBD) and the human ACE-2 receptor. This may block the virus from entering cells. It may also stop the virus from multiplying by reducing spike glycosylation.

Computer-based studies found that 2,3-Dihydrowithaferin 27-Deoxy-14-hydroxywithaferin and A can block both the spike protein with NSP3 protein of the virus[44].

Four other WS compounds were found to block the envelope (E) protein of COVID-19 by binding to its pore region, which may slow down viral growth.

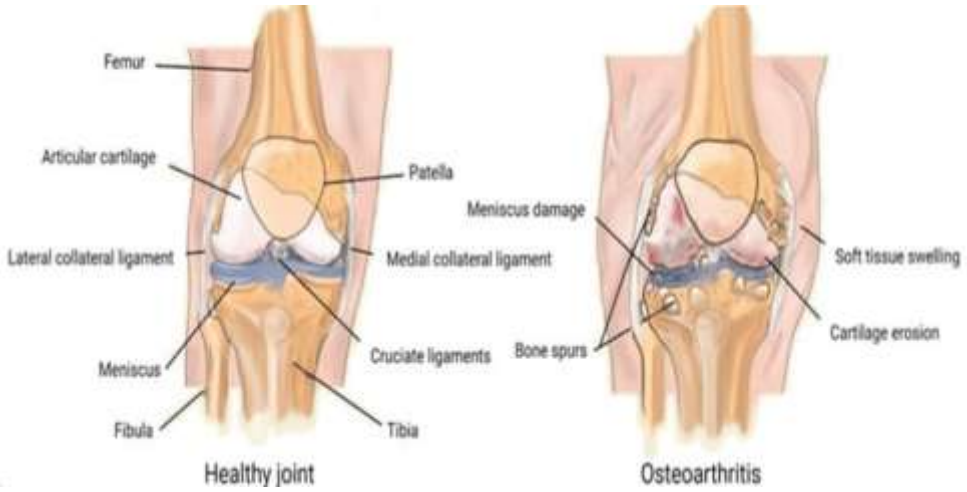
WS's aqueous root extract also lowered Death and stress rates Tilapia Lake virus (TiLV) is the cause, showing broader antiviral effects[45].

Other WS compounds like Along with rutin and isochlorogenic acid B, quercetin-3-rutinoside-7-glucoside was effective even more effective than withanone and withanolide against the main SARS protease-CoV-2[46].

Molecular docking research showed that Withanoside II, Sitoindoside, Withanoside IV, and Withanoside V attach strongly to the primary SARS-CoV-2 protease, suggesting strong antiviral activity[47].

Therapeutic potential in Osteoarthritis:

Osteoarthritis (OA) is a condition that impacts the joints, especially the ones that move. It happens when the smooth cartilage covering the bones wears down. Along with this, changes occur in the bone, new bony growths (osteophytes) may form, and the joint can become inflamed, leading to reduced normal movement. The problem usually starts with small or large injuries to the joint, which trigger abnormal repair processes and disturb the normal balance of joint tissues[48].



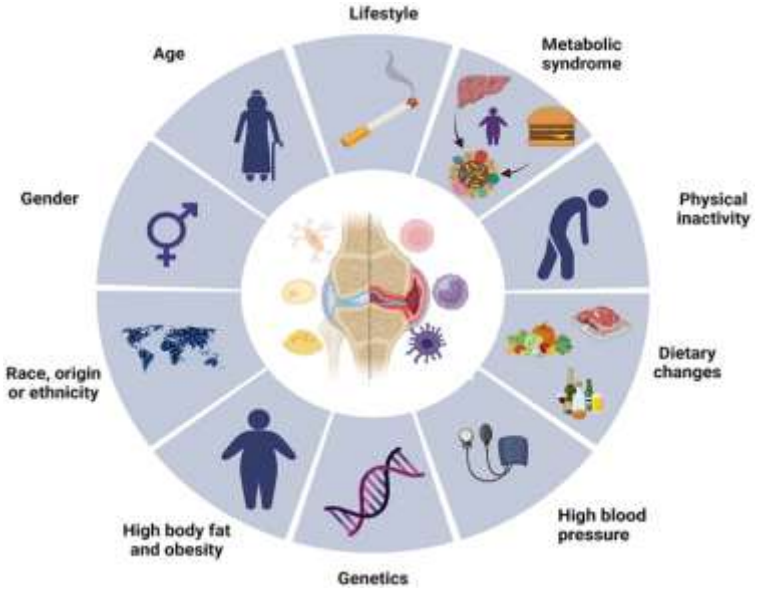
Overview of healthy and osteoarthritis joint

QA is one of the primary causes of long-term impairment, mainly because of joint pain, which is the most common complaint. In knee QA, pain often starts only during activity but later becomes more constant and long-lasting. Along with pain, stiffiness is also common, making it difficult to carry out daily activities. The more severe the pain, the more the person's movements and functions are restricted. Apart from affecting health, OA also creates a significant financial and social burden[49].

The chances of developing osteoarthritis increase due to several factors. These include family history (genetics), lifestyle habits, natural changes in the body like age and gender, and health problems such as obesity and high blood pressure[50].

For joint pain, doctors often use medicines like NSAIDs, painkillers, and corticosteroids. However, NSAIDs can cause heart and stomach problems, and strong painkillers may lead to addiction, which worries both doctors and patients. Studies have also shown that steroid injections in the joint can sometimes speed up osteoarthritis, cause small bone fractures, lead to bone tissue damage, or even rapid joint breakdown. Because

of these risks, safer treatment options are needed. The use of natural medicine has been around for a while to manage osteoarthritis and usually cause fewer side effects than standard drugs. Research also suggests that some herbs may help slow the worsening of the disease through different biological actions[51].



Some commonly studied herbal extracts include Boswellia serrata, Cortex Eucommia, Matricaria chamomilla, and Tripterygium wilfordii root & *Withania somnifera* [52].

Withania somnifera , also called Ashwagandha, is a well-known herb in Ayurveda. It is mainly used for its pain-relieving as well as anti-inflammatory qualities. Studies have indicated that extracts of this plant can block certain molecules in the body (such as IL-1β, IL-12, and TNF-α) by reducing the activity of specific pathways (AP-1 and NF-κB). It can also protect collagen (the main protein in tendons and cartilage) from breaking down by lowering the action of collagenase enzymes. In animal studies, Ashwagandha treatment reduced swelling, redness, joint deformity, and stiffness. Its effects may be due to lowering harmful molecules like MMP-8, ROS, TNF-α, IL-1β, and IL-6, while increasing protective ones like IL-10[53].

Sumantran and colleagues found that water extracts of Ashwagandha could protect damaged cartilage in people with osteoarthritis by reducing collagenase activity. Clinical studies also support its pain-relieving benefits in knee osteoarthritis. In a 12-week study, patients taking 125 mg or 250 mg of extract from ashwagandha reported less pain, stiffness, swelling, and disability compared to those on placebo. The higher dose worked faster (within 4 weeks), improved doctors' overall assessments, and reduced the need for painkillers like paracetamol[54].

A mixture of Maharasnadi Kwath, Bala oil, and Ashwagandha oil can be gently warmed and used for massage on affected joints. Massaging in circular motions for 10–15 minutes allows the herbal oils, including Ashwagandha, to penetrate the skin, helping to reduce pain and inflammation. The oil should remain on the skin for at least 30 minutes, and additional warmth—like a warm towel or compress—can enhance its effect. This therapy can be done once or twice daily, ideally before a bath or bedtime. While Ashwagandha contributes anti-inflammatory and pain-relieving effects, individual outcomes may vary, so

guidance from a qualified Ayurvedic practitioner is recommended[55].

CONCLUSION:

Ashwagandha plant *Withania somnifera* is a well-known medicinal plant valued for its anti-inflammatory, antioxidant, and adaptogenic properties. While historically, it has been utilized to increase strength and vitality, modern research shows its special potential in osteoarthritis (OA) management. Clinical and experimental studies report Ashwagandha also lowers joint pain, rigidity, swelling, and disability by lowering inflammatory mediators and protecting cartilage from damage. Thus, Ashwagandha acts as a safe and natural therapeutic option that bridges ancient Ayurveda with modern medicine, offering promising benefits in improving joint health and managing osteoarthritis.

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