

# Ashwagandha: A Flagship Herb of Ayurveda from Past to Present Nano Era

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## ABSTRACT

Plants are considered excellent resources for the generation of greener biomaterials. Plant extract are renewable in nature. Various metabolites present in plant extract are normally used in redox reaction for the formation of eco-friendly nano-particles. It is also considered as the main factory for the green synthesis of metal nano-particles. The plant-based nano-particles is very necessary for absolute harmony connection between plant science and nanotechnology. Ashwagandha is the non-toxic herb which used to treat a range of conditions and its life changing benefits runs over a long time. Its numerous medicinal values make this plant so popular. It is a stress buster which works for all "SUPERHERB". This super herb rejuvenates our body and brain from the inside out. Present review depicts the variety of assistance of Ashwagandha plant with or without nanoparticles, from the past to the present time of corona.

**Keywords:** Ashwagandha, Plant extract, Nanoparticles, COVID-19, Natural inhibitor.

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## INTRODUCTION

Treatment of Ayurveda always gives side benefits not side effects. Ashwagandha is an evergreen shrub which is found in India, Africa and many parts of the Middle East. It is known as Rasayana for more than 6000 years.<sup>1</sup> Its botanical name is *Withania somnifera* and commonly known as winter cherry or poison gooseberry which is the annual evergreen shrub from the family Solanaceae. The name of family Solanaceae means "dream carrier" with reference to restful sleep. This family plants supported sleep and use to provide daytime energy and stress. Sometime this herb is called "Indian Ginseng" although it is unrelated to the Ginseng species as Ginseng support energy and stamina and Ashwagandha gives claming and nourishing stress support.<sup>2</sup> The root of Ashwagandha smells (gandha) like horse (in Sanskrit *Ashwa* means horse), that's why the plant name is Ashwagandha.<sup>3</sup> The plant requires the dry stony soil with sun to partial requirement of shade. In most of the countries this herb is sold as dietary supplement. The various part of Ashwagandha works as anthelmintic, astringent, diuretics, narcotics, thermogenic and as tonic. Its powder is given to the children with milk and works as tonic and able to gives the power of horse. This herb is used against nervous breakdown, insomnia, vitiated conditions of vata, rheumatism, constipation, leukoderma

etc.<sup>4</sup> In Tanzania, the root of Ashwagandha is used to promote uterine constraction and sexual stimulant.<sup>5,6</sup> The plant is works as rejuvenative for men, strengthen muscles, bone marrow, muscle and semen. It also promotes longevity and youthful vitality.<sup>7</sup> The whole plant itself have medicinal importance (Figure 1). The leaves of plants are rich in iron and can be taken as herbal tea. The plant leaves are helpful during heavy periods and anemia. Its leaves are useful in painful swellings and fever. Its leaves also consume as energy sources and decreases fever and pain during swelling. The flower parts having diuretics, depurative, astringent and aphrodisiac property. The seeds are known for anthelmintic activity and used to treat memory loss, anxiety, hysteria, syncope etc. Drug-free and non-habit-forming herb of Ashwagandha contain melatonin, a hormone which is naturally produced in the brain and help for sound cycle asleep naturally. A Russian scientist N.V. Lazarez described the plant as adaptogen as it satisfied the criteria of non-toxic, benefit of overall well-being and reduce and regulate stress by helping the body adapt.

## ASHWAGANDHA AS A SUPPLEMENT

Ashwagandha is considered as "Real Potent Regenerative Tonic or Rasayana of Ayurveda". Because of the nature of adaptogen, the Ashwagandha is used for many states of stress which may be physical and mental. Ashwagandha extract is the best form to take in. Various forms of it are available in the market such as capsules, gummies, liquid drops and powders which can be mix in to drinks (Figure 2). Its two branded extract is KSM66 and Sensoril are very popular. Both brands are fully standardized,



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certified organic extracts, high potency with verified health benefits proved by clinical studies. A study in which the effect of Ashwagandha supplement is seen in type 2 diabetes. This study proves that the 250 mg/day may help to lower the blood sugar levels.<sup>8</sup> Daily dose of 125mg to 5 g for 1-3 months reduces the cortisol level by 11-32%.<sup>3</sup> Again 500 to 600 mg of Ashwagandha for 6-12 week per day may lower anxiety and insomnia in people with anxiety and stress disorder.<sup>9</sup> The supplements of it helps to boost fertility and promotes reproductive health particularly in men. Research have shown that 5 gm of Ashwagandha per day for 3 months may boosts fertility in men. At the end of 3 month 14% of their partners became pregnant.<sup>10</sup> Ashwagandha powder is sold as Kama Ayurveda's Nirvah face pack which is helpful in anti-acne treatment and also reduces scars, heals blackheads and pimples and ultimately improves skin tone. Ashwagandha is one of the main ingredient in very popular Ayurvedic tonic "CHAWANPRASH". In Ayurveda, a term "Anupama" is used which means vehicle or the way medicine is administrated. For the proper action of herb in Ayurvedic treatment this Anupama (vehicle) is very important. In the Ayurveda text, Charaka Samhita described that milk is the proper anupama for body's seven tissue system. Its overall effect is pleasing for mind and body with sweet post-digestive effect.<sup>11</sup> Milk and Ashwagandha having similar properties as both are known as rejuvenator so proved to an optimal combination. The combination of both created solid results in the case of tuberculosis and starvation and curbing malnutrition. A well-known scholar in Ayurveda "Sushruta" quoted that the combination of Ashwagandha with milk act as medicated clyster in anorectal bleeding and Vata disorder. The seed powder mixed with astringent and rocksalt is used to remove white spot from cornea. Ashwagandha is normally available as a fine sieved powder and the churna can be mixed with ghee or

honey and water which improves the memory and enhances the function of nervous system and brain.

## ASHWAGHANDHA CONSTITUENTS LOADED WITH BIOLOGICAL ACTIVITY

Chemical constituents of Ashwagandha contains fatty acid, glucose, tannins, potassium, nitrates and a rich source of flavonoids. The loss of melanin in the hair is repaired by the tyrosine and amino acid present in the Ashwagandha. The constituents of Ashwagandha stimulates the production of sebum through its stimulation of DHEA (Dehydroepiandrosterone: a precursor to both testosterone and estrogen)) for healthy hair growth. A steroid "Withaferin-A" is found in the plant leaves which are useful in the treatment of prostate cancer. During menopause its uses reduces the hormonal imbalance, hot flashes, anxiety, sleeping trouble etc. In children it boosts the immune system as it is immunomodulatory and helps in the development of antibodies by increasing the levels of white blood cells and platelets in the body. As per study several sitoindosides, 40 withanolides and 12 alkaloids present in different part of the plant (Figure 3). Various phytochemical such as Withafarin,<sup>12</sup> pubesenolide,<sup>13</sup> Withanolide,<sup>14</sup> viscosalactone,<sup>15</sup> 27-deoxywithaferin A,<sup>16</sup> jaborosalactone D,<sup>17</sup> 2,3-dihydrowithaferin A-3b-O-Sulfate,<sup>12</sup> 4b,27-dihydroxy-L-oxo-22R-with a-2,5,24-trienolide,<sup>18</sup> was reported (Figure 4). Different Withanolide viz. Withanolide A, D, E, F, L, withanone, quercetin, Kaempferol are found based on the degree of occurrence. An ergostane base steroidal compounds: Withanoides with a  $\delta$ -lactone functionally found between the C-22 and C-26 atoms and C-1 position is oxidized. The GC-MS studies proves the presence of different metabolites like fatty acids, organic acids, aromatics and aliphatic amino acids, sterols, sugar, polyols, phenolic acids and tocopherols. Many primary and secondary metabolites such as 1-deoxy-D-Xylulose-5-phosphate (DOXP), Mevalonic Acid (MVC), squalene, shikimic acid and phenylpropanoids were also reported.<sup>19</sup> Withanolides (a group of minimum 300 naturally occurring steroids) are the active constituents found in Ashwagandha. This steroid is sold in supplement form and a popular adaptogen. This is known for



**Figure 1:** Various parts of Ashwagandha Plants which shows good deal of medicinal value.



**Figure 2:** Different form of Ashwagandha used as supplements.

inhibiting tumor growth, cure inflammation and anxiolytic effect. The Ashwagandha extract contain 10% and non-concentrated powder 2.5% withanolides. The two constituents withanolide A and withaferin A are found in Ashwagandha which shows antioxidant, anti-stress, mild sedative, analgesic and immunomodulatory effect.<sup>20</sup>

Ashwagandha provides antioxidant supports by helping the pathways in the brain for Gamma-Aminobutyric Acid (GABA) which is a neurotransmitter that work for maintaining muscle tone and sustaining calmness.<sup>20,10,11</sup> One of the most asked about wellness concern of 21<sup>st</sup> century is heart health. Ashwagandha provides the natural way to support the heart. It gives anti-oxidant support to the heart by protecting it against free-radicals in the blood.<sup>22</sup> It supported healthy triglyceride and cholesterol level which are the major factors for cardiovascular system such as heart-attack, strokes etc.<sup>23</sup> In the same study, the researcher reported that highest dosage of standardized Ashwagandha extract decreases LDL (bad) cholesterol by 17% and 11% decrease in triglycerides.

### ASHWAGANDHA EXTRACT LADEN WITH BIOLOGICAL INTEREST

In the area of alternative and complementary medicine, the Ashwagandha (*W. somnifera*) works as a wonder drug. The ameliorative properties of this plant for human medical condition are very much discovered in the case of stress, diabetes, hypertension, cancer and asthma. Various psychological and

neurological diseases like ischemic stroke, Huntington's disease, amyotrophic lateral sclerosis, sleep deprivation, bipolar disorder, attention deficit hyper activity disorder, Schizophrenia, Parkinson's diseases, obsessive compulsive disorder, Alzheimer's disease etc. are especially treated with *W. somnifera* (Table 1). A systematic meta-analysis of Ashwagandha plant extract was reported by<sup>27</sup> 400 participant with five randomized controlled trials were analysed. The effects on sleep were diagnosed with insomnia with dosage  $\geq$  600 mg/day with  $\geq$ 8week duration. The plant extract was effective on mental alertness and decrease the anxiety level with no side effect. The methanolic extract of different parts of plants such as leaves, fruits and roots possess antibacterial and anti-oxidant properties. The results showed that the extract of leaves of plant showed remarkable antioxidant properties and showed highest activity against *S. typhi* whereas the minimum activity was against *K. pneumonia*.<sup>16</sup> Bioactive compound found in the leaf extracts of *W. somnifera* discovered as the DNA gyrase inhibitor.<sup>30</sup> A study by molecular docking proved that the compound Withanolide C present in the methanolic leaf extract binded strongly to DNA gyrase enzyme as compared to known DNA gyrase inhibitor namely chlorobiocin. This study forms the basis for the evolution of novel antimicrobial agents. The root extract of Ashwagandha showed anti-inflammatory effects in HaCaT cells by regulating cytokines and inhibiting the MAPK/NF-KB pathway.<sup>31</sup> This study reported the anti-inflammatory activity of ASH-WEX on skin due to suppression of NF-KB and mitogen-activated protein kinase pathways. ASH-WEX treatment enhanced the m-RNA expression of the anti-inflammatory cytokine TGF-B1 and suppress the m-RNA expression of the pro-inflammatory cytokine TNF- $\alpha$  *in vivo*. The leaf extract of Ashwagandha was investigated as selective killer of the cancer cells and identify as the tumor-inhibitor. By *in vivo* tumor formulation essay in mice and by invitro growth assay on human cells were apply on the leaf extract to check the tumor-inhibitory activity. A gene silencing approach were adopted to discover the cellular target of leaf extract and found the Withanae; a phytochemical present in the plant is identified as p-53-activity tumor-inhibitor. This study proves the ashwagandha as a natural source for anticancer activity and able to kill the tumor cells.<sup>32</sup> The protective effect of Ashwagandha was reported by.<sup>33</sup> This finding explains the neuroprotective effect of plant extract against  $AlCl_3$ -induced neurotoxicity. Al enhanced the levels of lipid peroxidation and nitric acid in cortex, striatum and hippocampus and reduced the glutathione level in the striatum and hippocampus. The rats who were protected with ashwagandha extract and non-significant changes were seen in lipid peroxidation, nitric acid and reduced glutathione. This study proved that the ashwagandha extract prevent the tumor necrosis factor- $\alpha$  induced by  $AlCl_3$  in the cortex and hippocampus. In addition, the decline in cholinergic activity is also shown by the protective effect of Ashwagandha extract by maintaining normal acetylcholinesterase activity. Later on, the extract also suggests as a memory enhancer. The extract



Figure 3: Different classes of phytochemicals present in Ashwagandha.<sup>21</sup>

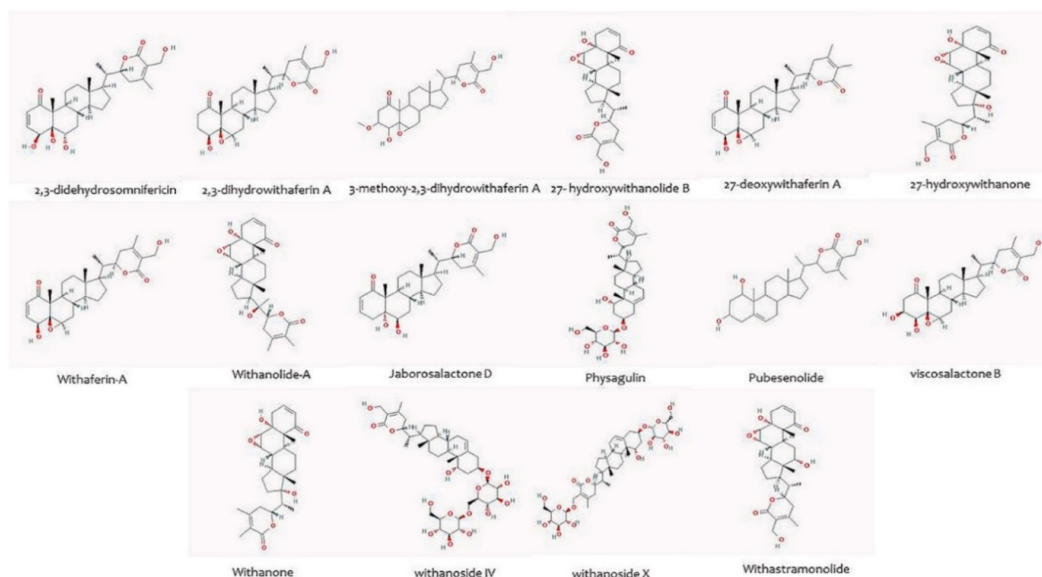
of *W. somnifera* was investigated for the protecting the liver from damage. The root extract of plant confirmed the protection of the rat's liver  $\text{CCl}_4$ -induced hepatotoxicity. The anti-hepatic damage effect is found in Ashwagandha root extract which improved the antioxidant enzyme liver.<sup>34</sup>

## ASHWAGANDHA EXTRACT WITH NANOPARTICLES AND THEIR BIOLOGICAL PURSUITS

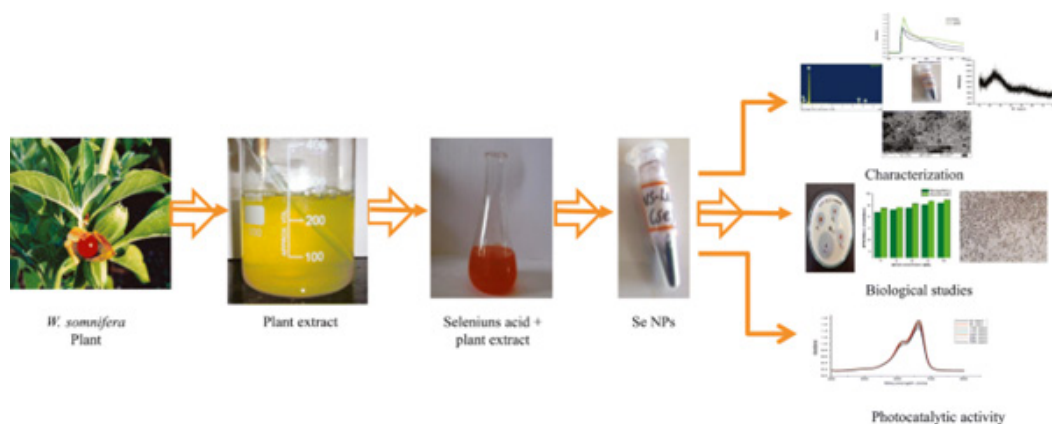
The use of nanoparticles in plant extract or oil needs much attention because of polydispersity and slow reduction rate of the final product. The development of nanoparticles with biological materials is much in demand as it is used in clinical setting and industries.<sup>35</sup> Various biological system such as plants,<sup>36</sup> and microorganism,<sup>37</sup> has gained momentum by the fabrication of bioinspired NPs. Nanoparticles with plants have advantages because of ecofriendly synthesis, clean, safe and low energy consumption.<sup>38</sup> Aqueous extract of different plant part such as roots, seeds, stems, fruits and leaves have been taken for the synthesis of metallic nano-particles. The phyto-constituents present in the extract behave as stabilizing and reducing agents for the production of non-toxic nano particles.<sup>39</sup>

The root extract of *W. somnifera* was used for the synthesis of  $\text{TiO}_2$  NPs biofilm and characterized. The newly prepared  $\text{TiO}_2$  NPs studied for its broad-spectrum anti biofilm potential as against *P. aeruginosa*, *S. aureus*, *L. monocytogens*, *E. coli*, *Serratia marcescens* and *Candida albicans* and for HepG2 cytotoxicity. Intracellular ROS generation in  $\text{TiO}_2$  causes cell death because of the formation of impaired biofilm which treated pathogens. These green  $\text{TiO}_2$  NPs have a great impact in the food industry by decreasing environmental biofouling. Furthermore, the synthesized biofilm sustains the cancer development.<sup>40</sup>

Topical delivery of *W. somnifera* crude extracts in Niosome and solid lipid nanoparticles as delivery vesicles was investigated.<sup>41</sup> The plant *W. somnifera* is known for their anticancer properties and investigated for anti-melanoma properties in this study. The ethanolic extract of *W. somnifera* was encapsulated in niosomes and Solid Lipid Nanoparticles (SLNs). The encapsulated extracts were used to determine the release and skin penetration of the phytomolecules Withaferin A and Withanolide A. In present study SLN formulations are managed to deliver only Withaferin A to epidermis-dermis layers and the stratum corneum-epidermis of the skin. A type of green synthesis with leaf extracts of *W. somnifera* was described.<sup>42</sup> Ethanolic extracts of plant leaf was biosynthesized with anisotropic gold nano-particles and their activity as IR blockers were investigated. The nanoparticles and presence of proteins were characterized by FTIR, UV-vis, TEM and fluorescence spectroscopy. The application of synthesized gold nanoparticles was suggested as chemical sensor. A study on the aqueous extract of *W. somnifera* with zinc nanoparticles was reported for their anticancer and anti-oxidant activity. The characterization was done by photochemical analysis, zeta-potentials and TEM and revealed that the large surface area and high stability of zinc nanoparticles. The antioxidant activity of the above synthesized nanoparticles has more antioxidant activity with  $\text{IC}_{50} = 0.701\text{mg/mL}$ . The extracted *W. somnifera* with its zinc nanoparticles were tested invitro for the anticancer activity on six human tumor and a normal cell line using MTT assay. The result showed most potent cytotoxicity on HeLa cell line with  $\text{IC}_{50} = 19.17\ \mu\text{g/mL}$  and proved to be a potent anticancer agent.<sup>43</sup> A research for the green synthesis of SeNPs by simple mixing of *W. somnifera* leaves extract and selenious acid ( $\text{H}_2\text{SeO}_3$ ) solution. In *W. somnifera* secondary metabolites is conjugate with SeNPs. The phyto constituents such as flavonoid, phenolic and tannic content were 12.74, 40.54 and 156.33  $\mu\text{g/mL}$  respectively in



**Figure 4:** Chemical structures of phytochemicals from *Withania somnifera* (from www.ChemSpider.com).



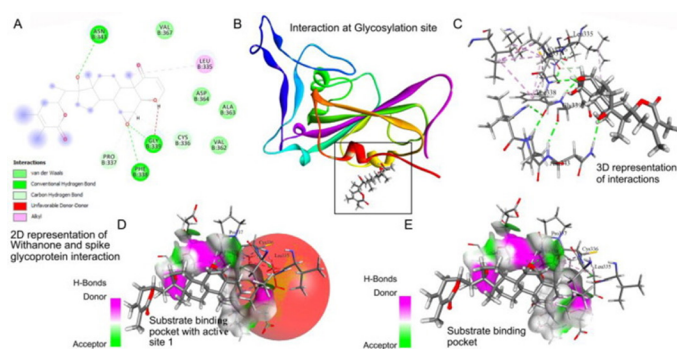
**Figure 5:** Green Synthesis of Selenium Nanoparticle Using Leaves Extract of *Withania somnifera* with Biological and Photocatalytic Activities.<sup>44</sup>

aqueous extract. The synthesized green SeNPs showed significant anti-oxidant activity of  $IC_{50} = 14.81 \mu\text{g/mL}$  and good antibacterial activity on *B. subtilis* (12mm), *K. pneumonia* (14mm) and *S. aureus* (19.66mm). Antiproliferative effects against A549 cells of SeNPs was  $IC_{50}$  at  $25 \mu\text{g/mL}$ . Above results indicates the potential application of SENPs in medical field. Although, these green SeNPs degraded MB under sunlight irradiation which was confirm by photo catalytical study so it can find its application in textile industries and water treatment plants (Figure 5).<sup>44</sup>

Ashwagandha root extract is investigated with silver nanoparticles for the antibacterial activity. The synthesis of AgNPs using roots of *W. somnifera* tested by UV-visible which showed maximum at 430 nm in the visible region. FTIR analysis proved the reduction of silver nanoparticles from  $\text{Ag}^+$  ions to  $\text{Ag}^0$  ions. The SEM proves the size of 5nm and spherical in shape. The results proves that plant root extract might be used as antibiotic with benefits of cost-effective, ecofriendly, non-toxic and most importantly highly effective against the bacteria.<sup>45</sup>

## ASHWAGANDHA AS NATURAL INHIBITOR DURING COVID-19

Various phytochemical present in the plant show a remarkable multi potency for human for various human biochemical pathways and biological process. The phytochemical obtained from plant targets the different biological pathways in COVID-19 infections. On the other way the phytochemical works as alternative therapy for the high-risk patients of diabetes, cancer and heart disease. Various natural compounds like quercetin, theflavin, caffeic acid phenethyl ester and with none are effective inhibitors of SAR-CoV-2.<sup>46-48</sup> As there is no proper medication of COVID-19, so there is an urgent requirement for the potential therapy to fight with the deadly infection of corona virus. A study reported<sup>49</sup> foretell that the plant *W. somnifera* have withanone which bind with Receptor-Binding Domain (RBD) complex of COVID-19 spike protein and human Angiotensin-Converting Enzyme 2 (ACE)-2 and suppress the viral entry. Withanone proved to be best fit due to the highest binding affinity at active site



**Figure 6:** Interaction of Withanone with Spike glycoprotein. (A) 2D representation; (B) Withanone fit at glycosylation site; (C) 3D representation; (D) Withanone within binding pocket and (E) active site 1 region.<sup>50</sup>

1 of glycosylation site and main protease 3CL pro. The constituent Withanone decreases the glycosylation of SAR-CoV-2 and inhibit viral replication via interaction with Asn343 (Figure 6).<sup>50</sup>

Molecular dynamics simulation analysis of phyto constituents from the plant *W. somnifera* and *Azadirachta indica* reported as potential inhibitors of SAR-CoV-2 agent (Table 2).<sup>51</sup> The Withanolide R (-141.96 KJ/mol) having the lowest free-energy of binding for the main protease spike proteins and can be used as potent therapeutic agents against SAR-CoV-2.

In the study the Ashwagandha plant is dock with main protease (NSP5) and the spike protein of SAR-CoV-2. The four phyto-chemical (P1-P4) and repurposed drug (PR5) with main protease of SAR-CoV-2 (NSP5) were analysed to 100ns MD simulation. Results shown that binding of P4 and PR5 with NSP5 produces a stable environment as compared to other phytochemical. Further the four best docked complexes (S1-S4) with phytochemicals were gone through to same MD simulation with repurposed drug (SR5) with spike protein (PDB). Results also proved that Withanolide R and 2,3-Dihydrowithaferin A (S4) shows lowest relative binding energy with spike protein (-87 KJ/mol) and main protease (-141.96 KJ/mol) in comparison to Baricitinib which is known as anti-Janus kinase inhibitor with greater for AP-2 associated protein kinase 1 (AAK1) for the

**Table 1: Various benefits of Ashwagandha with dosage and time with effects.**

Sl. No	Benefits Against	Dosages	Time	Effects
1.	Stress	125 to 5 mg/day	1-3 months	Cortisol levels reduces by 11-32%. <sup>3</sup>
2.	Anxiety	500 to 600 mg/day	6-12 weeks	Lowers anxiety and insomnia. <sup>9</sup>
3.	Type-2 Diabetes	250 mg/day	30 days	Reduces blood sugar level. <sup>8</sup>
4.	Infertility	5 mg/day	3 months	14% of their partner became pregnant. <sup>10</sup>
5.	Muscle growth and strength	500 mg/day	8 weeks	1% muscular power increased. <sup>24</sup>
6.	Inflammation	250 mg/day or 12 mL its extract	60 days	Reduces C-reactive protein level by 30%. <sup>25</sup>
7.	Memory	50 mg/day	14 days	Boost memory in terms of task performance, reaction time, cognitive and psychomotor performance. <sup>26</sup>
8.	Sleep quality	600 mg/day	8 weeks	Improve overall sleep in the patients of insomnia. <sup>27</sup>
9.	Maximum oxygen consumption (VO <sub>2max</sub> )	750 to 12550 mg/day	30 days	Improve VO <sub>2max</sub> in athletes. <sup>28</sup>
10.	Sexual function in women.	300 mg twice/day	8 weeks	Helpful for the treatment for female sexual dysfunction [FSD]. <sup>29</sup>

**Table 2: The top scoring drug like phytochemicals used for MD simulations.<sup>[51]</sup>**

Sl. No.	Sources	Phytochemical (Main protease NSP5 (PDB ID: 6lu7))	Abbreviation	Autodock docking score
1.	<i>W. somnifera</i>	27-Deoxy-14-hydroxywithaferin A c4	P1	-10.8
2.	<i>W. somnifera</i>	Nimoliinol c7	P2	-10.09
3.	<i>W. somnifera</i>	17-Hydroxywithaferin c6	P3	-10.08
4.	<i>W. somnifera</i>	Withanolide R c10	P4	-9.63
5.	Repurposed drug	Methylprednisolonc23	PR5	-8.57
		Spike protein (PDB ID: 6lzg, chain B)		
6.	<i>W. somnifera</i>	27-Hydroxywithanone c37	S1	-8.47
7.	<i>W. somnifera</i>	12-Deoxywithastramonolide c40	S2	-8.27
8.	<i>W. somnifera</i>	27-Deoxywithaferin A c36	S3	-7.82
9.	<i>W. somnifera</i>	2,3-Dihydroxywithaferin A c41	S4	-7.45
10.	Repurposed drug	Baricitinib C56	SR5	-7.62

treatment of COVID-19.<sup>52</sup> Four different compounds present in *W. somnifera* (WS) suppress COVID-19 envelop (E) proteins by binding with the pore region and decreases viral infection.<sup>53</sup> A research on WS phytochemical based on molecular docking emphasize the promiscuous activity. The study proved that withanoside II, IV, V with free energy (-11.30 Kcal/mol; -11.02 Kcal/mol; -8.96 Kcal/mol respectively and sitoindoside IX (-8.37 Kcal/mol) are discovered to be bind strongly with the main

protease of SAR-CoV-2.<sup>54</sup> These finding proves the phytochemical of *W. somnifera* have potent anti SAR-CoV-2 activity but finding are still needed to be authenticate *in vivo* and *invitro* system.

### ETHICAL ANALYSIS OF THE USE OF ASHWGANDHA

By the side with traditional Ayurvedic medicine, administration of Ashwagandha also furnished the desired result.<sup>55</sup> Proved ethical analysis and safety of the usage of Ashwagandha via

clinical studies have been reported initially together with stress and anxiety, reproductive issues, cardiorespiratory endurance and in further ailments.<sup>3,28,56</sup> A double-blind Randomized, Placebo-controlled study was reported for the efficacy and safety of *W. somnifera* root extract for the treatment of insomnia and anxiety. Remarkable improvement was seen in all the sleep parameter such as Sleep Onset Latency (SOL), Sleep Efficiency (SE), Pittsburgh sleep quality index and anxiety rating scales by the treatment for 10 weeks. The SE scores was reported 75.63 (2.70) for the test at the baseline and enhanced to 84.48(2.83) as compared to placebo (P, 0.002) after 10 weeks. The SOL was significant less (P, 0.019) after 10 weeks with test 29.00 (7.14) as compared to placebo 33.94 (7.65).<sup>57</sup> Another study for the safety of Ashwagandha root extract was reported and investigated that it did not interfere with any type of normal liver function. Ashwagandha 300mg or a placebo of the same dosage were given to the 80 healthy participants in 1:1 ratio, twice daily, orally for 8 weeks. For the sake of safety outcomes, various hematological and biochemistry related parameter were evaluated at the baseline and results showed no abnormality or significant changes were reported.<sup>58</sup> Efficacy, safety and tolerability of Ashwagandha was also investigated in the elderly person for the general wellbeing and sleep quality and it proved to be. All three parameter were tested by Physician's global assessment of efficacy and tolerability to therapy.<sup>59</sup> Research on Ashwagandha is carry on to prove its efficacy against a variety of diseases globally and many science-baked benefits are also reported. As modern science wants evidence of the safety and efficacy of any herb so many research about the consumption of Ashwagandha with varying dosage range are going on and need to explore for the efficacy of the herbal product and population wide safety.

### LIMITATION IN THERAPY AND MEDICAL CARE

Ashwagandha supplements were reported to well tolerated and safe after the study of various population. As far as limitation is concern, the first and most important thing is "varying dose range". If the consumption of Ashwagandha is in high doses that may lead to vomiting, stomach upset, diarrhea. Again, consultation with doctor is needed for breast feeding and pregnant ladies and the patients who is taking sedative, immunosuppressant and other medicine.<sup>60</sup> Ashwagandha may also interact with blood pressure, blood sugar and thyroid medicines. So, it is advisable to talk to your healthcare professional and dosage range can be vary that to keep in mind. Sources of supplement capsule are also be checked.<sup>61</sup> Sometimes heavy metals such as As, Cd, Pb and Hg is found in the product which causes damage to the body organ viz. central nervous system, immune system, reproductive system, kidney and liver.<sup>62</sup> One more thing is that the Ashwagandha's benefits are not immediate and can notice days to week but its non-toxic side effects make it popular adaptogen.

### CONCLUSION

Every single part of Ashwagandha plant is equally important. This plant is best suited for the concept of "Bioinspiration". It is the process that takes help from biological design for advantageous technologies for various biological activity such as antimicrobial, antiviral, anti-inflammatory, anti-cancer etc. Ashwagandha is one of the most popular herbs which uses as a traditional form of substitutes medicine with many proven benefits along with strengthen the immune system, easy to obtain, stabilizes hormones and metabolism with low cost and lesser side effects. Multiple health benefits are shown by the Ashwagandha are reducing stress and anxiety, enhances the athletic performance, improving mental health condition, boost testosterone, lowers blood sugar, reduce inflammation and improve memory and sleep. Around 69 studies proved that the Ashwagandha is completely safe and effective for controlling many health problems. In all it can be said that "*Ashwagandha is the vector for managing the quality of life*"

### FUTURE OUTCOME

Nanoparticles based on the Ashwagandha have great potential not in medical field but also for dressing and consumer products. So "Green-nanotechnology" provides a platform to investigate this plant for better results. Moreover, the way by which the active molecules present in extracts binds to the surface of MNPs and the presence of real molecular active groups in the molecules needs to be further attention. The MNPs *in vivo* toxicity and long-term effects on environment, animals or human are needed to address. Future research is expected for the better utilization of the green synthesis for the progress and development of human society. The large-scale research is needed to establish the stereotype of the plant-based treatment.

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### CONFLICT OF INTEREST

The authors declare that this review content has no conflict of interest.

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