



WORLD'S BEST ASHWAGANDHA

FROM THE ASHWAGANDHA EXPERTS. THAT'S ALL WE DO.

# Scientific Studies

**HIGHLY BIOAVAILABLE, CLINICALLY EFFECTIVE, SUSTAINABLY PRODUCED.**



**KSM-66 is from the world's ashwagandha experts.  
Ashwagandha is the only thing we do.**

## **KSM-66's Clinically Proven Benefits:**

**Stress Relief**

**Memory and Cognition**

**Muscle Strength**

**Endurance**

**Sleep**

**Sexual Health**

**Male Testosterone**

**Weight Management**

**Thyroid Health**

[www.ashwagandhaadvantage.com](http://www.ashwagandhaadvantage.com)

**Ashwagandha Advantage** is a website sponsored by KSM-66 and is brought to you by SupplySide. It is an informative new resource featuring premium reports, infographics, blogs and videos. Designed to deliver information on the powerful Indian adaptogenic botanical, the content site highlights clinical study results, formulation guidance, sourcing information and more.

## What Makes KSM-66 The “World’s Best Ashwagandha”

### The most extensive set of research studies and clinical trials

- Ixoreal is the industry leader in clinical trials and basic research investigating the effectiveness of ashwagandha.
- Largest pool of research studies with 24 studies: 10 published studies, 6 additional studies completed and in peer review and 8 ongoing studies.
- Following the gold standard: Double-blind, placebo-controlled, randomized studies.
- Our trials are on healthy populations to mirror our mainstream customer base.
- Our publications are of academia standard, all in PubMed-indexed medicine journals.
- The principal investigators are leading researchers with established publication records.

### Tight vertical integration for high quality and price advantage

Ixoreal is the only major branded ashwagandha manufacturer in the world to own the entire value chain in producing the extract. Ixoreal has its own farms, production facilities, testing laboratories, research center and distribution. Nothing is outsourced and no middlemen are involved. As a result, Ixoreal is unmatched in its ability to deliver high-quality ashwagandha with steady supply and batch-to-batch consistency.

### KSM-66 is highly bioavailable

KSM-66’s production process leads to it being highly bioavailable. A recent study demonstrated KSM-66 to be the most bio-available in a benchmark set of ashwagandha extracts produced using different extraction methods.

### Highest number of quality certifications:



### Highest Concentration

Created via a process that took 14 years of R&D to develop and refine, KSM-66 has the highest concentration of all major root-only extracts available on the market today. It is produced through a unique proprietary extraction process, based on Green-Chemistry principles, without using alcohol or any other chemical solvent.

### Winner of several awards and honors

“Sports Nutrition Ingredient of the Year 2018” by NutraIngredients Asia

“Herbal Industry Leader 2016” by Society for Ethnopharmacology

“Product Innovation in Botanicals Award” by Frost and Sullivan 2014

“Best Botanical Ingredient” at Engredea 2013

“Ingredient of the Year” at Panacea 2012

## For Stress and Anxiety



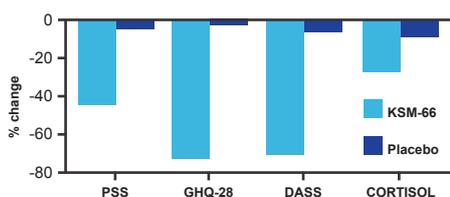
OBJECTIVE	DOSE	DURATION	NO. OF SUBJECTS
To evaluate the safety and efficacy of KSM-66 Ashwagandha in reducing stress and anxiety and in improving the general well-being of adults under stress.	300 mg Twice daily	8 Weeks	64 Healthy subjects

“A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety in adults,” published in *Indian Journal of Psychological Medicine*, 2012.

### EFFICACY MEASURES

- Perceived Stress Scale (PSS) score
- Serum cortisol level, General Health Questionnaire-28 (GHQ-28) score
- Depression Anxiety Stress Scale (DASS) score

### RESULTS



**PSS scores:** KSM-66 Ashwagandha caused a noticeable decrease in perceived stress among the subjects. At the end of the study, KSM-66 Ashwagandha produced a 44.0% reduction in PSS scores from the baseline, which is statistically significant ( $p < 0.001$ ) compared to the placebo.

**Serum cortisol levels:** A statistically significant decrease ( $p < 0.05$ ) of 27.9 % was observed in serum cortisol level as a result of KSM-66 Ashwagandha consumption.

**GHQ-28 scores:** KSM-66 Ashwagandha produced a marked reduction in GHQ-28 scores. It produced a 72.3% decrease ( $p < 0.001$ ) in total GHQ-28 scores from the baseline at the end of 60 days. The GHQ-28 domain scores for ‘somatic’, ‘anxiety and insomnia’, ‘social dysfunction’ and ‘severe depression’ reduced significantly by 76.1%, 69.7%, 68.1% and 79.3% respectively from the baseline ( $p < 0.001$ ).

**DASS domain scores:** KSM-66 Ashwagandha reduced depression, anxiety and stress in the study subjects, as evidenced in DASS scores. It produced a 71.6% decrease ( $p < 0.001$ ) in total DASS scores. The DASS scores for depression, anxiety and stress domains reduced significantly ( $p < 0.001$ ) by 77.0%, 75.6% and 64.2% respectively with KSM-66 Ashwagandha supplementation.

### MODES OF ACTION

- Stress is often accompanied by an increase in serum cortisol level. Ashwagandha, an adaptogen, can promote homeostasis, regulate HPA-axis function and reduce serum cortisol level.
- Ashwagandha is seen as a GABA-mimetic that reduces over-excitation of neurons, thereby producing calmness, reducing stress and increasing focus, mental well-being and self-control.
- There is emerging evidence suggesting the role of ashwagandha in suppressing stress-induced increase of dopamine receptors in the corpus striatum of the brain. It is also claimed to reduce stress-induced increase of plasma corticosterone, blood urea nitrogen and blood lactic acid.



## For Male Sexual Function

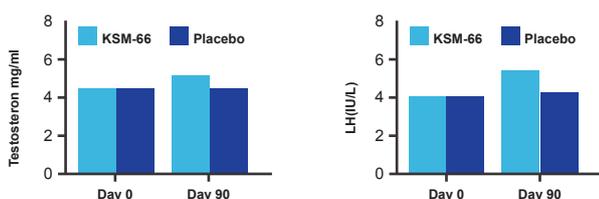
OBJECTIVE	DOSE	DURATION	NO. OF SUBJECTS
To evaluate the efficacy of KSM-66 Ashwagandha in improving male sexual function in otherwise healthy males.	225 mg Thrice daily	12 Weeks	46 Healthy male subjects

“Clinical Evaluation of the Spermatogenic Activity of the Root Extract of Ashwagandha (*Withania somnifera*) in Oligospermic Males: A Pilot Study,” published in *Evidence-Based Complementary and Alternative Medicine*, 2013.

### EFFICACY MEASURES

- Sperm concentration
- Semen volume
- Sperm motility
- Serum testosterone levels
- Serum luteinizing hormone levels

### RESULTS



**Sperm concentration:** KSM-66 Ashwagandha improved sperm concentration among the male study subjects. A significant ( $p < 0.001$ ) increase of 167% was observed in sperm concentration in the subjects supplemented with KSM-66 Ashwagandha.

**Semen volume:** A significant 53% ( $p < 0.001$ ) increase in semen volume was observed in the ashwagandha treatment group, significant when compared to the placebo group.

### MODES OF ACTION

- Stress is known to be a causative factor in male infertility. Ashwagandha’s proven adaptogenic effects, antioxidant action and its ability to modulate the stress response therefore may improve male fertility.
- Ashwagandha can result in significant decrease in cortisol levels, increase in testosterone, regulation of other reproductive hormones and improvement in overall semen quality.
- Ashwagandha is believed to help stimulate the hypothalamus gland to produce gonadotropin releasing

**Sperm motility:** The study showed a significant increase of 57% in sperm motility in the ashwagandha treatment group, significant when compared to the placebo group ( $p < 0.001$ ).

**Serum testosterone level:** Therapy with KSM-66 Ashwagandha produced a 17% increase in serum testosterone levels in the study subjects, significant when compared to the placebo ( $p < 0.001$ ).

**Serum luteinizing hormone:** Therapy with KSM-66 Ashwagandha produced an improvement ( $p < 0.001$ ) of 34% in serum luteinizing hormone levels, significant when compared to the placebo.

hormone, which in turn can stimulate the anterior pituitary gland to produce FSH and LH that stimulate the testes to produce testosterone.

- Ashwagandha may have a direct spermatogenic influence on the seminiferous tubules by exerting a testosterone-like effect.
- Ashwagandha may reduce serum cortisol level by regulating HPA-axis function. Increase in cortisol level can have a negative effect on sperm production.

## For Cardiorespiratory Endurance



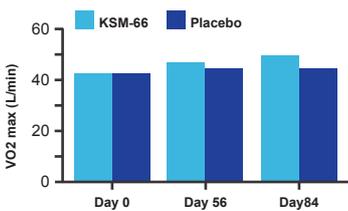
OBJECTIVE	DOSE	DURATION	NO. OF SUBJECTS
To evaluate the effect of KSM-66 Ashwagandha in improving cardiorespiratory endurance in healthy athletic adults.	300 mg Twice daily	12 Weeks	49 Healthy athletic adults

“Efficacy of Ashwagandha (*Withania somnifera* [L.] Dunal) in improving cardiorespiratory endurance in healthy athletic adults,” published in *AYU*, 2015.

### EFFICACY MEASURES

- $VO_2$  max by the shuttle run test
- World Health Organization Quality of life (WHO-QOL) questionnaire scores

### RESULTS



**VO<sub>2</sub> max:** The 12 week therapy of KSM-66 Ashwagandha showed a marked improvement in maximum oxygen consumption ( $VO_2$  max) in healthy athletic adults. Significant increase ( $p < 0.001$ ) of 11.8% and 13.6% were observed in  $VO_2$  max at Day 56 and Day 84 respectively in the ashwagandha supplemented group, significant when compared to the placebo group.

**WHO-QOL scores:** The supplementation with KSM-66 Ashwagandha produced a significant ( $p < 0.05$ ) improvement in Physical health, Psychological, Social relationship and Environmental domain scores in the WHO-QOL questionnaire, significant when compared to the placebo after the 12 week therapy. KSM-66 Ashwagandha produced 14.8%, 19.7%, 21.6% and 9.7% increases in WHO-QOL scores of Physical health, Psychological, Social relationship and Environmental domains respectively, from the baseline value.

### MODES OF ACTION

- Ashwagandha is believed to increase energy production in muscles through its beneficial effects on mitochondrial energy levels.

- Ashwagandha has been demonstrated to increase creatine levels, which can lead to more efficient phosphocreatine production, which leads to ATP activity to generate rapid energy for muscle contraction and movement.

- Ashwagandha can improve the hemoglobin count and

red blood cell (RBC) count. An increase in RBC mass leads to an increase in the capacity of blood to transport oxygen at a greater capacity to the peripheral system, thus ensuring a greater  $VO_2$  max.

- Ashwagandha can increase the level of succinate dehydrogenase (SDH). SDH in turn provides increased cellular energy. The ashwagandha root can help to support the nervous system and adrenals, helping to maintain energy levels during times of stress and prevent the body from ‘burning-out’.



## For Muscle Strength and Recovery

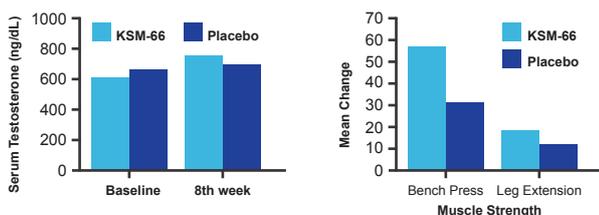
OBJECTIVE	DOSE	DURATION	NO. OF SUBJECTS
To evaluate the effect of KSM-66 Ashwagandha on muscle strength, mass and recovery, as an adjuvant to resistance training program and an ergogenic aid.	300 mg Twice daily	8 Weeks	50 Healthy male subjects

“Examining the effect of *Withania somnifera* Supplementation on Muscle Strength and Recovery: A Randomized Controlled Trial,” published in the *Journal of the International Society of Sports Nutrition*, 2015.

### EFFICACY MEASURES

- Serum testosterone level
- Muscle strength (maximal sustainable single repetition load -1RM)
- Muscle size
- Body fat percentage
- Serum creatine kinase level

### RESULTS



**Serum testosterone levels:** KSM-66 Ashwagandha produced a marked increase in serum testosterone levels, which can be associated with muscle growth and increased muscle strength. At the end of 8 weeks, a statistically significant ( $p<0.05$ ) increase of 15.3% in serum testosterone level was noticed for the ashwagandha group, significant when compared to the placebo group.

**Muscle Strength:** The effect of KSM-66 Ashwagandha on muscle strength was measured through bench press and leg extension exercise (1RM). KSM-66 supplementation produced 138.7% and 52% increases in muscle strength for the bench press ( $p<0.05$ ) and leg extension exercise

( $p<0.05$ ) respectively.

**Muscle growth:** KSM-66 Ashwagandha supplementation caused improved muscle growth as measured for the thigh, arm and chest ( $p<0.05$ ). At the end of the study, 8.1%, 17.1% and 3.3% increases in muscle size for thigh, arm and chest respectively were observed with ashwagandha supplementation.

**Body fat percentage:** KSM-66 Ashwagandha supplementation resulted in a 16% reduction ( $p<0.05$ ) in average body fat.

**Muscle Recovery:** Muscle recovery was measured through reduction in serum creatine kinase level. KSM-66 Ashwagandha supplementation produced a significantly faster recovery compared to the placebo.

### MODES OF ACTION

- Ashwagandha can increase muscle size by promoting muscle growth through increasing testosterone levels in body.
- Ashwagandha can inhibit reduction in muscle mass by decreasing the levels of cortisol, which is a catabolic agent.
- Ashwagandha may help the body improve its own natural production of steroids that in turn enhance protein synthesis. Ashwagandha is also believed to accelerate the cell repair process in the body. This is helpful not only in anti-aging but also in faster recovery between sessions of exercise and physical activity.
- Ashwagandha may promote muscle recovery through its antioxidant effects that combat free radical damage both at the muscle and central nervous system levels, anti-inflammatory and analgesic effects and reduction in lactic acid and blood urea nitrogen.



## For Female Sexual Health

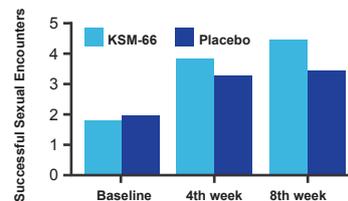
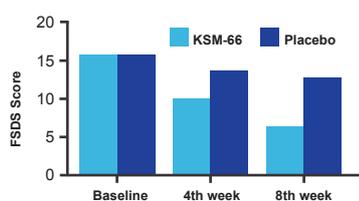
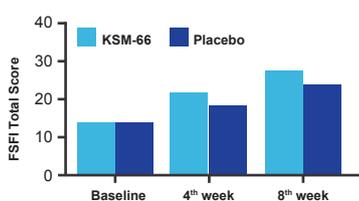
OBJECTIVE	DOSE	DURATION	NO. OF SUBJECTS
To evaluate the efficacy of KSM-66 Ashwagandha in improving the sexual functions in healthy females.	300 mg Twice daily	8 Weeks	50 Healthy female subjects

“Efficacy and Safety of Ashwagandha (*Withania somnifera*) Root Extract in Improving Sexual Function in Women: A Pilot Study,” published in *BioMed Research International*, 2015.

### EFFICACY MEASURES

- Female Sexual Function Index (FSFI) Questionnaire domain scores
- Female Sexual Distress Scale (FSDS) scores
- Number of total and successful sexual encounters

### RESULTS



**FSFI scores:** KSM-66 Ashwagandha caused a noticeable improvement in sexual function among the female subjects. It produced a 75.8% increase in total FSFI scores ( $p < 0.001$ ) from the baseline. The FSFI domain scores for Arousal, Lubrication, Orgasm and Satisfaction improved significantly by 62.4%, 59.4%, 82.4% and 62.4% respectively from the baseline score ( $p < 0.001$ ).

**FSDS scores:** KSM-66 Ashwagandha reduced sexual distress among the female subjects. The extract produced a 60.9% reduction in FSDS scores from the baseline

( $p < 0.001$ ).

**Number of Total and Successful Sexual Encounters:** KSM-66 Ashwagandha caused 14.3% and 126.1% increase in the number of Total Sexual Encounters and Successful Sexual Encounters respectively from the baseline. KSM-66 Ashwagandha also caused a significant ( $p < 0.001$ ) increase in successful sexual encounters. However, it did not produce a significant improvement in the number of total sexual encounters and in the FSFI domain for desire and pain.

### MODES OF ACTION

- Female sexual dysfunction is associated with reduced libido, dryness in vagina, reduced genital perception, reduced arousal, pain during intercourse, problems to achieve orgasm and is majorly due to neuro-vascular, hormonal or psychogenic manifestations.
- Stress enhances cortisol levels in the blood, which in turn may result in gonadal and sexual dysfunction. Under chronic stress, women are less motivated towards sexual activities. Excessive stress along with anxiety and fatigue can impede sexual arousal and increase vaginal pain.
- Ashwagandha reduces serum cortisol level, likely by regulating HPA-axis and maintains homeostasis in the body.
- The GABA-mimetic action of ashwagandha can reduce stress and anxiety.
- In females, ashwagandha improves libido probably by increasing LH and reducing FSH and prolactin.
- Ashwagandha can alter the gonadotrophin levels and increase the ovarian weight and promote folliculogenesis significantly.



## For Stress and Weight Management

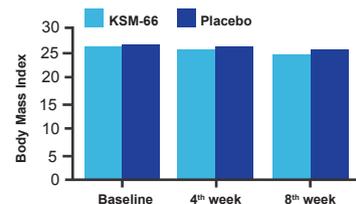
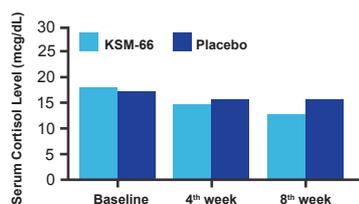
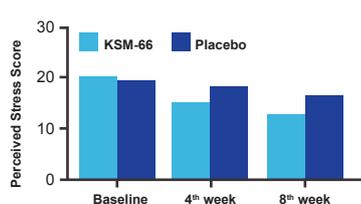
OBJECTIVE	DOSE	DURATION	NO. OF SUBJECTS
To evaluate the efficacy of KSM-66 Ashwagandha in reducing body weight in adults under chronic stress.	300 mg Twice daily	8 Weeks	50 Healthy subjects

“Body Weight Management in Adults Under Chronic Stress Through Treatment with Ashwagandha Root Extract: A Double-Blind, Randomized, Placebo-Controlled Trial,” published in the *Journal of Evidence-Based Complementary & Alternative Medicine*, 2016.

### EFFICACY MEASURES

- The efficacy measures were Perceived Stress Scale (PSS) and Food Cravings Questionnaire (FCQ) scores, Oxford Happiness Questionnaire (OHQ) score, Three Factor Eating Questionnaire (TFEQ) domain scores, serum cortisol levels, bodyweight and body mass index (BMI).

### RESULTS



**PSS scores:** KSM-66 Ashwagandha caused a significant reduction ( $p < 0.05$ ) in perceived stress among the subjects. By the end of the study, KSM-66 Ashwagandha produced a 32.74% reduction in PSS scores from the baseline, significant when compared to the placebo.

**FCQ domain scores:** KSM-66 Ashwagandha reduced desire or cravings for food in the study subjects. The FCQ scores for Planning, Positive and Negative reinforcement, Lack of control, Emotion and Environment domains were reduced significantly ( $p < 0.05$ ) in the Ashwagandha supplemented subjects.

**Serum cortisol levels:** A statistically significant ( $p < 0.05$ )

decrease of 22.2% was observed in serum cortisol (a stress hormone) levels as a result of KSM-66 Ashwagandha supplementation, significant when compared to the placebo.

**Bodyweight and BMI:** KSM-66 Ashwagandha supplementation resulted in a 3.0% and 2.9% reduction in bodyweight ( $p < 0.05$ ) and BMI ( $p < 0.05$ ) respectively.

**OHQ and TFEQ scores:** Supplementation with KSM-66 Ashwagandha resulted in a significant ( $p < 0.05$ ) increase in OHQ scores and a significant ( $p < 0.05$ ) reduction in TFEQ scores for ‘Uncontrolled’ and ‘Emotional Eating behavior’, significant when compared to the placebo.

### MODES OF ACTION

- Chronic stress is frequently accompanied by an increase in serum cortisol and food cravings and a decrease in dietary control and mental well-being, which are all associated with weight gain.
- Ashwagandha is seen as a GABA-mimetic that reduces over-excitation of neurons, thereby producing calmness, reducing stress and increasing focus, mental well-being and self-control.
- The role of ashwagandha in promoting homeostasis and regulating HPA-axis function may explain its role in the reduction of serum cortisol.
- Ashwagandha can therefore impart a positive impact on eating behavior and normalization of hunger.



## For Memory and Cognition

OBJECTIVE	DOSE	DURATION	NO. OF SUBJECTS
To assess the effect of KSM-66 Ashwagandha on working memory, immediate memory, general memory, visuospatial processing, executive function, attention and information processing speed.	300 mg Twice daily	8 Weeks	51 Healthy subjects

“Efficacy and Safety of Ashwagandha (*Withania somnifera* (L.) Dunal) Root Extract in Improving Memory and Cognitive Functions,” published in the *Journal of Dietary Supplements*, 2017.

### EFFICACY MEASURES

- Wechsler Memory Scale III: Logical Memory I and II, Associates I and II, Faces I and Faces II, Family Pictures I and II, Letter-Number Sequencing, Spatial Span and Visual Reproduction I & II
- Cognitive Battery Tasks: Shepard’s mental rotation task, Erikson Flanker task, Wisconsin card sort test, Trail making test part A, Mackworth’s sustained attention test

### RESULTS

**WMS-III Immediate Memory subtests:** The WMS-III Immediate Memory subtests relate to the ability to recall within a few minutes of stimuli presentation, and reflect learning ability. KSM-66 Ashwagandha supplementation enhanced immediate memory, as assessed by improving the WMS-III subtest scores for Logical Memory I ( $p < 0.01$ ), Verbal Paired Associates I ( $p < 0.05$ ), Faces I ( $p < 0.05$ ), Family Pictures I ( $p < 0.01$ ).

**WMS-III General Memory subtests:** The WMS-III General Memory subtests relate to the ability to recall after a substantial passage of time, which is associated with learning and productivity. KSM-66 Ashwagandha supplementation upgraded general memory in terms of WMS-III subtest scores for Logical Memory II ( $p < 0.01$ ), Verbal Paired Associates II ( $p < 0.05$ ), Faces II ( $p < 0.05$ ), Family Pictures II ( $p < 0.01$ ).

**WMS-III Working Memory subtests:** The WMS-III Working Memory subtests relate to the ability to hold

information for immediate sequential actions. KSM-66 Ashwagandha supplementation increased scores on the Spatial Span subtest ( $p < 0.05$ ), but not the Letter-Number Sequencing subtest ( $p > 0.10$ ), thus resulting in a mixed response on working memory.

**Executive Function:** Executive function, a higher-order cognitive process, facilitates the coordination, selection and execution of willful action. KSM-66 supplementation improved executive function as seen in the scores for the Eriksen Flanker Task ( $p < 0.01$ ) and Wisconsin Card Sort Test ( $p < 0.05$ ).

**Attention and Information Processing Speed:** This cognitive component governs the extent of time that the subject can receive information, filter out irrelevant information, focus on the relevant information, process that information and respond accordingly. KSM-66 improved performance in Trailmaking Test Part A ( $p < 0.05$ ) and Mackworth’s Sustained Attention Test ( $p < 0.01$ ).

### MODES OF ACTION

- Ashwagandha is seen to facilitate choline production in the body, which in turn influences key memory processes.
- As a GABA-mimetic agent, ashwagandha can decrease over-firing of neurons and increase the ability of the body to ignore distracting stimuli and improve executive function.
- Increased cortical muscarinic acetylcholine receptor capacity has been observed in animals and humans with extracts of ashwagandha.



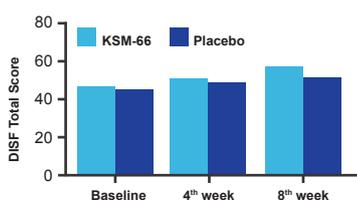
## For Sexual Wellness In Healthy Men

OBJECTIVE	DOSE	DURATION	NO. OF SUBJECTS
To evaluate the effect of KSM-66 Ashwagandha on sexual wellness of healthy male adults.	300 mg Twice daily	8 Weeks	50 Healthy male adults

### EFFICACY MEASURES

- Derogatis Interview for Sexual Functioning (male version) DISF(M)
- Serum testosterone levels

### RESULTS



**DISF scores:** Treatment with KSM-66 Ashwagandha caused significant improvements in sexual function among the male subjects compared to the placebo group ( $p < 0.0001$ ). It produced a 10.64% increase in total DISF scores ( $p < 0.0001$ ) from the baseline. The DISF domain

scores for Sexual fantasy/functions, Arousal, Orgasm and Sexual drive improved significantly by 3.65%, 18.23%, 6.12% and 11.35% respectively from the baseline score ( $p < 0.05$ ).

**Serum testosterone level:** Therapy with KSM-66 Ashwagandha produced a significant increase in serum testosterone levels in the treatment subjects compared to the placebo.

### MODES OF ACTION

- Stress is detrimental for male sexual health and wellness. Ashwagandha's adaptogenic activity, antioxidant properties and ability to modulate the stress response can result in improved sexual function in men. Ashwagandha can significantly increase serum testosterone levels, decrease serum cortisol levels, regulate other reproductive hormones and improve overall sexual health and wellness in men.
- Ashwagandha is traditionally thought to improve serum testosterone level and improve libido, arousal, sexual drive and other sexual responses.
- Ashwagandha may reduce serum cortisol level through regulating HPA-axis function. Increase in cortisol level can have a negative effect on male sexual desire and arousal.
- Ashwagandha may scavenge free radicals and protect the male reproductive system from their negative effects and restore normal sexual function in men.
- Ashwagandha can stimulate the hypothalamus gland to produce gonadotropin releasing hormone, which stimulates anterior pituitary gland to produce FSH and LH and stimulate the testes to produce testosterone.

# For Thyroid Function Support



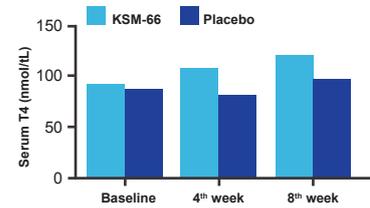
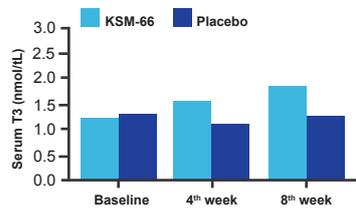
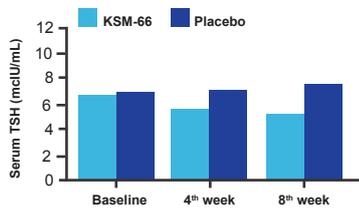
OBJECTIVE	DOSE	DURATION	NO. OF SUBJECTS
To evaluate the effect of KSM-66 Ashwagandha on sub-clinical hypothyroidism.	300 mg Twice daily	8 Weeks	50 Healthy subjects

“Efficacy and Safety of Ashwagandha Root Extract in Subclinical Hypothyroid Patients: A Double-Blind, Randomized Placebo-Controlled Trial,” published in the *Journal of Alternative and Complementary Medicine*, 2017.

## EFFICACY MEASURES

- Serum TSH level
- Serum free T3 level
- Serum free T4 level

## RESULTS



**Serum TSH level:** KSM-66 ashwagandha reduced the serum TSH level among the volunteers. Treatment with KSM-66 Ashwagandha produced a significant ( $p < 0.0001$ ) reduction of 18.59% in the serum TSH level, significant when compared to the placebo.

**Serum free T4 level:** The study showed an increase of 23.19% in serum free T4 level in ashwagandha treatment group, significant when compared to the placebo group ( $p < 0.0001$ ).

**Serum free T3 level:** A significant 47.16 % ( $p < 0.0001$ ) increase in serum free T3 level was observed in ashwagandha treatment group, significant when compared to the placebo group.

## MODES OF ACTION

- Ashwagandha is seen to regulate the hypothalamic–pituitary–thyroid (HPT) axis. It can reduce serum TSH to normal level and control subclinical hypothyroidism.
- Ashwagandha can scavenge free radicals and simultaneously reduce oxidative stress and protect the thyroid system from their negative effects and restore normal thyroid function.
- Ashwagandha, as an adaptogen, is believed to promote homeostasis, regulate HPA-axis function and reduce morning cortisol level. High levels of cortisol, dopamine, and inflammation are associated with thyroid dysfunction. Ashwagandha can reduce the levels of cortisol, dopamine, and inflammation and modulate the thyroid hormones to normal levels.



## For Anti-Aging

### OBJECTIVE

To evaluate the effect of KSM-66 Ashwagandha in enhancing lifespan of *Caenorhabditis Elegans*.

“*Withania somnifera* root extract extends lifespan of *Caenorhabditis Elegans*,” published in *Annals of Neurosciences*, 2013.

### METHODS

Wild type *C. elegans* (N2) or RB918: *acr-16* (*ok789*); and NL2099: *rrf-3* (*pk1426*) mutant worms were used. The lifespan assay of the worms is done after treating them with KSM-66 Ashwagandha.

### RESULTS

Sample	Median Lifespan + Std. Dev
NGM	14±3(109)
NGM+ethanol	15±1.3(127)
NGM+PI-KSM-100ng/ml	17±3.14(213)

Wild type worms (mutant for the human nicotinic acetylcholine receptor, nAChR,  $\alpha 7$  equivalent, *acr-16*), showed around 20% lifespan extension when treated with KSM-66 Ashwagandha. The authors concluded that KSM-66 Ashwagandha successfully enhanced the lifespan of *C. elegans*.

### MODES OF ACTION

- Ashwagandha as an adaptogen can increase the ability to adapt to environmental, physical and mental changes by modulating metabolism.
- In Ayurveda, ashwagandha has been claimed to enhance lifespan.
- Organisms which live to a very old age tend to

experience low stress either due to environmental factors or due to internal resilience. The adaptogenic action of ashwagandha can promote resilience to stress and in this way indirectly promote longer life.

- Ashwagandha enhances telomerase activity which may be responsible for anti-aging activity and enhanced lifespan of *C. elegans*.



## For Telomerase Activity

### OBJECTIVE

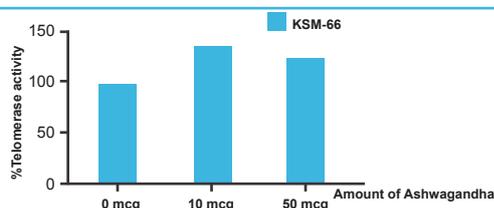
To evaluate the effect of KSM-66 Ashwagandha to increase telomerase activity in HeLa cells, an in-vitro human cell-culture model.

“*Withania somnifera* Root Extract Enhances Telomerase Activity in the Human HeLa Cell Line,” published in *Advances in Bioscience and Biotechnology*, 2016.

### METHODS

Telomerase activity of KSM-66 Ashwagandha was determined through the Telomere Repeat Amplification Protocol (TRAP) assay in HeLa cells, an in-vitro human cell-culture model.

### RESULTS



KSM-66 Ashwagandha increased telomerase activity, as assessed by TRAP assay, with highest enhancement of ~45% at 10-50 $\mu$ g concentration. Thus, ashwagandha root extract has an anti-aging potential.

### MODES OF ACTION

- Ashwagandha may elongate short telomeres and thereby enhance telomerase activity.

## Toxicity Studies On KSM-66 Ashwagandha

**Acute oral toxicity study:** KSM-66 Ashwagandha did not cause mortality in the treated rats at any studied dosage level, according to the Globally Harmonized System (GHM) ranking. The results revealed that KSM-66 neither caused adverse effects nor produced any toxicity in the set of measures studied. It was found to be safe up to 2000 mg/kg dose level by oral route, observed for 14 days.

**28-day sub-acute repeated oral toxicity study:** KSM-66 Ashwagandha did not cause mortality or some specific negative symptoms and adverse effects in the

treated rats at any dose level studied. KSM-66 was found safe up to 2000 mg/kg dose level by oral route given daily for 28 days.

**Genotoxicity acute and 28 days repeated dose study by Comet Assay:** It was observed that there was no significant increase in percentage tail DNA at all studied time intervals after treatment when compared to control. There was no evidence of genotoxicity by KSM-66 at any studied dose levels in acute and 28-day subacute repeated oral dose toxicity studies.

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## Substantiated Structure/Function Claims

KSM-66 Ashwagandha's substantiated structure/function claims are in accordance with the requirements of the Dietary Supplement Health and Education Act of 1994. Backed by peer reviewed studies, numerous claims have been deemed acceptable for KSM-66. Some examples include:

### Stress

- Helps to reduce stress and anxiety
- Helps to promote relaxation
- Helps to improve the quality of sleep
- Helps to reduce and maintain normal cortisol levels
- Helps in the calming-down and relaxation of the body and mind

### Memory And Cognition

- Helps to improve memory
- Helps to improve learning (adaptation and recognition of systematicities)
- Helps to improve alertness (rapidity of recognizing changes in stimuli)
- Helps to improve concentration (the ability to filter out distracting stimuli and increase performance speed)

### Sexual Performance

- In women, helps to increase sexual arousal, orgasm and satisfaction
- In men, helps the body to increase and maintain healthy levels of testosterone
- In men, helps the body to increase sperm concentration and volume

### Women's Health

- Helps to moderate normal symptoms of PMS
- Helps to support a healthy response to common conditions associated with menopause

### Sports Function

- Helps to boost stamina and endurance
- Helps to increase muscle size in men
- Helps to increase muscle strength in men
- Helps to reduce body fat percentage in men
- Helps to increase the speed of muscle recovery in men
- In men, helps the body to increase and maintain healthy levels of testosterone
- Helps to enhance sports performance

### Weight Management

- Helps to control stress-related food cravings
- Helps to reduce and maintain healthy body weight
- Helps to improve overall body composition when used as part of a healthy diet and exercise program

### Thyroid FunctionSupport

- Helps to normalize thyroid hormone levels
- Helps to maintain normal thyroid health

## Studies On KSM-66 Ashwagandha In The Publication Process

1. “Efficacy of KSM-66 Ashwagandha on quality of sleep in healthy adults”
2. “Efficacy of KSM-66 Ashwagandha for perimenopausal symptoms in healthy women”
3. “Efficacy of KSM-66 Ashwagandha for general health improvement in elderly subjects”
4. “Efficacy of KSM-66 Ashwagandha on VO<sub>2</sub> max, oxidative stress and cardiorespiratory endurance in athletes”
5. “The effect of KSM-66 Ashwagandha on creatine, muscle size and muscle strength in athletes”
6. “Efficacy and safety of KSM-66 Ashwagandha in reducing the effects of stress and anxiety, a multi-continent study”  
(Data collection still in process.)

## Ashwagandha Adoption

KSM-66’s maker, Ixoreal Biomed Inc., is pleased to partner with the American Botanical Council to be the adopter of the Ashwagandha herb, under its “Adopt-an-Herb” program. Ixoreal helps the American Botanical Council keep its repository of research articles on ashwagandha up-to-date and aids the council in collecting and distributing research information on Ashwagandha.



## KSM-66 Ashwagandha Is GRAS

KSM-66 is a self affirmed GRAS (Generally Regarded as Safe) ingredient, qualified by a reputed panel of toxicologists.

## KSM-66 Ashwagandha And Health Canada



Health  
Canada

Health Canada has granted approval to KSM-66 for a broad range of compelling functional claims based on KSM-66’s impressive set of clinical studies, which have been published in respected peer-reviewed journals indexed in the PubMed database of the U.S. Government’s NIH.

Under Health Canada’s NPN (Natural Product Number) 80047973, a few of the end-product claims that formulators can make using KSM-66 at the clinically-relevant dosage are: (1) Helps increase resistance to stress/anxiety in individuals with a history of chronic stress, thereby improving their overall quality of life; (2) Athletic support or Workout/Exercise supplement; and (3) Helps promote healthy testosterone production in males. (4) Helps support physical aspects of sexual health in women.

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FROM THE ASHWAGANDHA EXPERTS. THAT'S ALL WE DO.

