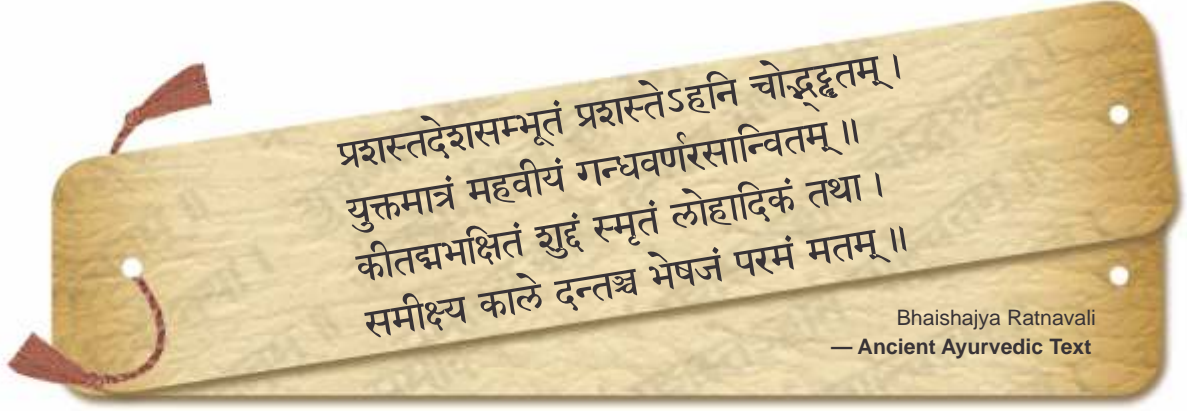


KSM-66[®] ashwagandha



KSM-66[®] 
a s h w a g a n d h a



Bhaishajya Ratnavali
— Ancient Ayurvedic Text

Having taken care of the place of collection of the herb at proper time, having right smell, colour and chemical composition, not infested by microorganisms, properly purified, potentiated and administered at proper dose and time, that medicine alone is considered as the 'Best Medicine'.

WHAT MAKES KSM-66 THE WORLD'S BEST ASHWAGANDHA?

- KSM-66 is the highest concentration full-spectrum extract on the market today, retaining all the natural constituents of the herb in the original balance.
- KSM-66 is the ashwagandha extract with the most extensive set of research studies and clinical trials.
- KSM-66 has the highest percentage of withanolides of all root-only extracts available today. It has more than 5% concentration of withanolides as measured by HPLC.
- The production of KSM-66 has tight vertical integration for high quality and price advantage. KSM-66's maker is the only ashwagandha manufacturer in the world with its own farms, production facilities, testing laboratories, research center and distribution.
- KSM-66 is the only major ashwagandha extract in the world that is 100% Organic certified.
- KSM-66 has a neutral taste and is not bitter like other ashwagandha extracts, making it an excellent choice for use in foods and beverages.
- KSM-66 has negligible levels of Withaferin A, a widely recognized cytotoxic withanolide.
- KSM-66 is produced using a first-of-its-kind, unique extraction process, based on "Green Chemistry" principles, without using alcohol or any synthetic solvents.
- KSM-66 is manufactured at an ISO 9001:2008- and GMP-certified state-of-the-art cleanroom facility, conforming to WHO-cGMP and US-FDA standards.
- KSM-66 is GRAS Affirmed, Kosher, Halal, Non-GMO, Vegetarian and Gluten free; Safe and Shelf-stable.

Award Winning: For several of the factors listed above, KSM-66 was chosen as the recipient of "Best Botanical Ingredient" award for 2013 at Natural Products Expo West and "Innovative Ingredient of the Year" award for 2012 at Panacea.

KSM-66 Ashwagandha has been clinically proven to:

- Reduce stress and anxiety
- Enhance memory and cognition
- Increase endurance and strength
- Improve sexual function and testosterone levels in men

KSM-66 Ashwagandha promotes balance in the body for men, women and children.

SOME EVALUATION FACTORS TO LOOK AT WHEN CHOOSING ASHWAGANDHA EXTRACT

- Make sure that your ashwagandha extract is drawn from roots alone and that leaf components are not added.

There are some ashwagandha makers who make the extract using the plant's leaves instead of just the root. However, KSM-66 uses ONLY the roots with no adulteration by leaves. This is because, for maximum clinical effectiveness, the ashwagandha extract is conceptualized primarily as a root extract, not only in ayurveda textbooks, but also in the standard references like the Indian, the British and the U.S. Pharmacopeias (their specifications are based entirely on the root, the leaf appears nowhere). There are dozens of studies documented in PubMed and conducted by universities and research hospitals, virtually all of which use root-only extracts and no leaves. While there are numerous human clinical studies using the root extract, pretty much the only clinical evidence for a root+leaf extract is from research sponsored by such extracts' manufacturers themselves. Moreover, the extracts containing leaves have so little safety and efficacy data supporting them that most European countries' regulatory authorities explicitly disapprove extracts with leaves and allow solely root-only extracts. Therefore, KSM-66's approach of using only roots is on vastly better scientific and historical foundation than the approach of these other ashwagandha extract makers who use leaves.

- Make sure that the clinical studies are published in high quality, high credibility outlets like PubMed-indexed journals.

PubMed is an index, maintained by the U. S. Government's National Library of Medicine, of articles published in what academics consider to be high-quality biomedical journals. Journals not indexed in PubMed are considered to be of a distinctly lower tier than Pubmed-indexed journals. Ixoreal is the industry leader in clinical trials investigating the effectiveness of ashwagandha, and KSM-66 is the ashwagandha extract with the most extensive set of research studies. KSM-66's research publications are in PubMed-indexed journals. Most other ashwagandha makers' clinical trials are not published in PubMed journals. Also noteworthy is that KSM-66's clinical trials are conducted by well-established physicians and scientists with strong publication records.

- **If your end-product is for wide appeal, make sure that the clinical trials on your ashwagandha extract use normal, healthy populations.**

Some ashwagandha makers' clinical studies try to show the effectiveness of their ashwagandha by demonstrating improvement in clinically compromised populations or otherwise less than fully healthy populations. However, if your finished product is targeted toward normal healthy populations, this is very problematic because clinically compromised populations are systematically different from normal healthy populations and, therefore, demonstrations of improvement in clinically compromised populations may not hold true for normal healthy populations. Broadly speaking, because of the physiological law of diminishing marginal improvements, it is easier for a drug or ingredient to achieve improvements in clinically compromised populations than in normal healthy applications: for example, it is relatively easy for an obese person of weight 300 pounds to lose 5 pounds than it is for a healthy person of weight 165 lbs to lose 5 pounds. The makers of KSM-66 have taken great pains to ensure that KSM-66's clinical studies are all on normal healthy populations having no pre-existing clinically adverse conditions. Recruiting people from normal healthy populations is frequently difficult because they are less interested in participating in clinical studies. However, for the makers of KSM-66, it is critically important that the clinical trials be on normal healthy people because most of KSM-66 customers target their end-products at normal healthy people who want to develop some extra function or strength. Therefore, it is important to have efficacy data available for those kinds of normal healthy people.

- **Make sure that you assess the concentration of Withaferin A.**

Not all withanolides are beneficial. Withaferin A is one withanolide which is cytotoxic, as has been established in multiple scientific studies. So, it is undesirable to have Withaferin A in an ashwagandha extract when the intended use is for classical applications like building anti-stress ability, energy, cognition and immunity. Some ashwagandha extracts have high levels of Withaferin A because the manufacturers use ashwagandha leaves. Using leaves spikes up the overall withanolide content, but it also brings in the undesirable withanolide 'Withaferin A'. KSM-66 consists of negligible levels of Withaferin A, making it very safe for human consumption.

- **Make sure your ashwagandha extract is a full-spectrum extract.**

Botanicals are complex substances with many constituents in them. With many botanicals, modern research has proven clinically beneficial effects but oftentimes has not been able to definitively identify which specific constituents in the botanicals cause the effects. Many herbalists and scientists believe that, with Ashwagandha and several other herbs, it is not just one or two constituents that cause the clinical effects, but rather it is the combination and synergy of several constituents that gives the clinical effects. For this reason, it is important to use a "full spectrum" extract. A "full-spectrum" extract is an extract which maintains the balance of the various constituents as in the original herb, without over-representing any one constituent like, say, the withanolides. KSM-66 is a full spectrum extract different from other hydro-alcoholic extracts because its innovative extraction process does not upset the delicate balance of various constituents found in crude ashwagandha root; rather, it retains and potentiates the synergism in the whole root.

- **Make sure that withanolide content is high and that the content assessment is by HPLC only.**

The vast majority of manufacturers across the world estimate withanolide content by gravimetric analysis, which does not provide accurate results. Unfortunately, gravimetric analysis often overestimates withanolide content by a factor of 2.5 to 3! This is because gravimetry does not adequately discriminate between withanolides and some other constituents, thereby bundling withanolides with other compounds and over-assessing the extent of withanolides. Furthermore, gravimetric analysis is idiosyncratic and shows too much inter-batch and intra-batch variation. In contrast, the HPLC method of withanolide assessment operates near the molecular level and is much more discriminating and accurate. KSM-66 withanolide content is measured by HPLC and is found to be of >5% concentration. As an aside, when measured by gravimetry, the concentration is found to be in the 8% to 15% range.

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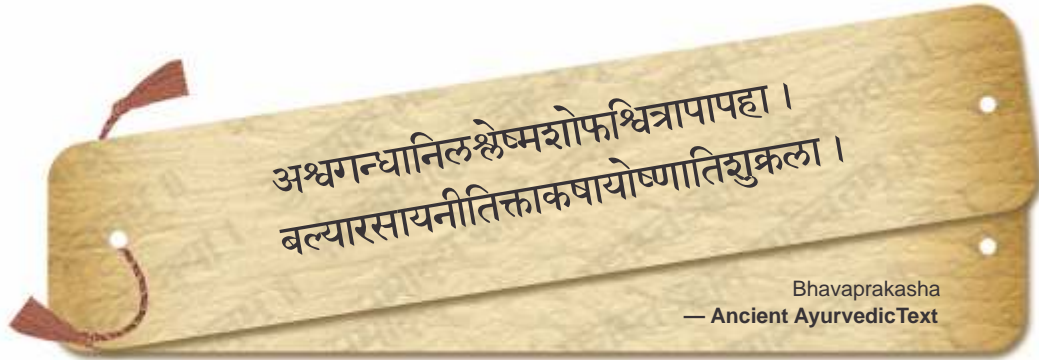
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Ashwagandha roots

Ashwagandha (*Withania somnifera* (Dunal)) Plant



Ashwagandha is katu, tikta, kashaya rasa, ushna veerya and it is madhura vipaka. Important therapeutic effects are balya, dhatu vruddi and kantiprada. Ashwagandha is beneficial in geriatric disorders. It provides sharira pushti and exerts anabolic effect. In two different nighantus, It is mentioned as madhagandhika at one place and madhugandhika at another place; madhagandhika connotes possible aromatherapy property and madhugandhika connotes underlying sweet principles, perhaps on account of glycoside activity. It pacifies vata and kapha. It is a potent emmenagogue. It rejuvenates and promotes strength.

Ashwagandha promotes strength, bestows youthful vigour and gives mental power. Besides bringing robustness, it also gives longevity.



ASHWAGANDHA: THE FLAGSHIP HERB OF AYURVEDA

Ashwagandha (*Withania somnifera* Dunal) is the most popular Indian Medicinal plant and has been in use in Ayurveda, the 5,000 year old Indian system of medicine, as a rejuvenative and life sustainer for many centuries. It is only now that ashwagandha is experiencing major growth worldwide because of a burst of recent studies in pharmacology and medicine.

Ashwagandha embodies the very essence of the preventative and curative approach to health in Ayurveda. Ashwagandha operates at the level of the overall body system by maintaining balance in the substances and processes running in the human body. For instance, if some hormones are lower than they should be, ashwagandha increases them. On the other hand, if some hormones are higher than they should be, ashwagandha decreases them. In this sense, ashwagandha maintains balance in the body; in scientific terms, ashwagandha serves the very critical function of maintaining "homeostasis" in the human body. A central idea in Ayurveda is that disease, aging and stress cause the body to fall out of balance. And the reverse is also true, that if the body is out of balance it tends to be more susceptible to disease, aging and stress. Therefore by creating homeostasis when the body falls out of balance, and by maintaining homeostasis once the body is in balance, ashwagandha performs an important function in supporting good health. Specifically, ashwagandha maintains balance in the body's neurological, immune, reproductive, endocrinal and energy production systems. A side comment to be made is that dysfunction in the hypothalamic-pituitary-adrenal axis (HPA-axis) is frequently interpreted as the body losing its state of homeostasis. For this reason, ashwagandha is frequently used to ameliorate HPA -axis dysfunction.

Ashwagandha is a small, woody shrub in the Solanaceae family that grows to about two feet in height. It can be found growing extensively in India as well as in a few parts of the Mediterranean and Africa. As a result of this wide ranging habitat, there are considerable morphological and chemo-typical variations in local species. However, the root phytoactives of both the wild and the cultivated species appear to be the same. The roots are the main portion of the plant that are used therapeutically.

ORIGINS AND HISTORY

Ashwagandha is also often referred to as 'Indian ginseng' because it is used in Ayurveda the same way as Panax ginseng is in Traditional Chinese Medicine. However, for reasons that we will give in a moment, the more accurate nomenclature may be to describe Ginseng as "Chinese Ashwagandha"! We know from historical records that ashwagandha was popular in the Buddhist monasteries of India for centuries. As Buddhism spread to China and the Far East from India, Buddhist scholars from Indian monasteries very likely carried this herb further east into China.



Due to variations in geoclimatic conditions in China, an alternative may have been found in 'Ginseng'. Therefore, the more historically accurate nomenclature may be to refer to 'Ginseng' as 'Chinese Ashwagandha' rather than refer to 'Ashwagandha' as 'Indian Ginseng'. Modern research has shown that ashwagandha is in many ways more therapeutically effective than ginseng and is less stimulating.

Apart from its long history of over 4,000 years of use in India, we find that this herb was favored outside the Indian subcontinent too. According to Robin Lane Fox, a reputed English scholar, during the period of Alexander the Great, wine prepared from ashwagandha was widely used by his army to build energy and rid themselves of various ailments. According to Anne Van Arsdall, there is a legend that Apollo, the Greek God of Medicine and Healing, found ashwagandha and gave it to the healer Aesculapius. That is why ashwagandha was called 'apollinaris' and also 'glofwyrt' in *'The Old English Herbarium'*. Aesculapius was a Greek and later Roman, God of Medicine.

ACTIVE CONSTITUENTS

Ashwagandha is referred to as the "Prince of Herbs" in Ayurveda because it has an impressively broad range of therapeutic effects. Such a broad range of effects arises perhaps because ashwagandha is one of the more complex herbs with many phytochemical constituents in it. While in the natural products marketplace, much of the discussion on ashwagandha is centered around the withanolides constituents or alkaloid constituents, Ayurvedic experts and doctors emphasize that there is much more to ashwagandha than just the withanolides. The synergistic effect from this diverse set of active constituents is believed to be responsible for the multiple therapeutic properties of ashwagandha. Some of these constituents found are: alkaloids (including withanine, somniferine, isopelletierine, anafierine, tropine, pseudotropine, anahygrine, beta-sisterol, cuscohygrine, scopoletin, somniferinine, tropanol, withananine), flavonoids, saponins, sitoindosides, iron, choline, acylsteryl glucosides, coumarins (scopoletin and aesculetin), triterpene (beta-amyrin), phytosterols (stigmasterol and beta-sitosterol), minerals, essential oils (ipuranol, withaniol), somnine, pseudowithanine, 3-a-gloyloxytropane, cuscohygrine, isopelletierine, anahydrine.

Withanolides are an important (though by no means the sole critical) set of the major bioactive constituents of the ashwagandha root. At present, more than 35 withanolides from this plant have been isolated and are being studied. Withanolides serve as important hormone precursors that can be converted into human physiological hormones as needed. Ashwagandha is thought to be an amphoteric, meaning that it can help regulate important physiological processes. The theory is that when there is an excess of a certain hormone, the plant based hormone precursor occupies cell membrane receptor sites so that the actual hormone cannot attach and exert its effect. If the hormone level is low, the plant-based hormone exerts a small supporting effect, allowing actual hormones to take over.

It is ashwagandha's unique combination of phytonutrients in their natural proportion and their synergistic effects that ultimately confers the many beneficial health effects associated with ashwagandha.



ASHWAGANDHA AS AN ADAPTOGEN

Adaptogens are medicinal plants that are said to enhance the "state of nonspecific resistance" of an organism to stress, which means that they help bring into balance, and create homeostasis, in our entire being, rather than exert influence on only certain biologic processes. These adaptogen plants are understood as having the ability to augment resistance to physical, biological, chemical, and psychologic stresses and to increase concentration, performance, and endurance. So, conceptually one must see these plants within a qualitative paradigm, rather than the quantitative paradigm of Western medicine, in which medicines are used to increase or decrease certain physiological measures, such as blood pressure, serum cholesterol or blood sugar. The mechanism by which adaptogens exert these effects is associated with the hypothalamic-pituitary-adrenal (HPA) axis, which is a major part of the neuro-endocrine system that controls reactions to stress and regulates many body processes. The mode of an adaptogen is also via the body's stress-system (neuro-endocrine-immune complex) and can be directed at various targets of the system involved in regulation (activation and inhibition) of stimulus response coupling.

Ashwagandha has been the focus of extensive scientific research the world over for a variety of health promoting effects with no associated toxicity. It is an adaptogen par excellence. Centuries of Ayurvedic medical experience and extensive recent scientific research using ashwagandha have revealed it to have pharmacological value as an antioxidant, anti-inflammatory, immunomodulatory, neuroprotective, diuretic, aphrodisiac and tonic.

Ashwagandha helps people adapt to a wide variety of stressors and health conditions. Thus, ashwagandha root has been used to increase vitality and longevity and relieve fatigue, anxiety, nervous exhaustion, and sleeplessness. Ashwagandha has hematopoietic and rejuvenating properties.

Most adaptogens are stimulants in disguise. In contrast, ashwagandha can give energy in the morning to run a marathon and yet taken before bed, put you to a calming sleep like that of a baby. Interestingly, ashwagandha neither stimulates nor sedates. Rather, it offers a deep rejuvenation to the whole body and mind in a manner unmatched by any other herb.

Ashwagandha stands out because of its uniqueness in that it is pretty much the only herb which offers the twin functions of stress-reduction and cognition-expansion. Other herbs reducing stress tend to sedate (which is counter to increased cognition) and other herbs increasing cognition tend to over-excite and stimulate (which is counter to reducing stress).



PHARMACOLOGY

Ashwagandha promotes “homeostasis” in the human body, as described earlier in this brochure. This means that ashwagandha amplifies the body’s ability to self-regulate key systems, specifically, the neurological, immune, reproductive, endocrinal and energy production systems. For a herb to operate at this systemic level, it needs a complex blend of phytochemicals with a wide range of actions on the human body. Ashwagandha is one of the very few herbs in the world with a complex blend of this type. For this reason, it is called the “prince of herbs” in the traditional Indian medicine system of “Ayurveda”. Because ashwagandha operates at the systemic level, it has 20+ distinct applications described in Ayurveda textbooks. However, Ixoreal being a very science and evidence based company, we limit our stated applications to only those that we can substantiate with rigorously-conducted biological studies using our KSM-66 extract. The following listing gives our stated applications of KSM-66 and respective mechanisms of action.

ASHWAGANDHA FOR ANXIETY AND STRESS-RELIEF

In stress, a series of biological changes occurs in a body. There is activation of the sympathetic nervous system, which in turn activates the adrenal medulla, which secretes adrenaline and noradrenaline, leading to increased physiological arousal. There is also activation of the HPA (hypothalamic-pituitary-adrenal) axis. Activation of the hypothalamus leads to the release of hormones that travel through the bloodstream to the pituitary gland, which in turn secretes other hormones and activates the adrenal gland, which releases the stress hormone, cortisol.

As an adaptogen, ashwagandha demonstrates a non-specific enhancement of the body's activity to resist a stressor. It exerts a normalizing influence on the body, neither over-stimulating nor inhibiting normal body function. Ashwagandha's potent antioxidant action is also thought to contribute to these adaptogenic effects.

Extracts of ashwagandha produce GABA-like activity, which may account for the herb's anti-anxiety effects. GABA (Gamma Amino-butyric acid) is an inhibitory neurotransmitter in the brain. Its function is to decrease neuronal activity and inhibit nerve cells from over-firing. This action produces a calming effect. Excessive neuronal activity can lead to restlessness and sleeplessness, but GABA inhibits the number of nerve cells that fire in the brain, and helps to induce sleep, uplift mood, and reduce anxiety. There is emerging evidence suggesting a 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 increases of plasma corticosterone, blood urea nitrogen, and blood lactic acid. Overall, ashwagandha helps the body in coping with stress by restoring hypothalamic and peripheral receptor sensitivity to the effects of cortisol and other adrenal hormones.



ASHWAGANDHA FOR MEMORY AND COGNITION

Ashwagandha has a memory-and cognition-enhancement effect. It is found that ashwagandha can significantly improve memory deficits and prevent loss of axons, dendrites and synapses. It appears to be mediated by a cholinergic effect. Increased cortical muscarinic acetylcholine receptor capacity has been observed in animals and humans with extracts of ashwagandha. Several withanolides exert calcium antagonistic ability, together with anticholinesterase activity, by inhibiting butyrylcholinesterase and acetylcholinesterase enzymes. The presence of choline in the herb may also contribute to the production of acetylcholine and further increase cholinergic effects. Additionally, ashwagandha has been reported to have potent antioxidant, anti-peroxidative and free radical quenching properties which are considered to contribute to its neuroprotective effects. The induced increase in cortical muscarinic acetylcholinereceptor capacity might partly explain the cognition- enhancing and memory-improving effects of ashwagandha extracts in animals and in humans.

Ashwagandha significantly restores glutathione and acetylcholinesterase levels in the striatum, cortex and hippocampus regions of the brain. A clinical trial investigated the potential anti-dementia effects of ashwagandha and its effects on neuronal networks in the damaged brain. Withanoside significantly induced axonal and dendritic regeneration and synaptic reconstruction. Hence it can ameliorate neuronal dysfunction and help healthy brain function. Ashwagandha significantly reverses some parameters, including lipid peroxidation, glutathione, activities of glutathione -S-transferase, glutathione reductase, glutathione peroxidase, superoxide dismutase, dopaminergic binding and tyrosine hydroxylase.

ASHWAGANDHA FOR ANTI-AGING

The correlation between ashwagandha consumption and lifespan longevity has been long noted in the ayurvedic literature. This is an area where the exact mechanism of action is not widely understood. From a modern scientific perspective, the only studies directly connecting ashwagandha consumption and lifespan longevity are the animal studies using models where the metabolic processes closely resemble those in human beings. At a high-level, it is well known across cultures that humans who live to very old age tend to experience low stress either due to environmental factors or due to internal resilience. The adaptogenic action of ashwagandha promotes resilience to stress. Ashwagandha in this way at least indirectly promotes longer life. Premature aging associated with chronic nervous tension may be related to increased oxidative stress, which is greatly ameliorated by the potent antioxidant properties of ashwagandha extract.



ASHWAGANDHA FOR ENERGY AND STRENGTH

At a macro level, ashwagandha promotes homeostasis, makes the body as a whole more energy-efficient and improves processes associated with energy management and production. At a micro-level, it results in increase in levels of ATP, which is associated with energy processes at a cellular level. The Adenosine Triphosphatase (ATPase) enzyme is responsible for the breakdown or destruction of ATP, which can have a direct negative effect on energy stores and energy levels in the body. Ashwagandha reduces the activity of the ATPase enzyme in liver mitochondria. This is also supported in the longer-term by ashwagandha's cardiopulmonary-protective action, anti-inflammatory action and antioxidant action.

Several studies have shown that ashwagandha enhances energy levels. Ashwagandha increases the level of succinate dehydrogenase (SDH). SDH in turns provides increased cellular energy. The ashwagandha root helps to support the nervous system and adrenals, helping to maintain energy levels during times of stress and prevent the body from "burning-out". It has rejuvenative properties that produce energy, increase stamina and endurance. It is an "energy-balancing" herb that improves the body's ability to metabolize sugars as well as cortisol.

Ashwagandha is known to also help in muscle development and muscle recovery. It is believed that ashwagandha helps the body improve its own natural production of steroids that in turn enhances the 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 helping recover faster between sessions of exercise and physical activity.

ASHWAGANDHA FOR SEXUAL FUNCTION

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 improves male fertility. Ashwagandha results in significant decrease in cortisol levels, increase in testosterone, regulation of other reproductive hormones and improvement in overall semen quality.

Apart from via stress-reduction, there are other ways in which ashwagandha is thought to promote fertility and sexual function.

- Ashwagandha may have a direct spermatogenic influence on the seminiferous tubules by exerting a testosterone like effect.
- Ashwagandha may engender nitric oxide stimulation in the male genitals.
- In females, ashwagandha is thought to improve libido by increasing LH and reducing FSH and prolactin levels.
- Ashwagandha can reduce oxidative stress and regulate reproductive hormones, thereby having a significantly beneficial effect on overall fertility.
- Ashwagandha can elicit significant changes in gonadotrophin levels coupled with a significant increase in ovarian weight and profound folliculogenesis.



ASHWAGANDHA FOR IMMUNITY

It is well known that chronic stress suppresses immune function and disturbs homeostasis. Ashwagandha is known for its ability to restore health and immune function after periods of stress. Therefore, at a systemic level, ashwagandha's adaptogenic effect also enhances immune response.

Apart from this systemic view, there is a lot of evidence that supports ashwagandha's role in boosting the immune system. Studies have shown immunomodulating effects of withania, such as an increase in white blood cell, platelet and neutrophil counts, increases in Interferon-gamma (IFN γ) and interleukin-2 (IL-2) and a reduction in tumour necrosis factor. Ashwagandha reduces hypersensitivity reactions. Researchers have reported significant increases in hemolytic antibody responses toward human erythrocytes which indicate immuno-stimulatory activity. It has been found that administration of ashwagandha causes significant recovery of stress induced depletion of T-cell population, causing an increase in cytokines associated with Th-1 helper cells and a decrease in the concentration of cortisone. Ashwagandha has also been shown to help in a reversal of stress induced increase of ALT, AST and hepatic lipid peroxidation as well as an improvement in the stress induced decrease of hepatic glutathione and glycogen levels, thus demonstrating significant antistress and immunomodulating activity. Ashwagandha was found to suppress and down-regulate IgE antibody production and be effective against tested allergens. Research has revealed immune modulating effects by up-regulation of Th-1 immune response measured by significant increases in CD4 and CD8 levels with ashwagandha root supplementation. Ashwagandha also can activate certain cells in the immune system, priming them to become more effective at fighting off disease by recognizing and neutralizing pathogens. Recent research suggests a possible mechanism behind the increased cytotoxic effect of macrophages exposed to ashwagandha extracts. Nitric oxide has been determined to have a significant effect on macrophage cytotoxicity against microorganisms and tumor cells.





KSM-66 ashwagandha extract



KSM-66 ASHWAGANDHA

KSM-66 is Ixoreal's ashwagandha extract, created via a process that took 14 years of R&D to develop and refine. KSM-66 is the best ashwagandha extract on the world market today in the sense that it is the highest concentration full-spectrum extract available today. A "full-spectrum" extract is an extract which maintains the balance of the various constituents as in the original herb, without over-representing any one constituent. The ashwagandha herb's efficacy is believed to be derived from a complex blend of active constituents, mainly alkaloids like withanine, somniferine, tropine, and steroidal lactones called withanolides. All these constituents need to be present in their natural proportions, which is why it is important for an extract to be full-spectrum. However, producing a high concentration full-spectrum extract is technologically very challenging. Only Ixoreal has managed to create a process that surmounts these challenges, and that too only after many years of R&D. The Ixoreal science team sought to introduce to the world the true quintessence of ashwagandha with all its benefits. Convinced that the essence of the ashwagandha root could be extracted without losing its potency, the science team dedicated itself to learning the nuances of plant chemistry and did what no one was able to achieve until then. With `Green Chemistry` processing, they were able to holistically extract all the root essence while preserving its natural healing potency. This proved to be immensely successful.

KSM-66 has been clinically proven to be effective. It leads the industry in clinical trials and basic research related to ashwagandha. Ixoreal has conducted numerous clinical studies using KSM-66 ashwagandha extract in collaboration with major academic and research institutes. All of Ixoreal partnered clinical studies follow gold standards of substantiation: randomized, double-blind, placebo-controlled designs.

KSM-66 ashwagandha is standardized to the highest percentage of withanolides in the world, >5% by HPLC, derived only from the roots of the plant. Standardization implies that an extract provides consistent dosage delivery and guaranteed potency. Standardization ensures that manufacturers and formulation developers can use a certain amount of extract and be assured of a commensurate amount of active constituents without much random variation from batch to batch. In addition to the desired quantum of withanolides, the nutrient rich KSM-66 also contains short and long chain amino acids, fructo-oligosaccharides, Vitamin A, calcium and Iron.

There are several other important ways in which KSM-66 is superior to other extracts for use in nutrition supplement and foods: KSM-66 ashwagandha has superior sensory characteristics and is not bitter. Unlike KSM-66, most other ashwagandha products use hydroalcoholic extraction. An effect of hydroalcoholic extraction is that the end-product is very bitter. In contrast, KSM-66 extract has a pleasant aroma and is neutral in taste, making an excellent choice for use in food and beverages.



COMPARISON OF KSM-66 WITH OTHER EXTRACTS

KSM-66 ashwagandha scores over other ashwagandha extracts on the market in the following aspects.

	KSM-66	Most other ashwagandha extracts
Active Constituent	Holistic extract, yet exhibits highest withanolide content in the world derived from roots alone (>5%by HPLC). Hence high therapeutic activity.	May be adulterated with leaf constituents. High values advertised may be from the gravimetry method of analysis.
Taste	Neutral.	Extremely bitter.
Full Spectrum Nature and Nutrients	Unique extraction process resulting in a full Spectrum extract, retaining the natural constituents of the herb intact. Hence rich in nutrients like fructooligosaccharides, vitamin A, amino acids, calcium and iron.	Nutrients often get lost during the extraction. Not a full spectrum extract.
Withaferin A	Negligible quantity of cytotoxic Withaferin A.	May contain substantial amount. Present in large quantity in leaf extracts.
Process	Extraction without using any alcohol or chemical solvents, based on the principles of "Green Chemistry".	Process of extraction sometimes requires the use of harsh chemicals and solvents, traces of which are difficult to remove completely from the final product.
Clinical Evidence	Has the most extensive set of clinical studies for various therapeutic benefits.	Lack clinical evidence for efficacy and safety.
Organic Status	Because of vertical integration from own farms to distribution, certified 100% Organic by USDA.	Do not have Organic certification; usage of alcohol too being a major barrier to get certified.



ANALYTICAL SPECIFICATIONS OF KSM-66 ASHWAGANDHA

No	Tests	Limits	Protocol
1	Description	Light yellowish brown, hygroscopic powder	
2	Physico-chemical analysis Loss on drying (%w/w) Ash content (%w/w) Acid insoluble ash (%w/w) pH of 5%w/v solution	<5.0 <15.0% <5.0 4.0-6.5	As per USP 24<561> Vegetable Drugs pg.1885 As per USP<791> pg.1977
3	Density Bulk density(g/cc) Tapped bulk density	0.2-0.6 0.2-0.8	As per USP 24<616> 1913-1914 Method-I
4	Heavy metal analysis Lead Cadmium Arsenic Mercury	<10ppm <1ppm <2ppm <0.1ppm	AOAC-Chap 49/HPLC AOAC/AAS AOAC/AAS AOAC/AAS
5	Microbiological analysis as per FIP guidelines Total viable aerobic count Total enterobacteriaceae Total fungal count	<10 ⁴ cfu g ⁻¹ <10 ² org g ⁻¹ <10 ² fs g ⁻¹	
6	Test for specific Pathogens as per FIP guidelines <i>E-coli</i> (1g) <i>Salmonella sp.</i> (10g) <i>S.aureus</i> (1g)	Absent Absent Absent	As per WHO/pharma/92.559/Rev.1 pg 49-52
7	Mycotoxin analysis Aflatoxins (B1,B2,G1,G2)	<5ppb	AOAC Chap 49/HPLC
8	Pesticide residue analysis as per USP and BP limits Organochlorine pesticides Organophosphorous pesticides Organosulphur pesticides	Comply with USP	As per AOAC/USP 24 IS : 13832-1993
9	Phyto-chemical analysis Total withanolides(%w/w) (Withaferin A)	>5% < 0.1 %	By HPLC

The production process of KSM-66 ashwagandha is completely free of alcohol and synthetic chemicals.



SCIENTIFIC STUDIES ON KSM-66

Ixoreal, the maker of KSM-66 ashwagandha is the industry leader in clinical trials and basic research investigating the effectiveness of ashwagandha. It collaborates with major academic and research institutes. KSM-66 has considerably more supporting clinical trials than any other ashwagandha available on the world market today. All of KSM-66's clinical studies follow the gold standard of substantiation: randomized, double-blind, placebo-controlled designs.

KSM-66 ashwagandha has been clinically proven to:

- Reduce stress and anxiety
- Enhance memory and cognition
- Increase endurance and strength
- Improve sexual function and testosterone levels in men

KSM-66 Ashwagandha promotes balance in the body for men, women and children.

Here is a summary description of each of the studies on KSM-66.

1. KSM-66 For Anxiety And Stress-relief:

Study Type	: Randomized Double Blind Placebo Controlled Study
Subjects	: 64 healthy adults
Dosage	: 300 mg twice a day
Duration of study	: 8 weeks

2. KSM-66 For Cardio-respiratory Endurance:

Study Type	: Randomized Double Blind Placebo Controlled Study
Subjects	: 50 sports athletes
Dosage	: 300 mg twice a day
Duration of study	: 12 weeks

3. KSM-66 For Male Fertility And Testosterone:

Study Type	: Randomized Double Blind Placebo Controlled study
Subjects	: 50 adults male volunteers (age group between 22-40 years)
Dosage	: 225 mg thrice a day
Duration of Study	: 12 weeks



4. KSM-66 For Muscle Strength, Size, Recovery and Testosterone:

Study Type : Randomized Double Blind Placebo Controlled study
Subjects : 50 healthy strength athletes
Dosage : 300 mg twice a day
Duration of Study : 8 weeks

5. KSM-66 For Stress Resistance and Weight Management:

Study Type : Randomized Double Blind Placebo Controlled study
Subjects : 50 healthy adults
Dosage : 300 mg twice a day
Duration of Study : 8 weeks

6. KSM-66 For Memory and Cognition:

Study Type : Randomized Double Blind Placebo Controlled study
Subjects : 50 healthy adults (age >35 years)
Dosage : 300 mg twice a day
Duration of Study : 8 weeks

7. KSM-66 For Female Sexual Function:

Study Type : Randomized Double Blind Placebo Controlled study
Subjects : 50 healthy women
Dosage : 300 mg twice a day
Duration of Study : 8 weeks

8. KSM-66 For Muscle Strength:

Study Type : Randomized Double Blind Placebo Controlled study
Subjects : 55 strength athletes
Dosage : 300 mg twice a day
Duration of Study : 8 weeks



9. KSM-66 For Immunity:

Animals : 72 Swiss Albino Mice
Duration of Study : 28 days
No. of groups : Six groups

10. KSM-66 For Lifespan Extension:

Animals : Caenorhabditis elegans worms
Duration of Study : 2 months
No. of groups : Two groups

11. Toxicity Studies On KSM-66:

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

Sub-acute or 28 days repeated oral toxicity study- KSM-66 ashwagandha did not cause mortality, symptoms and any other adverse effects in the treated rats at any dose level. The results revealed that KSM-66 has not produced any toxicity in the treated animals and 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 time intervals after treatment when compared to control. There was no evidence of genotoxicity by KSM-66 at any dose level in acute and 28 days repeated oral dose toxicity studies.

Please contact us for more information on ongoing studies, published papers and technical reports.



AWARDS WON BY KSM-66

KSM-66 has won some major industry awards because of its unique extraction process and extensive clinical trials.

"Best Botanical Ingredient 2013" at Engredea / Natural Products Expo West, Anaheim, U.S.A



"Innovative Ingredient of the Year 2012" at Panacea, Mumbai, India



"Finalist-Best Botanical" for Functional Ingredient's Editors Choice Award 2012 at Engredea / Natural Products Expo West, Anaheim, U.S.A



One botanical – Innumerable applications



KSM-66 ashwagandha APPLICATIONS IN DIETARY SUPPLEMENTS

KSM-66 ashwagandha is a multifunctional phyto-pharmaceutical and nutraceutical, which can be utilized as either a standalone ingredient or as a potential complementary ingredient in various herbal, phyto-pharmaceutical and dietary formulations.

KSM-66 ashwagandha processing technology retains and enhances the biological activity of ashwagandha herb. Phyto-active-nutrient dense KSM-66 ashwagandha offers wide therapeutic benefits. It can serve as a crucial ingredient in poly-ingredient herbal and dietary formulations. Some of the specific areas of health-related applications of KSM-66 ashwagandha for which interest may prevail:

- anti-aging support
- cognitive support
- cardiac support
- joint support
- sexual health function support
- anti-inflammatory support
- metabolic support
- immune support
- anti-oxidant support
- hematopoietic support
- free-radical scavenging support



The Food and Beverage world can use ashwagandha in numerous beneficial ways



KSM-66 ashwagandha APPLICATIONS IN FUNCTIONAL FOODS AND BEVERAGES

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

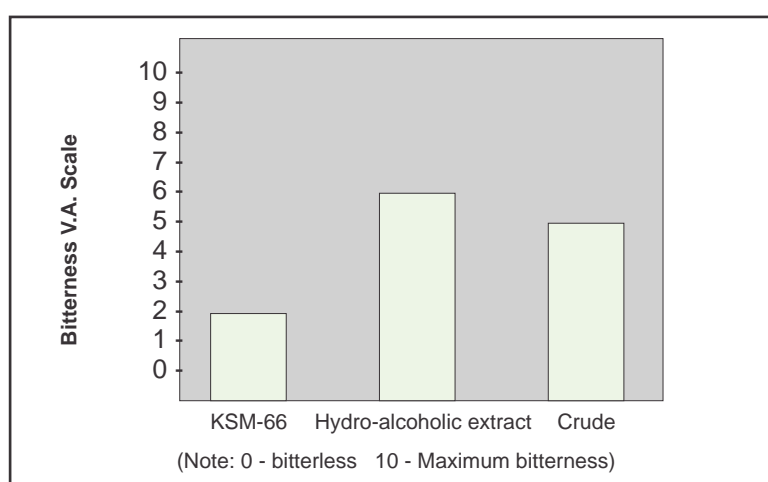
Consumers are looking for ingredients in their food with 'wellness benefits'...and ashwagandha suits this need with its time-tested, proven health benefits.

Nutrient-dense KSM-66 ashwagandha, ideal for food and dietary supplement formulations with its superior sensory characteristics, blends well with:

Functional Foods and Beverages

- * Bakery products / Cookies
- * Dairy Products- Yogurt, Ice creams, Smoothies, Shakes, Flavored milk
- * Cereals / Nutritional bars
- * Chocolates / Confectionery
- * Candies / Toffees
- * Honey / Spreads
- * Tea / Green Tea / Coffee
- * Malted beverages
- * Juices and Fruit blends
- * Wine
- * Soups

During a sensory evaluation, KSM-66 was found to be the least bitter with neutral taste, when compared to hydro-alcoholic extracts and raw powder of ashwagandha (which were extremely bitter to taste). This makes KSM-66 an excellent choice for food and beverage manufacturers.



Comparative analysis of bitterness of KSM-66 ashwagandha, hydro-alcoholic ashwagandha extract and crude ashwagandha powder.



Get - Set - Go for a power ride with KSM-66 ashwagandha



KSM-66 ashwagandha APPLICATIONS IN SPORTS NUTRITION

Other nutritional products in the sports world have focused on synthetic ingredients for the enhancement of sports performance. However, the push for 'natural' within mainstream markets is crossing over to the sports category too. Ashwagandha represents the latest emerging trend as a natural performance enhancer. Recent scientific research suggests that ashwagandha promotes better health, well being and greater levels of physical performance. It enhances the user's ability to cope with stressful situations by promoting faster corticosteroid release and rapid return to normal. It is safe, efficacious and well-tolerated.

Ashwagandha is an excellent non-hormonal anabolic sport supplemental ingredient with ground breaking health benefits:

- Helps improve the rate of recovery following strenuous exercise
- Enhances energy and endurance
- Assists muscle recovery
- May improve mental function, alertness and memory
- May improve oxygen usage
- Enhances the capacity to cope with physical and mental stressors

KSM-66 ashwagandha is of the highest quality and the most effective form of ashwagandha for body builders, for athletes who train and compete at peak levels and for active men and women of all ages in search of health and wellness. The Sports Authority of India accepts that ashwagandha is a non-dope ingredient and an energy booster par excellence.

- KSM-66 ashwagandha acts through GABA receptors and thus reduces stress. It increases neurological drive.
- High concentrations of withanolides in KSM-66 ashwagandha exert non-hormonal anabolic effects, raise endurance threshold, assist muscle recovery, improve physical fitness and reduce both mental and physical fatigue.
- KSM-66 contains branched chain amino acids such as leucine, associated with building and maintaining lean muscle mass.
- KSM-66 enhances the immune system via the increase in glutathione due to the inbuilt amino acid profile.
- Natural fructoligosachharides in KSM-66 ashwagandha promote healthy digestion, prevent infection and are crucial for overall health, colon health, bone health and mineral metabolism.

KSM-66 ashwagandha technology allows easy integration of ashwagandha into a wide range of sports foods and supplements: **Vitamin and mineral supplements, Nutrition bars, Meal replacements, Whey protein mixes and Hybrid sport drinks**



"KSM-66 enhances my ability to focus for long hours during my games. Most importantly, it helps me stay calm and composed when under pressure. My sport requires a sustained level of concentration. Thanks to KSM-66, I'm playing harder and performing better."

ADITYA MEHTA

ASIA RANKED #1, SNOOKER
GOLD MEDALIST, ASIAN GAMES



"I'm in constant search for the best fuel for my competition and recovery. I've been astounded at the effects that KSM-66 has brought to my program. Clinicals are one thing, but real life race testimony is another. KSM-66 is now a MUST have for me and my athletes."



PAUL ROMERO

ADVENTURE RACER OF THE YEAR
ONE OF THE WORLD'S TOP ADVENTURE ATHLETE

"Since I've been a child, I've learned to rely on natural extracts and have learned the value of extremely good nutrition- I'm relying on KSM-66 during my extremely demanding travel, school and athletic life; it's been a total game changer."



JORDAN ROMERO

WORLD RECORD HOLDER FOR BEING YOUNGEST CLIMBER TO REACH MT. EVEREST AND THE SEVEN SUMMITS OF THE WORLD

"I rely on KSM-66 Ashwagandha these days.... It gives me strength and energy with quick reflexes. It also makes me feel empowered to cope with stressful situations."



SHARATH KAMAL

GOLD MEDALIST, COMMONWEALTH GAMES
WINNING CHAMPION, U.S. OPEN TABLE TENNIS

Although, no one seems to watch how you make the medicine,
the heavens know the sincerity that you put into it.
- Anonymous



QUALITY CONTROL & QUALITY ASSURANCE

An overview of Ixoreal's commitment to Good Agricultural and Collection Practices (GACP), Current Good Manufacturing Practices (GMP) and Current Good Laboratory Practices (cGLP) and Quality Assurance:

GOOD AGRICULTURAL AND COLLECTION PRACTICES (GACP)

The ashwagandha root contains a variety of bio-active constituents. Different geographic locations determine the amounts and ratios of bio-active compounds in the ashwagandha root. Depending on soil conditions, the withanolide content in the ashwagandha root varies. The lower grade and older root stock is virtually useless and therapeutically shows poor response. At Ixoreal, we source high grade ashwagandha from the best geographic locations. It requires well-drained, sand loamy or light red soils with pH of 7.5-8.0. Ashwagandha is a late rainy season crop and requires relatively dry season. Areas receiving 650-750 mm rainfall are best suited for its cultivation. The state of Rajasthan in India is one of the most suited terrains known to grow the best quality ashwagandha and that is where, our certified organic farms are located. We do not use old root stock. This is important. And also, we use only high or A-grade root pieces. These are solid and bright, up to 7 centimeter approximately and with a diameter of 1 to 1.5 centimeters.

CURRENT GOOD MANUFACTURING PRACTICES (cGMP)

Ixoreal stringently follows WHO guidelines on GMP. We invite our valued business partners for a tour of our state-of-the-art manufacturing unit, located at the Government of Andhra Pradesh (India) allocated Pharma zone. Our KSM-66 ashwagandha processing is based on 'Green Chemistry' principles and ensures an effective overall approach to product quality control and risk management. We have set internationally approved standards and practices for product testing, manufacturing, storage, handling and distribution. Ixoreal firmly believes in offering a safe and effective product and therefore does not compromise on systems and documentation.

All bulk and raw products are stored in quarantine before being subjected to KSM-66 ashwagandha processing. To ensure KSM-66 ashwagandha's consistency and high quality and to prevent raw material and pre-finished material from being adulterated, contaminated or spoiled, Ixoreal, has established quality controls at every stage. KSM-66 ashwagandha processing is done in exclusively designed clean room systems. Our internal manufacturing controls provide documented proof that correct procedures are consistently followed at each step of processing and every time a batch extraction is made.



Extensive controls cover the sanitation and hygiene of our facilities, personnel, utensils and machinery are strictly ensured. Controls are also in place for handling materials throughout each step of the production process, such as work sheets, assuring consistency from batch-to-batch, easy monitoring and averting any chances of contamination and adulteration.

CURRENT GOOD LABORATORY PRACTICES (cGLP)

KSM-66 ashwagandha is subjected to various internationally prescribed quality standards in its state-of-the-art laboratory. All raw and finished material is inspected by the in-house quality control unit. Freshness labeling guidelines are followed. Trained and qualified personnel handle all the material, from raw stock to finished product.

Based on client requirements, Ixoreal also offers to get its product tested in independent testing laboratories anywhere in the world. We welcome third party verification of our analytical reports. In short, Ixoreal Quality Control & Quality Assurance stages include:

- Quality on the farm
- Quality on receiving the raw material
- In-house laboratory testing and segregation of raw material
- Organoleptic testing
- Bioactives testing
- Moisture content analysis
- Microscopy and petri-grid analysis
- Microbiological testing
- Ash testing
- pH testing
- Aflatoxin testing
- Heavy metal analysis
- Pesticide analysis

Every sample and every dispatched batch is accompanied by certificate of analysis (COA).

GOOD PACKAGING PRACTICES (GPP)

Strict protocols are followed at every stage, right from storing of raw herb to dispatch of finished product. Precise labeling and hygienic handling are ensured. KSM-66 ashwagandha packaging is done as per the Standard Exports Packaging policy.



COMPANY PROFILE

Ixoreal Biomed is a new division of the Baldwa Group, an industrial house that has been in business for the last 100 years. The group has \$320 million in annual revenues through 4000 employees in 85 cities across the world. It is diversified in chemicals, logistics, power, textiles, paper and agriculture. Ixoreal is headquartered in Hyderabad in the state of Andhra Pradesh, a city that is rapidly becoming a life sciences hub with the largest concentration of scientific institutes and scientists in India

There are two distinctive characteristics about Ixoreal Biomed. First: it truly believes in achieving scientific excellence. It invests heavily in basic research and development. One outcome of this is that it has managed to create a truly unique process for creating high-concentration extracts from the ashwagandha plant's root. Second: Ixoreal is unusually committed to superior product quality and customer satisfaction. For this reason, it never outsources any key function. It owns and manages the entire value chain in producing its extracts: the farms, the testing laboratories, the production facilities and the distribution. Because of these two distinctive characteristics, Ixoreal's extracts are unmatched for their quality worldwide.

KSM-66 ashwagandha is manufactured at the state of the art manufacturing unit of Ixoreal, located at a very picturesque location in the pharmaceutical zone of the government of Andhra Pradesh (India). Lush green plantations along with a small botanical garden adorn the facility and serve as a constant reminder for the Ixoreal family of their obligation towards safeguarding Mother Nature. The facility uses special energy saving light bulbs that last around ten times longer than ordinary light bulbs. This apart, motion sensors at the premises add to the energy conservation. A solar water heating system saves hundreds of litres of fuel, reducing CO₂ emissions by tons. Also, the entire facility is a "zero discharge plant".

Ixoreal's research and development activity focuses on three major areas: standardization, therapeutic efficacy and new drug delivery systems.

Ixoreal constantly strives to use the latest technology to redefine ancient concepts. It accords the utmost importance to human health and employs conventional as well as advanced techniques to guarantee high-quality end products. In its continuous commitment to protect 'Life Forms', Ixoreal avoids the use of petro-based chemicals in its products. Thus, Ixoreal's products and processes are eco-friendly and are based on the principles of 'Green Chemistry'.





Proud
Adopter
of

Ashwagandha
Withania somnifera

ADOPT - AN - HERB
HerbMedPro™ P R O G R A M

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.

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DISCLAIMER

The statements in this brochure have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. The brochure has been prepared with utmost care taking into account our internal records as well as the extensive available national and international literature on the subject of usage. However, the information is given by way of educating health professionals and consumers. Ixoreal Biomed takes no responsibility for any unexpected incidents of side reactions due to other drug and dietary interactions.

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KSM-66 ashwagandha
for a healthy mind and body



