



**KSM-66 Ashwagandha:  
The High-potency, Full Spectrum Ingredient  
for  
Stress Relief, Energy, Cognition and Immunity**

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# OUTLINE OF TODAY'S PRESENTATION

- Company Background
- Basic facts and findings on Ashwagandha
- Overview of KSM-66
- Research studies on KSM-66
- Applications

# THE BALDWA/INLAND GROUP OF COMPANIES

- Annual Revenues \$320 Million
- 4000 employees in 85 cities across Asia
- Major Clients include Unilever, GSK, Voltas, Philips, Sony, Tata, Ranbaxy
- Invests heavily in R&D
- Obsessive about quality and getting the best for this customers
- Very active in philanthropy and social causes
- Latest venture: Ixoreal Biomed



**Chemicals**



**Logistics**



**Power**



**Paper**



**Jewelry**



**Real Estate**



**Tea Estate**



**Food & Beverages**

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# IXOREAL BIOMED: KSM-66 ASHWAGANDHA FROM FARMS TO FINISHED PRODUCTS

- Own 2000 acres of agricultural farms, cultivated organically
- Modern clean-room facilities in a state-of-the-art manufacturing unit
- Natural Products Chemistry Lab
- Instrumentation Lab - Analytical/QC Lab (HPLC, GC, AS)
- Microbiology Lab
- Follows global best practices
  - Good Agricultural and Collection Practices (GACP)
  - Good Manufacturing Practices (GMP)
  - Good Laboratory Practices (GLP)
- Direct Distribution from company

# ASHWAGANDHA



**Scientific Name :** *Withania Somnifera*

**Active Constituents :** Steroidal lactones (withanolides, withaferin A), alkaloids (withanine, somniferine, isopelletierine, anaferine, tropine), bioflavonoids, saponins, sitoindosides, choline, iron, acylsteryl glucosides, coumarins (scopoletin and aesculetin), minerals, essential oils

**Plant part used most commonly:** Roots

## CORE EFFECT OF ASHWAGANDHA

- Ashwagandha is an excellent adaptogen that helps the body maintain and return to “Homeostasis”, a balanced state for the body as a whole, specially the endocrine system, the immune system and the nervous system.
- Disease, Aging, Stress result in and cause a disturbance of homeostasis

## DERIVATIVE EFFECTS OF ASHWAGANDHA :

- Anti Stress
- Energy- and strength-enhancing
- Nootropic, expanding cognition and memory
- Sexual function-enhancing
- Immunomodulatory



## ANTI - STRESS EFFECT OF ASHWAGANDHA

- Acts like a GABAergic drug binding to GABA receptors, producing calming, anti - anxiety, anti - convulsive, highly - stabilizing effects.
- Influences the hypothalamic - pituitary - adrenal (HPA) axis and adrenaline and cortisol levels, which in turn influences stress response. Overexposure to stress hormones increases the risk of:  
Hypertension, Hyperglycemia, Heart Disease,  
Sleep problems, Depression,  
Memory/cognitive impairment,  
Decrease in muscle tissue, Obesity
- Reduces stress - induced increases in dopamine receptors in the corpus striatum, thereby reducing effects of dopamine dysregulation.

# ENERGY AND MUSCLE ENHANCING EFFECT OF ASHWAGANDHA

**Macro - Level:** Promotes homeostasis which in turn makes the body as a whole more energy - efficient. Improves processes associated with energy management and production. Allows the body to self - regulate in response to physical stress.

**Micro - Level:** Results in increases of levels of ATP, which is associated with energy processes at a cellular level.

## **Supported by:**

Cardiopulmonary - protective Action

Anti - inflammatory Action

Antioxidant Action

# NOOTROPIC EFFECT OF ASHWAGANDHA

- Increases cortical muscarinic acetylcholine receptor capacity, mediating memory and cognition improvement
- Contains choline, which may aid the body's production of acetylcholine, which has a critical function in the initial formation of memory
- Has potent free radical quenching properties as a strong antioxidant, anti - peroxidative, leading to neuroprotective action.
- Recommended to correct for neurodegeneration, neuronal atrophy and synaptic loss and to promote dendrite formation
- Attenuates cerebral functional deficits

# SEXUAL FUNCTION ENHANCING EFFECT OF ASHWAGANDHA

- Balances hormone levels
- Diminishes oxidative stress
- Controls stress response and detoxifies
- May increase diameter of seminiferous tubules, number of cell layers
- May significantly improve gonadotrophin levels needed for puberty and fertility in females

# IMMUNOMODULATORY EFFECT OF ASHWAGANDHA

- 100+ articles on Ashwagandha as an adjuvant to cancer treatment
- Ashwagandha offsets the effects of multiple stressors that compromise immune function
- Increases cytokines, T - cell counts, neutrophils, white - blood cells
- Decreases hepatic lipid peroxidation, AST, ALT
- Suppresses and down - regulates IgE antibody production

# WHY IS KSM-66 UNIQUE?

# WHY KSM-66 IS UNIQUE

## 1. FULL SPECTRUM HIGH POTENCY EXTRACT

- Unique processing technology, retaining all the natural constituents of the herb intact
- Highest percentage of withanolides of all root only extracts in the world, standardized to >5% withanolides by HPLC
- Negligible levels of Withaferin A, a widely recognized cytotoxic withanolide

**ATTRACTED  
ATTENTION AND  
APPRECIATION  
OF  
INDIA'S PREMIER  
NATURAL PRODUCT'S  
RESEARCH INSTITUTE**



**INDIAN INSTITUTE OF INTEGRATIVE MEDICINE**  
(Formerly; Regional Research Laboratory)ased  
**Council of Scientific and Industrial Research**  
Canal Road , Jammu-Tawi - 180001 ( India)

**Dated : 10.11.2010**

Sub:- Research discussion with respect to Formulations based on Ashwagandha

Dear Dr. Shridhar,

Best wishes and season's greetings. As our research groups here at IIIM has developed lot of data on *Withania somnifera* with respect to Chemistry ,/preclinical pharmacology/ Biotechnology etc.and able to develop five positive health promoters which are under clinical trails at three different centers in India.

Your company is also engaged for production of KSM66,Which attracted our interest as your KSM66 root extract consistently contained the full range of substances found in the raw root. Withanolide /glycowithanolide content to be consistently around 5% (HPLC). Because of KSM-66's strength and full representation of the raw herb, the herbal medicine literature would suggest that KSM-66 could be very effective in a wide range of clinical applications. We are therefore interested to know more about KSM66 from your research team and invite yourself or senior member of Ixoreal's R&D staff to visit at IIIM Jammu and give brief presentation of your product at the forth coming brainstorming / Research discussion most probably in the third week of December.

Kindly contact us so that we can discuss further details and co-ordinate a visit.

Thanking you,

(K.A.Suri)

Director Grade Scientist  
Chairman Natural Products Chemistry &  
Instrumentation Divisions.



# WHY KSM-66 IS UNIQUE

## 2. PROVEN FOR EFFICACY

- Clinically proven to decrease stress, anxiety and depression and to improve overall quality of life
- Enhanced sexual function health by increasing testosterone, sperm count, motility and libido
- Shown to create high improvement in cardio respiratory endurance in healthy adults
- Shown as an effective immunomodulator in drug induced neutropenia in mice
- Exhibited life-span extension(anti-aging) in C.elegans model
- 2 more human clinical trials in progress for muscle strength in athletes and memory & cognition in children respectively
- All the clinical trials follow the Gold Standard of Substantiation - the Randomized, Double-Blinded, Placebo-controlled

# WHY KSM-66 IS UNIQUE

## 3. VERTICALLY INTEGRATED FOR HIGH QUALITY AND PRICE

- Own farms (organically cultivated)
- State of the art cleanroom production facility (conforming to US-FDA standards)
- Unparalleled research and expertise on ashwagandha
- Testing laboratories (HPLC, GC-MS, AAS)
- Direct distribution, no middle men involved

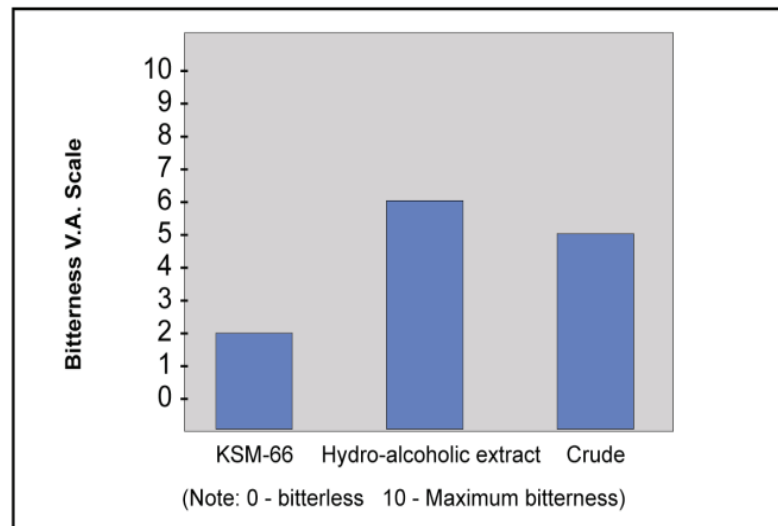


**Ensures Highest Quality + Value Pricing**

# WHY KSM-66 IS UNIQUE

## 4. SUPERIOR SENSORY CHARACTERISTICS

- Not bitter like all the other ashwagandha extracts, making it an excellent choice for food & beverage manufacturers



- Free flowing, less hygroscopic and pleasant aroma
- Special water soluble grade for beverage developers

# WHY KSM-66 IS UNIQUE

## 5. ROOTS ALONE ARE USED

- Ayurveda suggests the usage of roots alone of ashwagandha for strengthening of mind and body
- Leaf extracts suggested for external, topical usage
- Most of the modern studies validate the efficacy of root extracts

# WHY KSM-66 IS UNIQUE

## 6. NOVEL, NATURAL AND SAFE

- GRAS affirmed, qualified by a reputed panel of toxicologists
- Novel extraction process based on the principles of “Green Chemistry”
- No alcohol or any chemical solvents are used
- Non-GMO, Organic, Kosher, Halal, Gluten-free and Vegetarian

# WHY KSM-66 IS UNIQUE

## 7. AWARDS & RECOGNITION

- “Innovative Ingredient of the Year” award at Panacea 2012, South Asia’s largest tradeshow and conference on natural products
- Finalist for the “Best Botanical” award by the editors of New Hope Media’s “Functional Ingredients” magazine at Engredea 2012 in Anaheim

# SOME STUDIES INVESTIGATING THERAPEUTIC EFFICACY OF KSM-66

- Anti - stress study
- Sexual function enhancement study
- Cardio-respiratory endurance study
- Immuno-modulation study
- Lifespan extension study
- Muscle-strength performance
- Cognition and memory study

# 1. ANTI-STRESS STUDY

- **OBJECTIVE:** To evaluate the safety and efficacy of KSM-66 in reducing stress and anxiety and in improving general well being of healthy adults under stress
- **STUDY DESIGN:** Randomized, Double blind, Placebo-controlled
- **SAMPLE SIZE:** 64 healthy adults under stress
- **STUDY DURATION:** 8 Weeks
- **DOSAGE:** 300 mg twice a day
- **EFFICACY ASSESMENT PARAMETERS:**  
GHQ-28, DASS, PSS questionnaires scores  
serum cortisol levels
- Investigators are leading psychiatrists in India



## **General Health Questionnaire - 28 (Goldberg and Hillier, 1979)**

- Scale often used as a measure of psychological well - being
- Derived by factor analysis of the full 60 - item GHQ
- Incorporates four subscales: somatic symptoms, anxiety and insomnia, social dysfunction, and severe depression

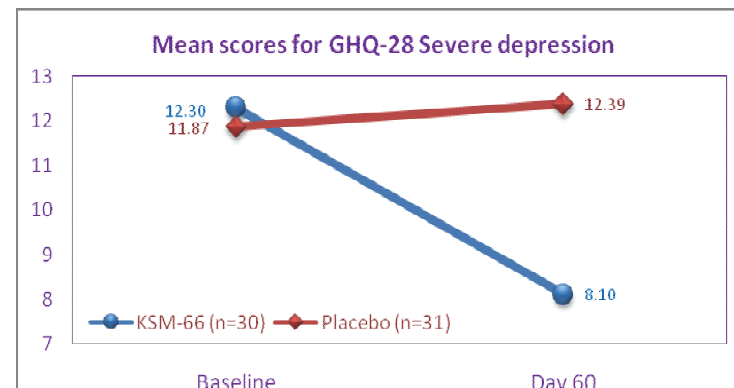
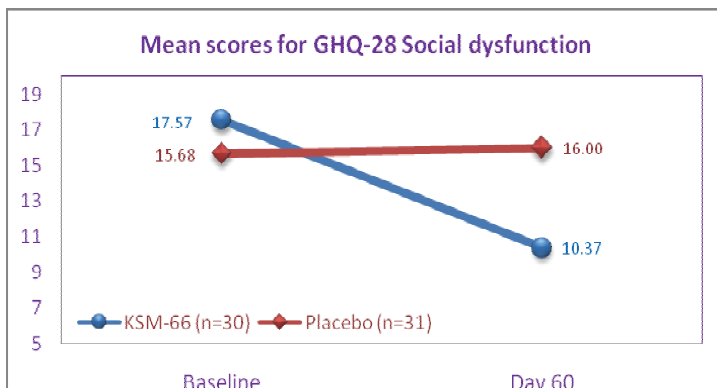
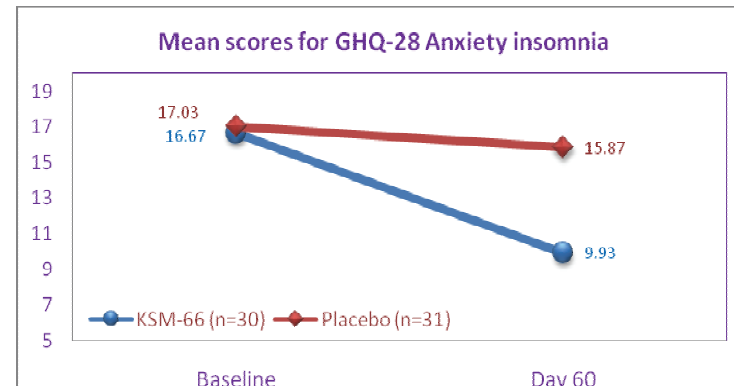
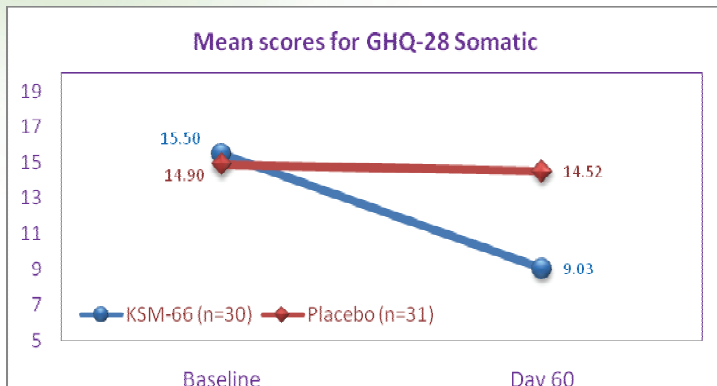
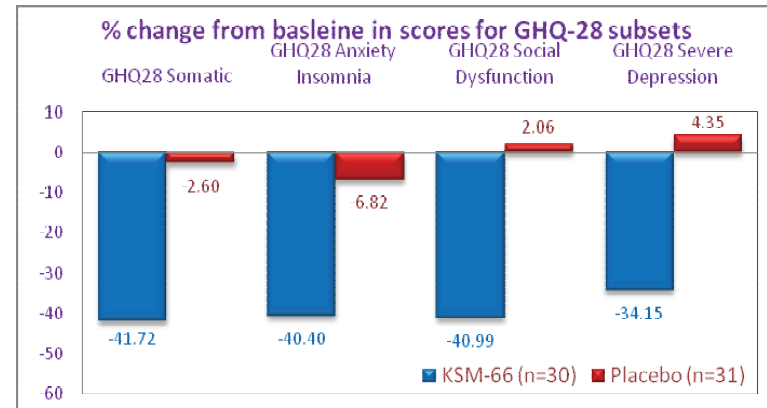
## **Depression Anxiety Stress Scale (Lovibond & Lovibond, 1995)**

- A set of three self - report scales to measure the negative emotional states of depression, anxiety and stress.
- Based on a dimensional conception of psychological disorder: differences between the depression, the anxiety, and the stress experienced by normal subjects and the clinically disturbed may be essentially differences of degree.

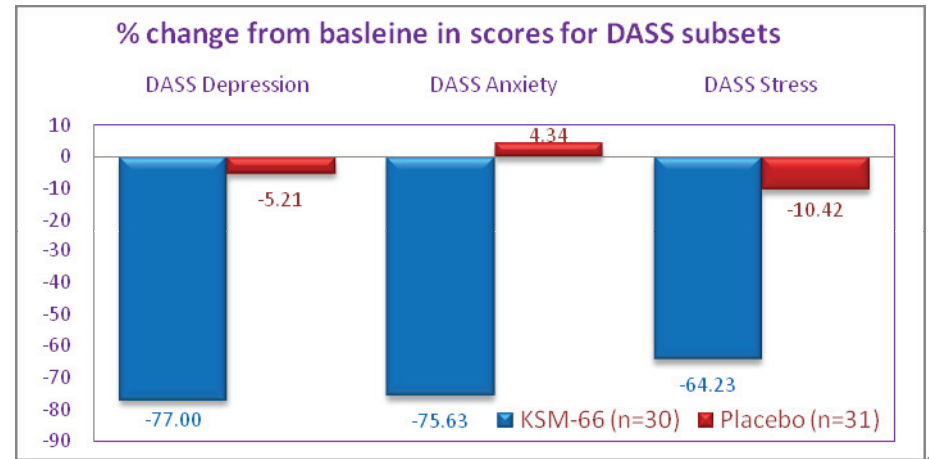
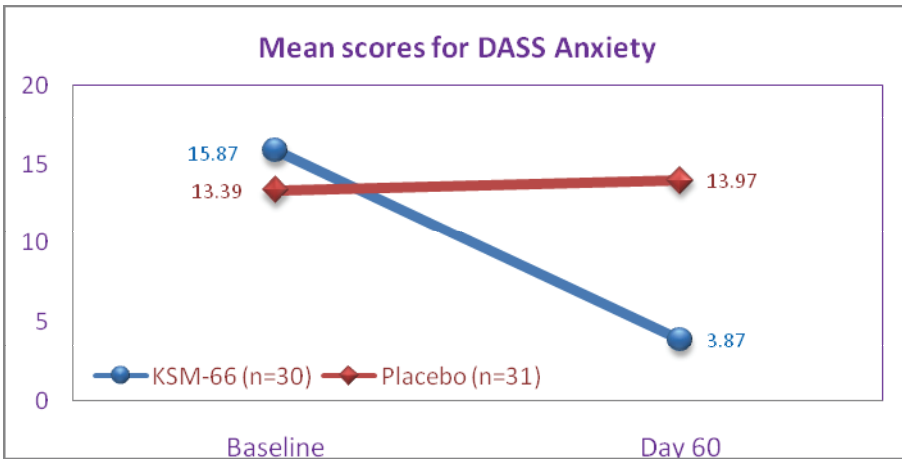
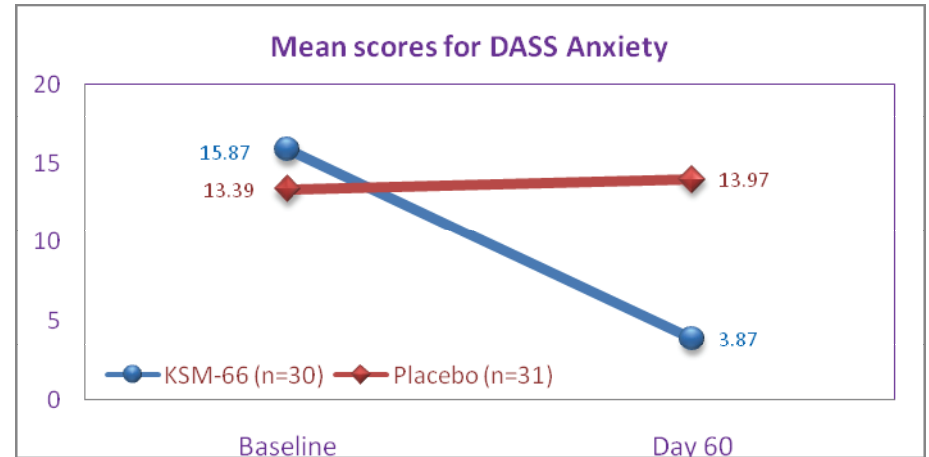
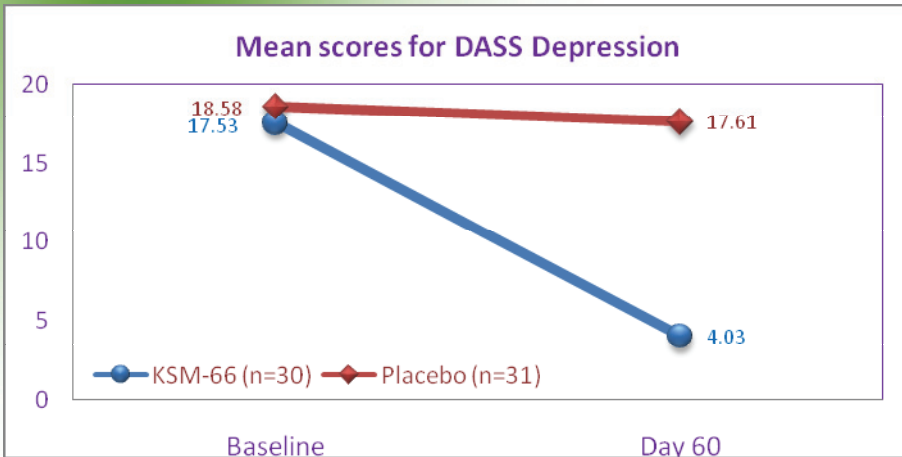
## **Perceived Stress Scale (Cohen and Williamson, 1988)**

- Items designed to assess how unpredictable, uncontrollable, and overloaded respondents find their lives.
- Includes a number of direct queries about current levels of experienced stress.

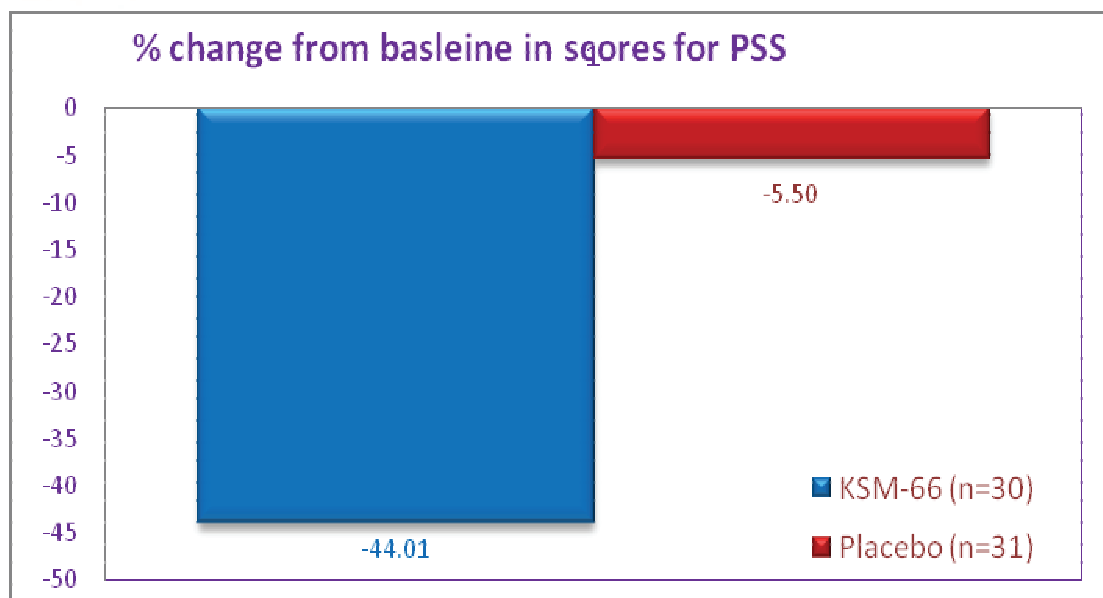
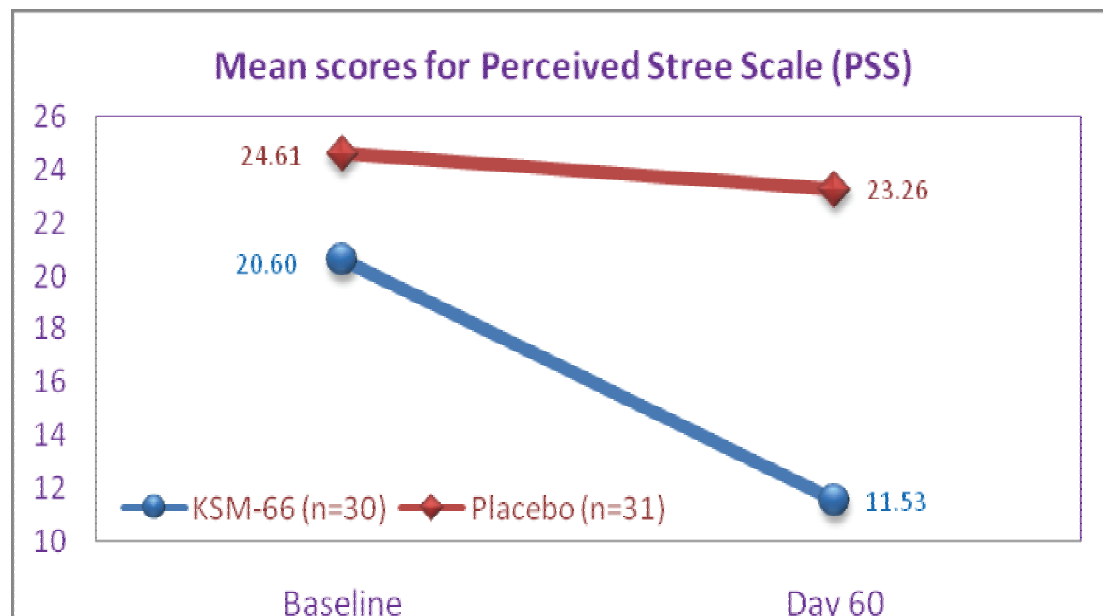
# GHQ SCALE



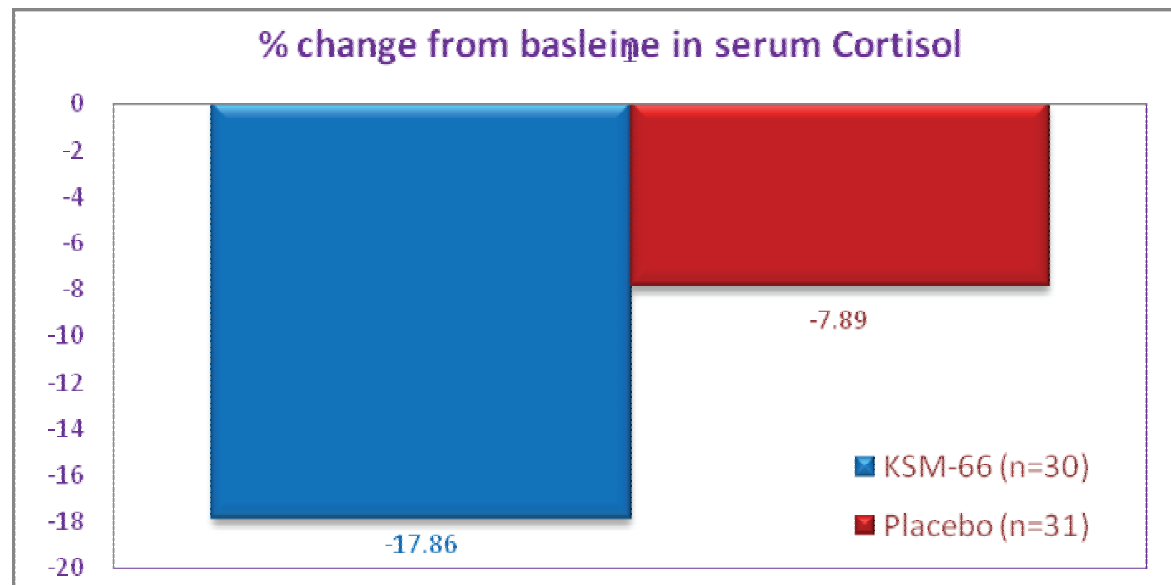
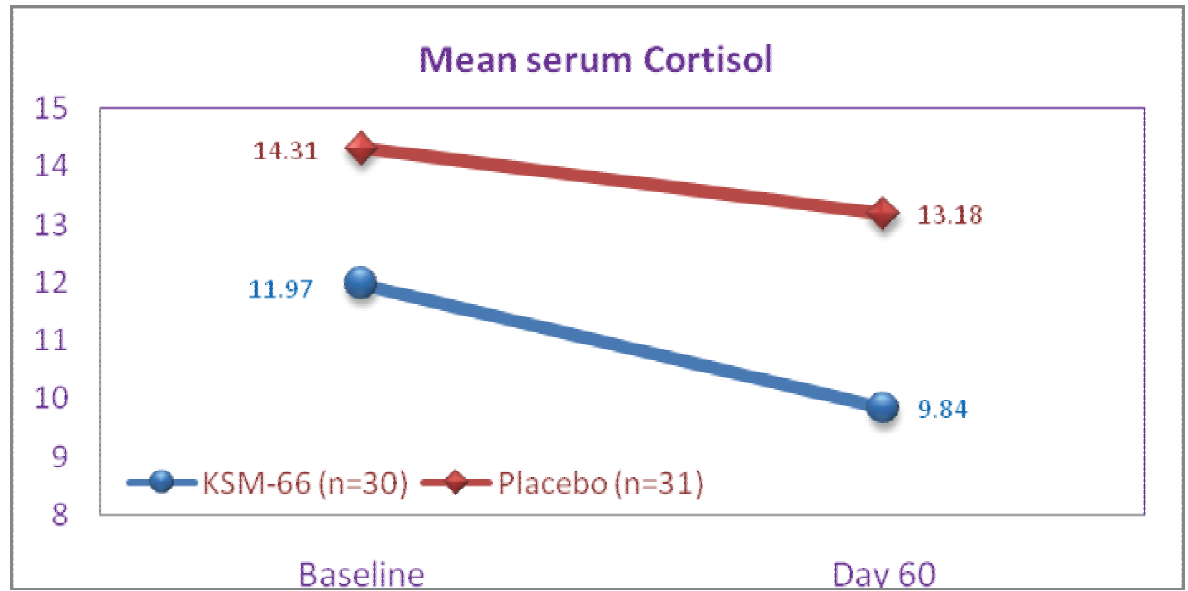
# DASS SCALE



# PSS SCALE



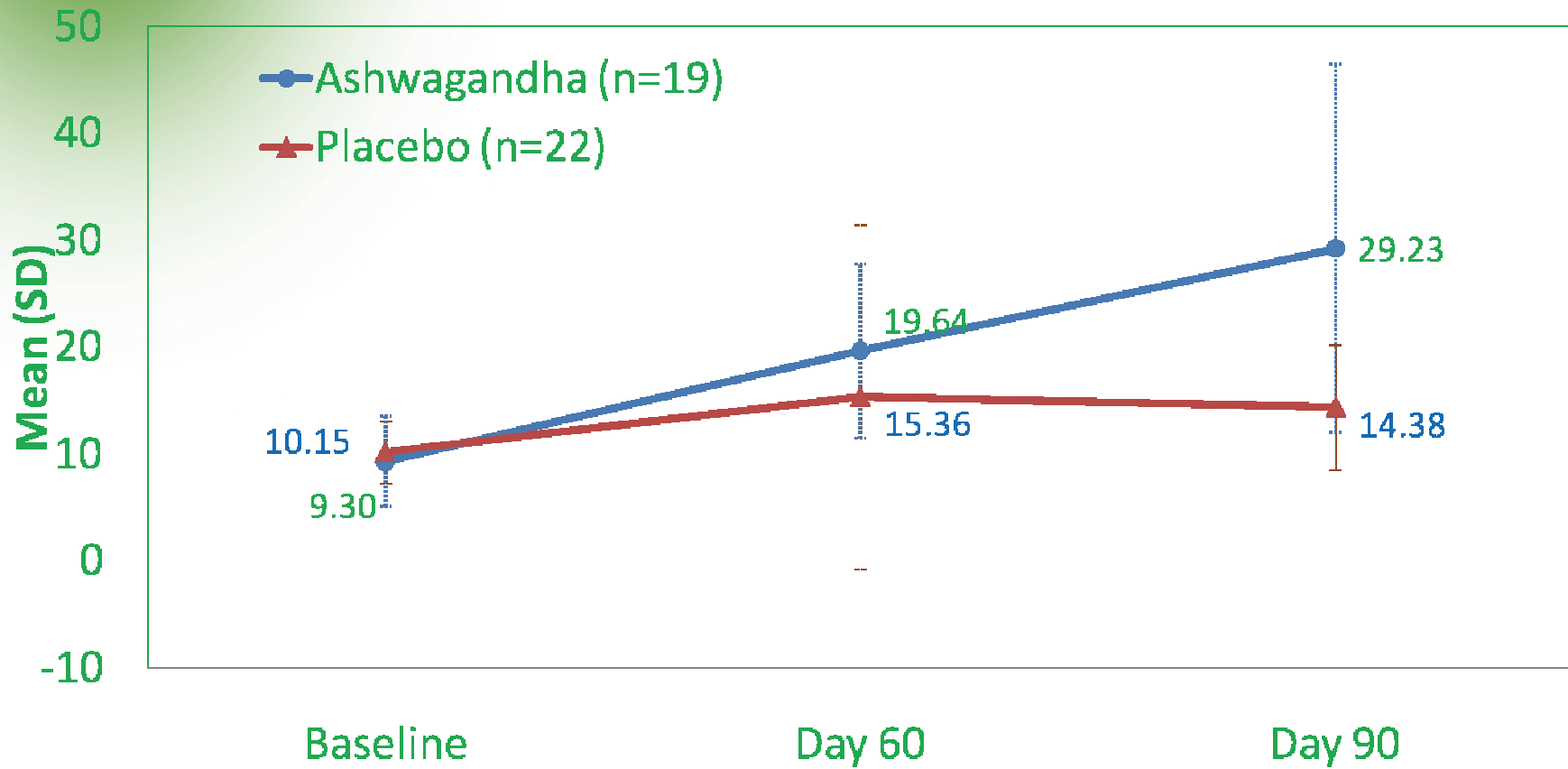
# SERUM CORTISOL LEVELS



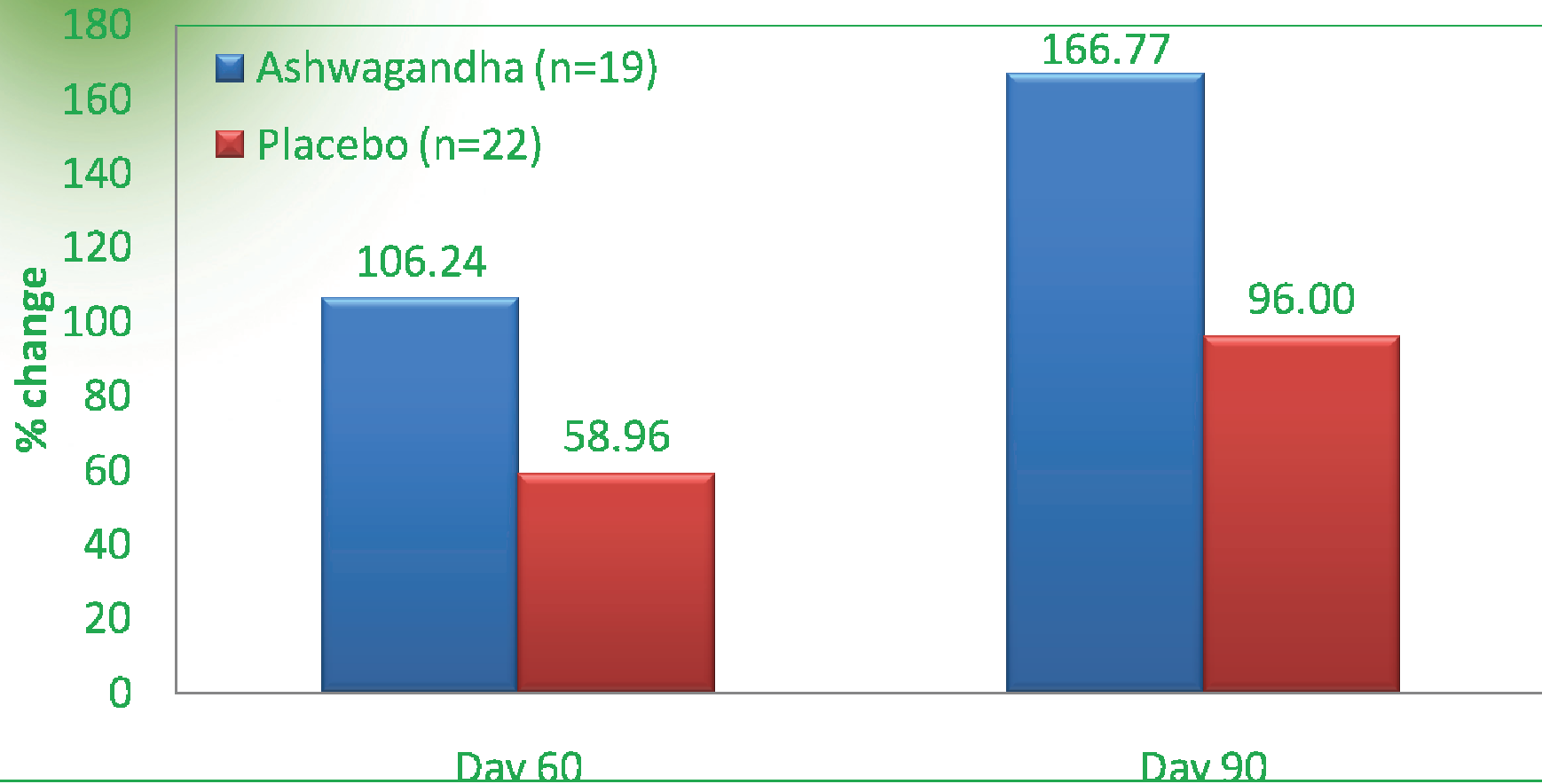
## 2. SEXUAL FUNCTION ENHANCEMENT STUDY

- **OBJECTIVE:** To evaluate the safety, tolerability and efficacy of KSM-66 in oligo-spermia and male sexual dysfunction
- **STUDY DESIGN:** Randomized, Double blind, Placebo-controlled
- **SAMPLE SIZE:** 50 subjects planned; 46 subjects enrolled
- **STUDY DURATION:** 12 Weeks
- **DOSAGE:** 225 mg thrice a day
- **EFFICACY ASSESMENT PARAMETERS:**  
Volume & pH of ejaculate, total sperm count, total & forward motility, morphology, Serum Testosterone, Serum FSH, Serum LH, Serum PRL
- Multiple centre study with 5 leading investigators

## Sperm count (millions/ml)

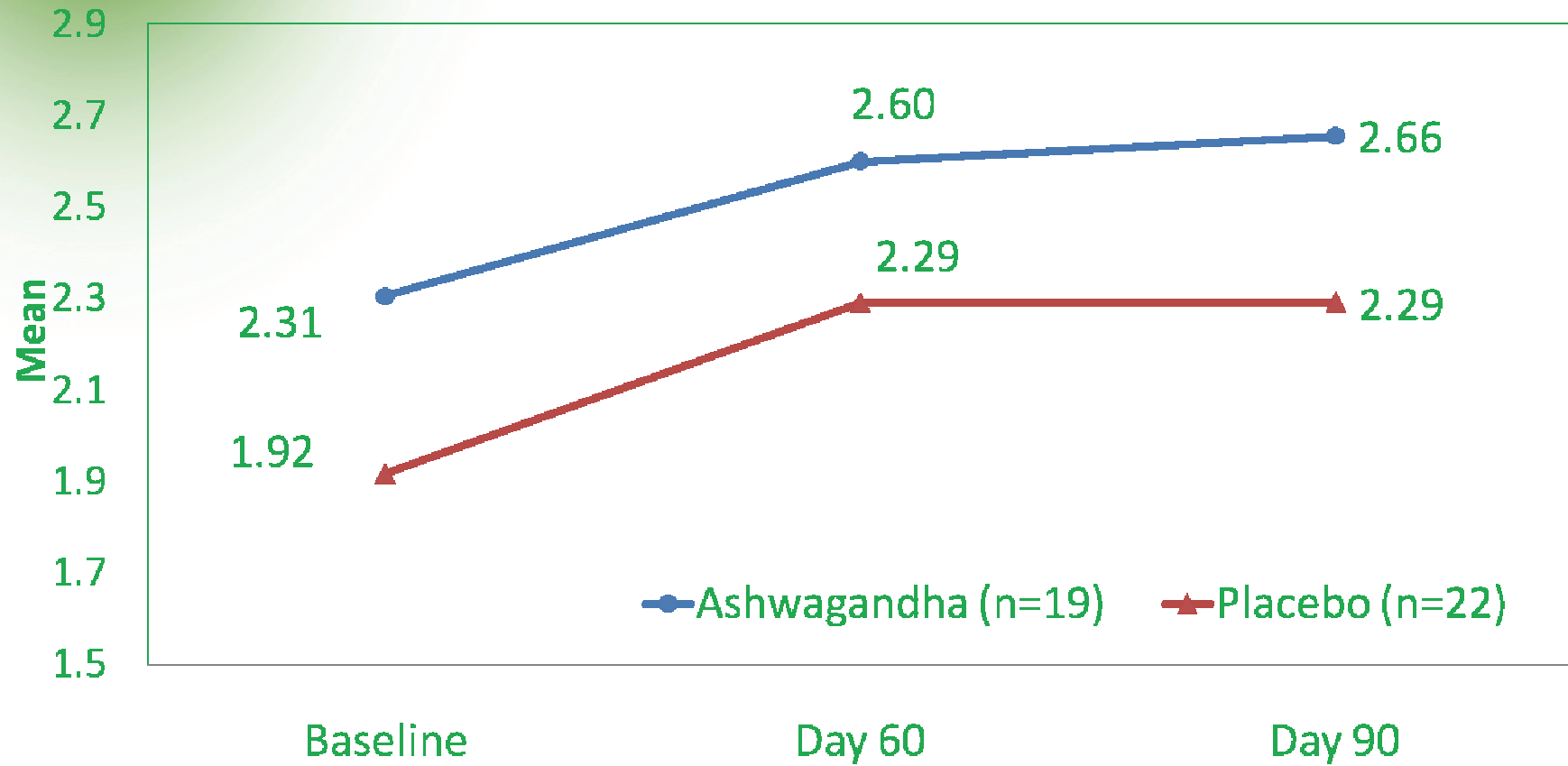


## % change from baseline in Sperm count

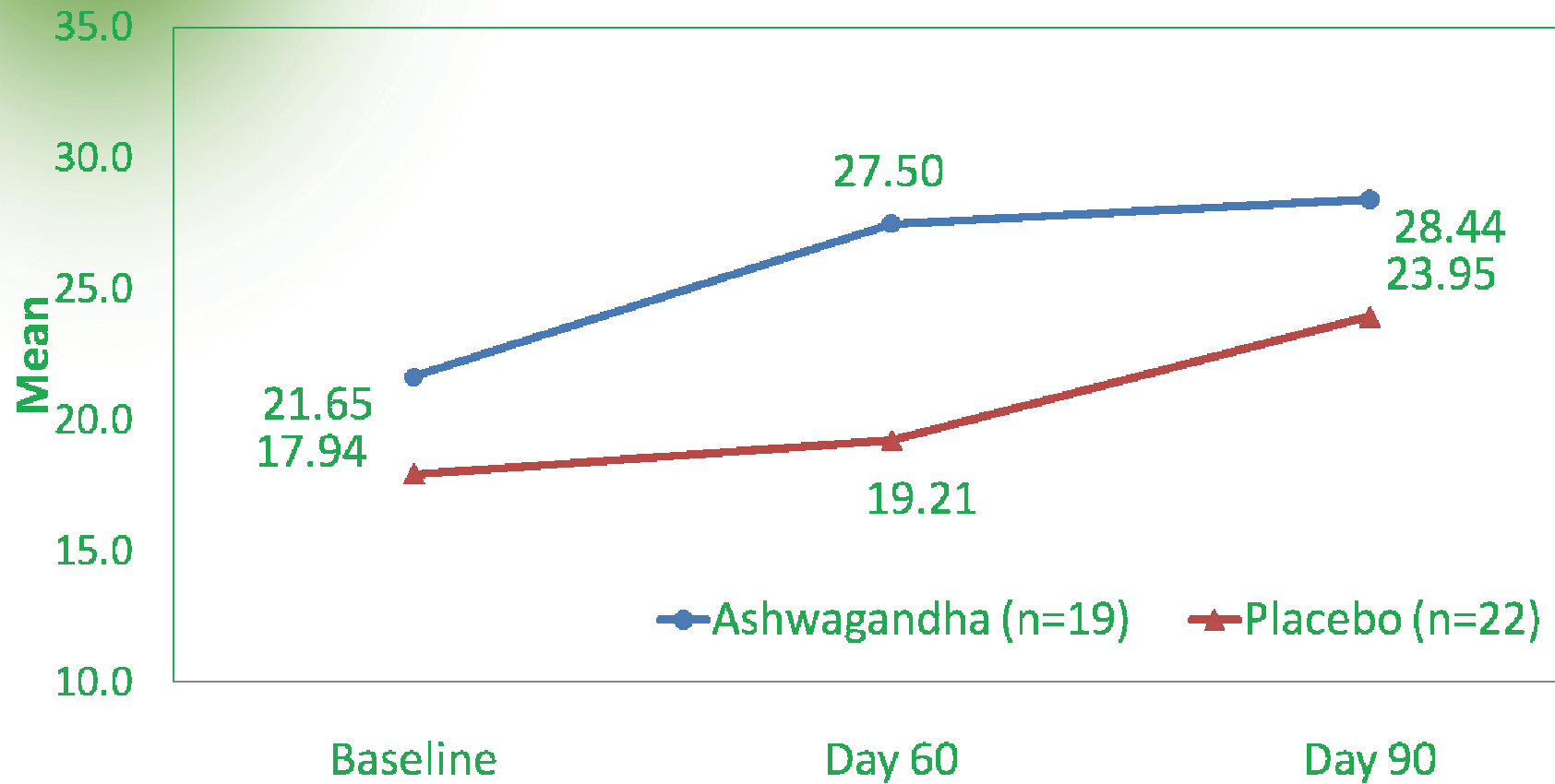




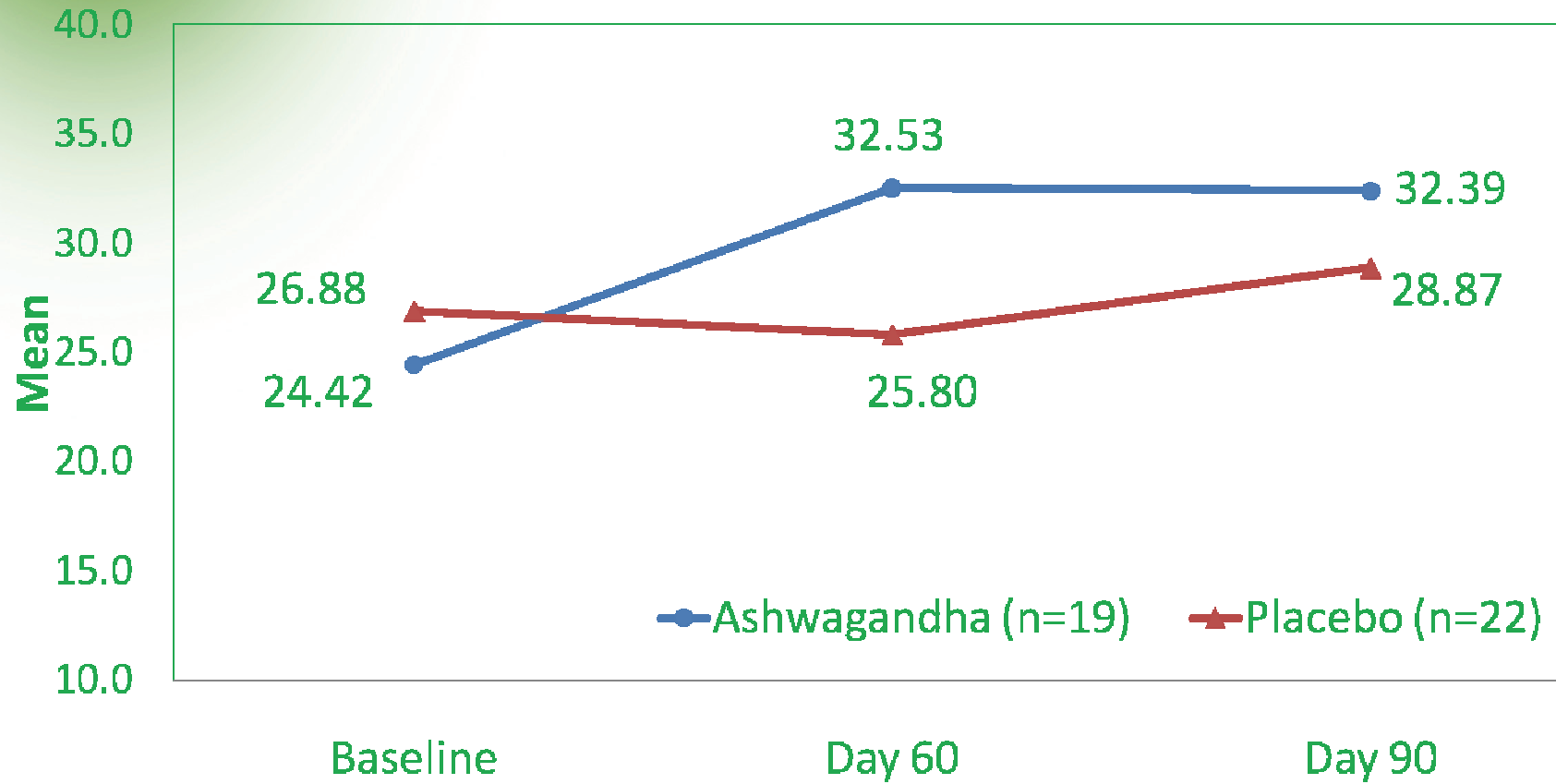
## Semen volume (ml)



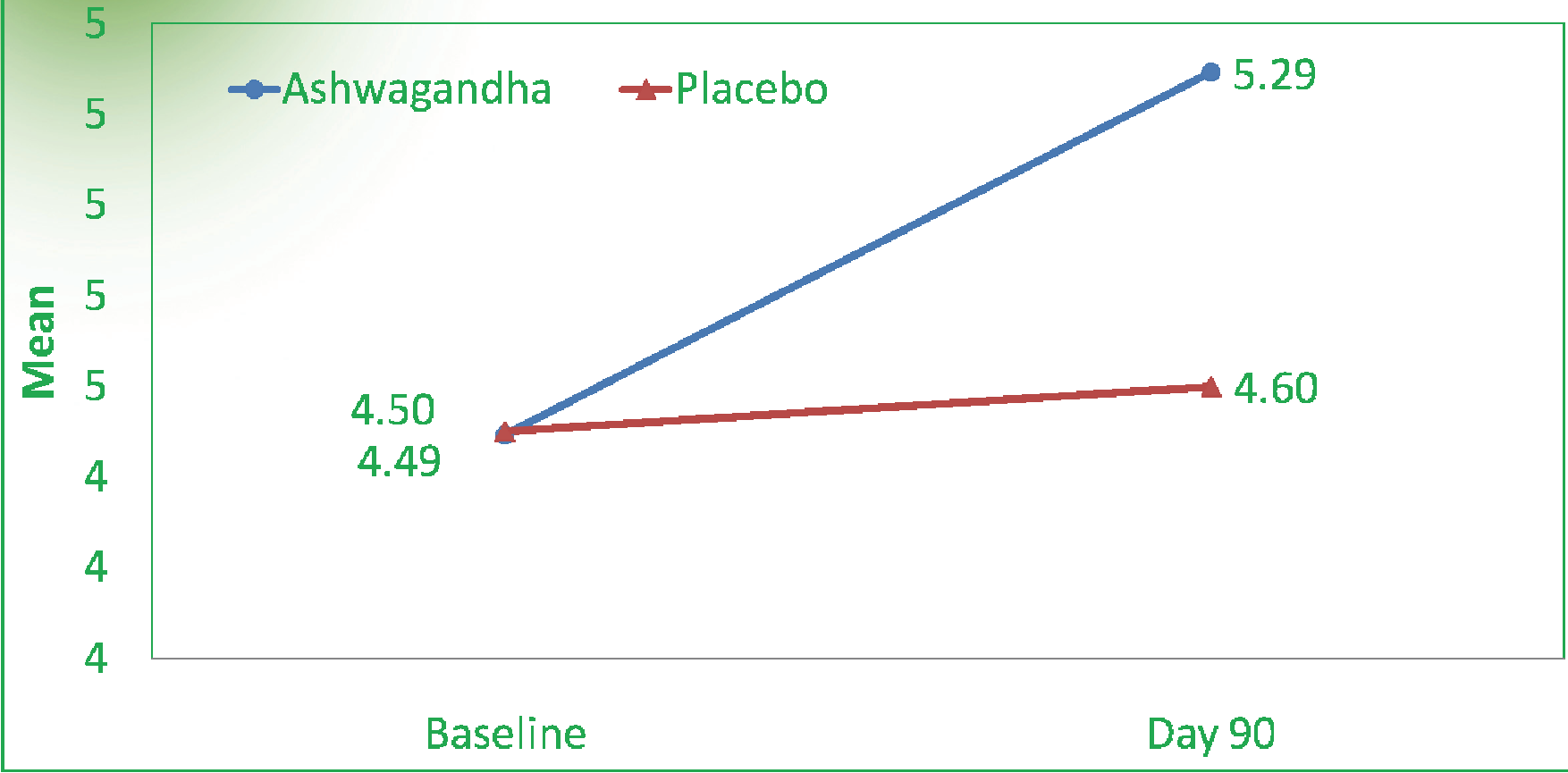
## Sperm total motility



## Sperm % motility



# Serum Testosterone



### 3. CARDIO-RESPIRATORY ENDURANCE STUDY

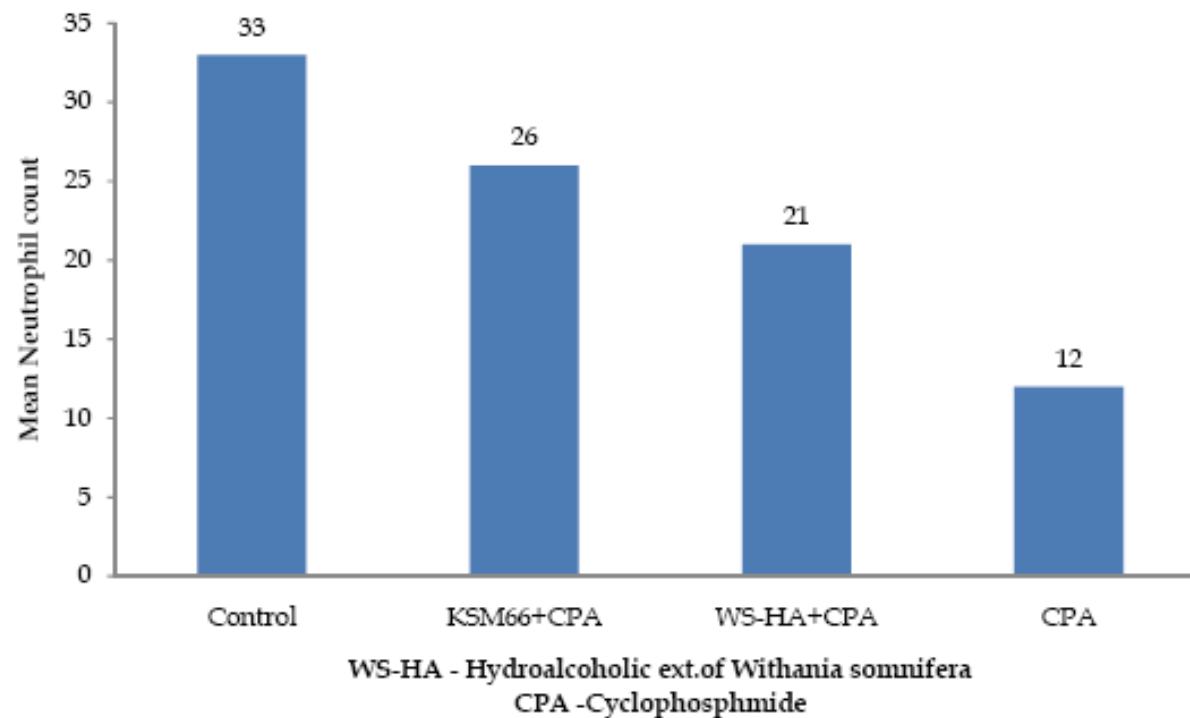
- **OBJECTIVE:** To evaluate the efficacy and safety of KSM-66 in improving Cardio Respiratory Endurance in healthy athletic adults
- **STUDY DESIGN:** Randomized, Double blind, Placebo-controlled
- **SAMPLE SIZE:** 50 subjects
- **STUDY DURATION:** 12 Weeks
- **DOSAGE:** 300 mg twice a day
- **EFFICACY ASSESMENT PARAMETERS:**  
VO<sub>2</sub> Max (maximum oxygen consumption) by 20 meter shuttle run test, perceived exertion test by Borg CR-10 Scale, Quality of Life questionnaire
- Investigator is a world renowned sports medicine doctor

## 4. IMMUNO-MODULATION STUDY

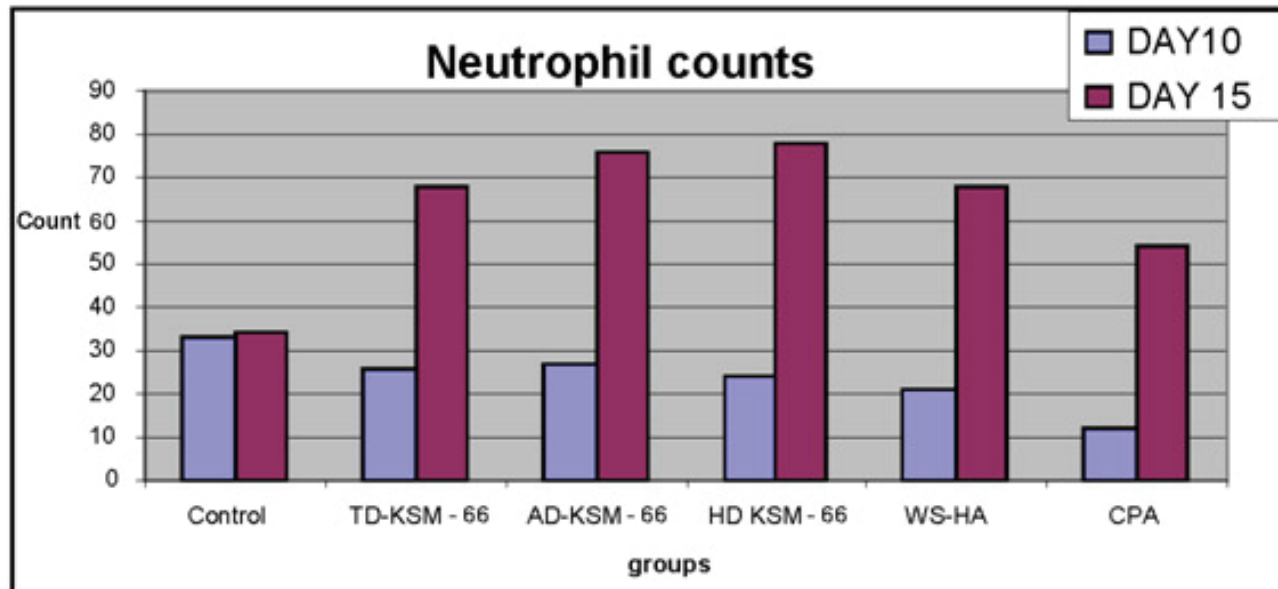
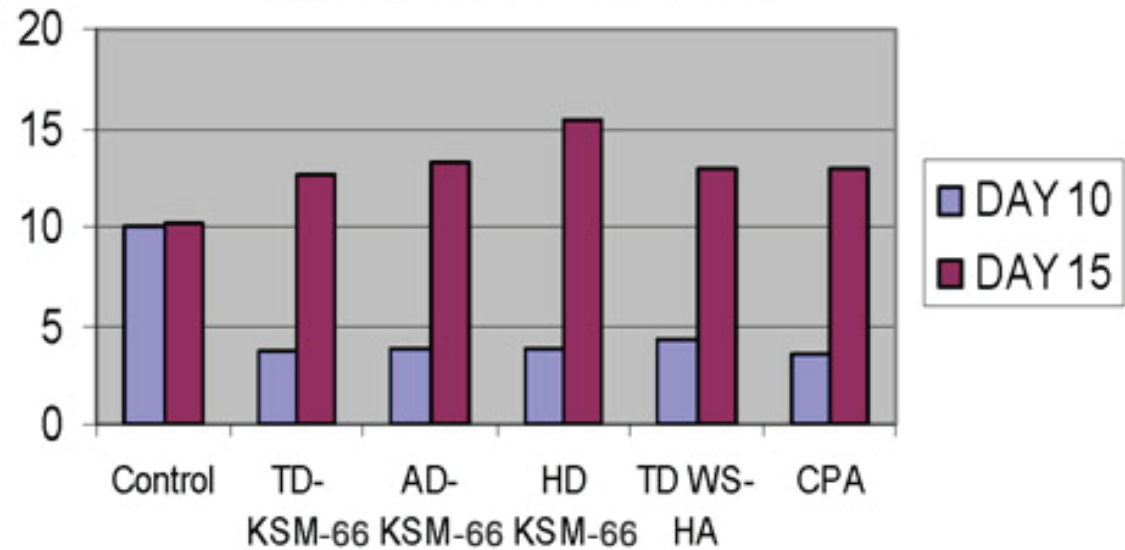
- 72 Swiss Albino Mice, randomized into control and 14 - day treatment groups
- 8<sup>th</sup> day: all treatment groups were administered Cyclophosphamide intramuscularly at dosage 200mg/kg body weight
- Days 10 & 15: Fasting blood samples collected for hematological analysis
- Day 15: Gross Lesions observed and measured

S.No	Test group	Dosage schedule	Duration*	Number of animals	
		(gm / Kg)	(weeks)	Males	Females
1	Vehicle control (VC)	Water / honey	3	6	6
2	Therapeutic dose (TD) KSM-66	0.26gm /Kg	3	6	6
3	Average dose (2.5 x TD) KSM-66	0.65gm /Kg	3	6	6
4	High dose (5.0 x TD) KSM-66	1.3 gm /Kg	3	6	6
5	Therapeutic dose (TD) WSHA	0.26gm /Kg	3	6	6
6	Experimental control Cyclophosphamide	200mg /Kg single dose on 8 <sup>th</sup> day	3	6	6

## KSM-66 ashwagandha -Immunomodulatory activity – Neutrophil count - Day 10



## INFLUENCE ON WBC





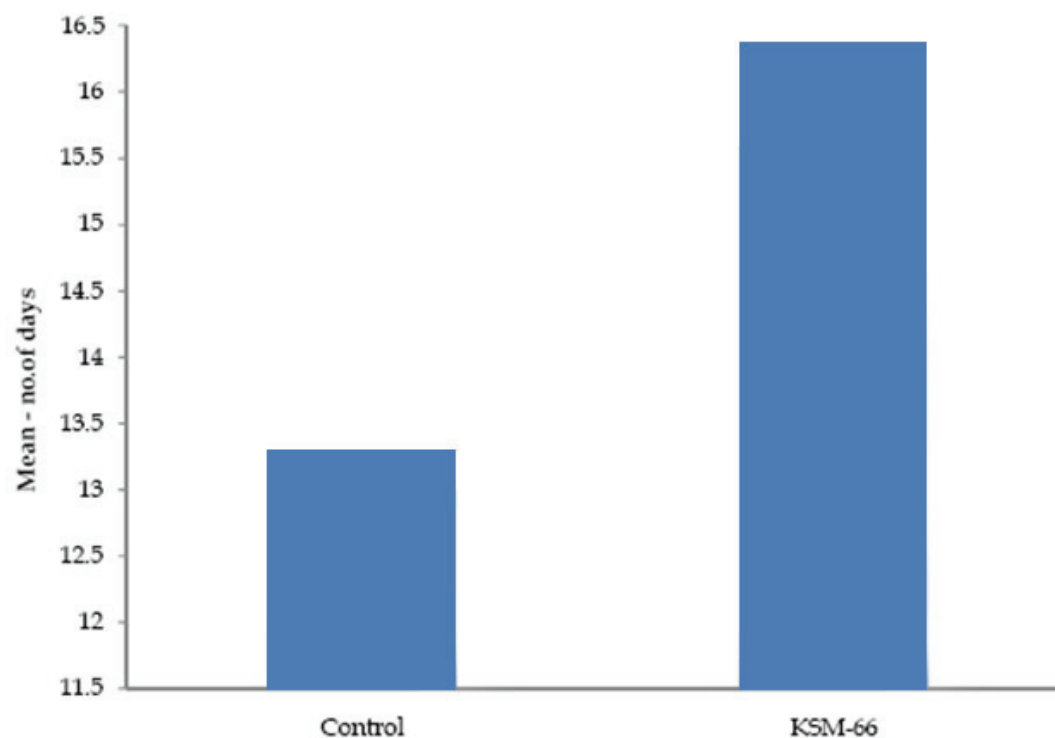
## 5. LIFESPAN EXTENSION STUDY

- Lifespan is correlated with stress
- We selected *Caenorhabditis Elegans* as the animal model because  
(A) fundamental mechanisms are similar to those in mammalian systems,  
(B) normal lifespan short enough for lab studies
- Constructs Measured: Lifespan, Locomotion, Pharyngeal pumping

### KEY RESULTS:

- Lifespan longer by 23% at 25°C  
Mean lifespan of control worms-13.3 days  
Mean lifespan of KSM-66 treated worms – 16.3 days
- 35% increase in thermo - tolerance at 35°C temperature
- More active locomotion and pharyngeal pumping and at later age

## KSM-66 – Absolute Lifespan extension of 3 days in *C.elegans* (n=296) at 25°c



## **CURRENTLY ONGOING STUDIES**

**6. EFFICACY AND SAFETY OF KSM-66 IN IMPROVING MUSCLE STRENGTH AND SIZE IN STRENGTH ATHLETES**

**7. EFFICACY AND SAFETY OF KSM-66 IN ENHANCING MEMORY AND COGNITION IN SCHOOL CHILDREN**

## TOXICITY STUDIES ON KSM-66

- Acute Toxicity - No Toxicity found up to 2000 mg/kg body weight
- Sub - acute 28 days repeated toxicity – No Toxicity found up to 2000 mg/kg body weight
- Genotoxicity (Acute and 28 days repeated oral BY Comet Assay) – Non mutagenic up to 2000 mg/kg body weight

# APPLICATIONS OF KSM-66

## DIETARY SUPPLEMENTS



## SPORTS NUTRITION



## FOODS AND BEVERAGES

