

*ClinWorld (P) Ltd.*

CONTRACT RESEARCH ORGANISATION

# Study Report

Study Protocol Number: FL-005/2005

## **BODY COMPOSITION AND HORMONAL ADAPTATIONS ASSOCIATED WITH FORSKOLIN CONSUMPTION IN OVERWEIGHT AND OBESE WOMEN.**

**Principal Investigator:**

Dr. Pankaj Gandhi, M.D (BOM)

**Investigator:**

Dr.J.R.Parekh, MBBS (BOM)

**Study Sponsor and Coordinating Group/CRO Addresses:**

**Sami Labs Limited**

19/1 & 19/2, 1<sup>st</sup> Main

2<sup>nd</sup> Phase

Peenya Industrial Area

Bangalore – 560 058

Tel: 91-80-8397973 – 75

Fax: 91-80-8373035

**ClinWorld (P) Ltd**

102,Arvind Chambers

Western Express Highway

Andheri (E),

Mumbai - 400069

Tel : 91-22-66981992/3

Fax: 91-22-66981994

**Study Drug : Sami Labs Limited Forslean® (extract of coleus forskohlii root,  
standardized for 10% Forskolin)**

**Study Protocol Number: FL-005/2005**

**Study Title: Body composition and hormonal adaptations associated with  
forskolin consumption in overweight and obese women.**

**Principal Investigator**

**Dr. Pankaj Gandhi, M.D (BOM)**

\_\_\_\_\_

\_\_\_\_\_

Signature

Date

**Co-Investigator**

**Dr.J.R.Parekh**  
MBBS (BOM)

\_\_\_\_\_

\_\_\_\_\_

Signature

Date

**Date of Study Initiation: 26/02/06**

**Date of Study Completion: 13/08/06**

# CONTENTS

<b>ETHICAL COMMITTEE APPROVAL LETTER .....</b>	<b>4</b>
<b>STUDY OVERVIEW.....</b>	<b>5</b>
<b>STUDY REPORT.....</b>	<b>10</b>

# ETHICAL COMMITTEE APPROVAL LETTER

# IEC

**Independent Ethics Committee**

4, Sharavati; Worli Sea Face, Mumbai 400 030  
Phone +9122-55748188; Fax +9122-24966602

Date: 5/12/2005

Dr.M.M.Jain, M.D.  
Chairman

Dr.Shubha Thatte, Ph.D.  
Member

Dr.Rajesh Yadav, M.S.  
Member

Mr. Kailash Gandewar  
Member

Dr.B.Pethambkar, M.D.  
Member-Secretary

Ad. Pradeep Pillai, LLB  
Member

Dr.Hemant Gupta, M.D.  
Member

Mrs. S. karajgikar

To,  
Dr. Pankaj Gandhi, M.D.  
Consulting Physician,  
**Amar Nursing Home**  
Opp. Kandavli Telephone Exchange,  
S.V.Road, Kandavli (W), Mumbai 400 067

Sub: Ethical approval of Clinical Trial entitled "Body Composition and Hormonal Adaptations associated with Forskolin consumption in Overweight and Obese Women"

Dear Dr.Gandhi,  
The Independent Ethics Committee meeting was held on 14/11/2005 and 03/12/2005 between 6.30 & 8.30 pm at Hotel Flora, Worli, to review your above research project. Following members were present for the meeting: -

1. Dr. M.M.Jain
2. Adv Pradeep Pillai
3. Mr. Kailash Gandewar
4. Dr. Shubha Thatte
5. Dr. Hemant Gupta
6. Mrs.Smita Karajgikar

Following documents were examined by the members: -

1. Study Protocol
2. Informed Consent Form
3. Patient's Information Sheet
4. Case Record Form
5. Investigator's Brochure
6. Investigator's Consent and his CV

After thorough discussion, the members unanimously approved the trial to be conducted in its presented form. The Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient's information/informed consent. On conclusion of the study, a final report should be provided to the Committee.

Yours sincerely,



Chairman, Ethics Committee

**Chairman**

**Independent Ethics Committee**

**4, Sharavati Worli Sea Face**

**MUMBAI-400 030.**

# STUDY OVERVIEW

## 1. INTRODUCTION

ForsLean® is Sabinsa's new proprietary composition extract of *Coleus forskohlii* root, standardized for 10 percent forskolin. ForsLean has shown promising results in three areas; enhancing lean body mass, promoting fat loss and promoting weight loss. In September of 1998 Sabinsa was granted a US patent for this application of forskolin in its ForsLean Composition.

The importance of maintaining or regaining lean body mass has recently come to light for two important reasons. First is the increased recognition that lean body mass plays a vital role in any successful weight training regimen, and second there is a growing awareness that lean body mass is proportionate to the overall health of an individual.

Lean body mass is composed of muscle, vital organs, bone and bone marrow, connective tissue and body water. The ratio of lean body mass to fat not only determines the body's aesthetic appearance, but more importantly, it is also an index of physical fitness, health status, and susceptibility to disease and premature mortality. Because the body's metabolic rate is directly proportional to the amount of lean body mass, there is substantial interest in products that safely maintain lean body mass because these products are most likely to work. The use of ForsLean may help to increase lean body mass and optimize body composition with the effects being fat loss and / or weight loss.

A sluggish metabolic rate is an undesirable effect of many weight-loss regimens. It was observed in one study that formerly obese subjects had a 3-5% lower resting metabolic rate than control subjects. The occurrence of a low resting metabolic rate is likely to contribute to the high rate of weight regain in formerly obese persons.

Clearly, we need to change and broaden our thinking on the objectives of weight management regimens for both active and not-so-active individuals. In particular, it should be emphasized that healthy functioning of the body depends not so much on a lower fat content, but rather obtaining a higher percentage of lean body mass. Again, it should be kept in mind that it is not only fat, but also lean body mass that is, or can be, lost through dieting. This fact often escapes our attention when we reduce our total body weight. The excessive loss of lean body mass offsets any benefits derived from the reduction of body weight, and can potentially increase one's chances for diabetes, cardiovascular disease and possibly some forms of cancer due to poor metabolic activity.

Sabinsa Corporation conducted 4 preliminary, clinical studies that evaluated the effect of ForsLean® on the body mass composition of overweight individuals. In the first study ForsLean® was orally administered to 4 overweight female volunteers for 12 weeks. Each volunteer received one capsule, which contained 250 mg of *C. forskohlii* extract (equivalent to 25 mg forskolin), twice daily. Each participant was informed about healthy eating and the benefits of regular exercise, and they were seen by a physician at the inception of the study and after 4, 8, and 12 weeks. The results showed that mean lean body mass significantly increased by 7.2 pounds from week 0 to week 12. Although not

significant, percent body fat was reduced by 2.9% from week 0 to 12. No significant differences were observed in blood biochemistry or vital signs (e.g. pulse rate, systolic blood pressure values, and appetite and energy levels).

In the second trial, six overweight healthy women were selected for the trial. The trial subjects were instructed to take one capsule of 250 mg of the extract standardized for 10% forskolin one in the morning and one in the evening half an hour before a meal. During the eight week trial the mean values for body weight, and fat content were significantly decreased whereas lean body mass was significantly increased as compared to the baseline. Weight loss was statistically significant ( $p < 0.05$ ) after four and eight week, and the mean amounted to 4.3 and 9.17 pounds respectively. The body fat values expressed as percent body fat were - 0 weeks  $33.63 \pm 3.02$ , four weeks 30.10. This preliminary data obtained with 250-mg b.i.d of forsklean, a proprietary 10% forskolin extract from *coleus forskohlii*, indicate that this plant is a safe and effective weight loss regimen. The effect of *coleus forskohlii* is particularly valid in the absence of change in frequency and intensity of physical exercise and without diet restrictions during the course of the trial.

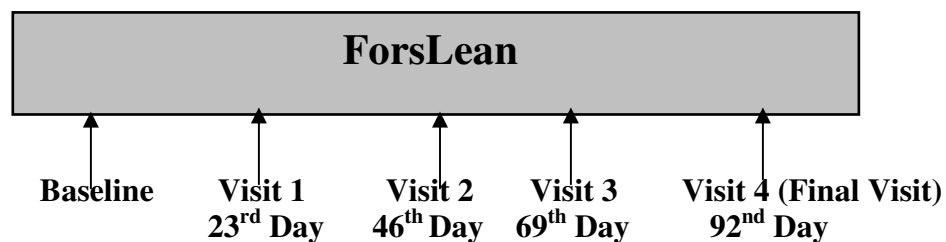
In the third trial, 60 overweight healthy subjects were selected for the trial. The trial subjects were instructed to take one capsule of 250 mg of the extract standardized for 10% forskolin one in the morning and one in the evening half an hour before a meal. During the 12 week trial the mean values for body weight, and fat content were significantly decreased whereas lean body mass was significantly increased as compared to the baseline. Weight loss was statistically expressed as percent weight loss and was - 0 weeks  $79.97 \pm 12.66$  and  $78.23 \pm 12.94$ , 12<sup>th</sup> week. The body fat values expressed as percent body fat were - 0 weeks  $39.73 \pm 6.09$  12<sup>th</sup> week  $39.27 \pm 6.23$ . This preliminary data obtained with 250-mg b.i.d of forsklean, a proprietary 10% forskolin extract from *coleus forskohlii*, indicate that this plant is a safe and effective weight loss regimen. The effect of *coleus forskohlii* is particularly valid in the absence of change in frequency and intensity of physical exercise and without diet restrictions during the course of the trial.

In the fourth trial, 50 overweight healthy subjects were selected for the trial. The trial subjects were instructed to take one capsule of 250 mg of the extract standardized for 10% forskolin one in the morning and one in the evening half an hour before a meal. During the Twelve week trial the mean values for body weight, and fat content were significantly decreased whereas lean body mass was significantly increased as compared to the baseline. Mean (95% CI) difference in weight decrease was -3.6 (-4.5 to -2.7,  $P < 0.001$ ) and % body fat score was -2.0 (-3.1 to -0.9,  $P < 0.001$ ). This preliminary data obtained with 250-mg b.i.d of forsklean, a proprietary 10% forskolin extract from *coleus forskohlii*, indicate that this plant is a safe and effective weight loss regimen. The effect of *coleus forskohlii* is particularly valid in the absence of change in frequency and intensity of physical exercise and without diet restrictions during the course of the trial.

## 2. OBJECTIVES

- a) The primary objective is to demonstrate the effect of Forslean on the hormonal levels and on the BMD (Bone Mineral Density)
- b) Secondary objective is to observe the effect of Forslean on Lean body mass and on Weight Loss.

## 3. STUDY DESIGN OVERVIEW



This study will involve 24 subjects who will be administered 250 mg. of ForsLean capsules twice a day (morning and evening) half an hour before meals for 3 months.

### STUDY DESCRIPTION:

A total of 24 Obese female subjects aged 25-35 yrs and with body mass index ranging from 28 to 45 (I degree to III degree obesity) will be enrolled in the study. After meeting the inclusion and exclusion criteria the informed consent will be obtained before enrolling the subjects in the study. On baseline visit, physical examination and the laboratory test like estrogen, progesterone, testosterone, Lutienizing hormone (LH) and BMD by DEXA will be recorded and the subject will receive study drug. The subject is asked to use the medication half an hour before breakfast and dinner.

The subject will be given medication enough to last for 23 days. Subsequently subjects are called visit 1 (23<sup>rd</sup> day), visit 2 (46<sup>th</sup> day), visit 3 (69<sup>th</sup> day) and visit 4 (92<sup>nd</sup> day) i.e., the final visit.

Laboratory tests will be recorded on Baseline, 46<sup>th</sup> day, 92<sup>nd</sup> day and physical examination in all visits. Also the signs, symptoms and adverse effect if any will be recorded in the CRF.

#### 4. OUTLINE OF PROCEDURES

Procedures	Baseline	Visit 1 23 <sup>rd</sup> Day	Visit 2 46 <sup>th</sup> Day	Visit 3 69 <sup>th</sup> day	Visit 4 92 <sup>nd</sup> Day
Informed Consent	X				
Inclusion / Exclusion Criteria	X				
Medical History	X				
Demographics	X				
Physical Examination	X	X	X	X	X
Concomitant therapy	X	X	X	X	X
BMI	X	X	X	X	X
Body Fat measurement	X	X	X	X	X
<b>Laboratory tests</b>					
<b>Estrogen</b>	X		X		X
<b>Testosterone</b>	X		X		X
<b>Progesterone</b>	X		X		X
<b>LH</b>	X		X		X
<b>BMD</b>	X				X
Adverse Events		X	X	X	X
Serious Adverse Events		X	X	X	X

#### 5. STUDY COHORT

##### 5.1 Number of Subjects / Duration of the study

24 obese Female subjects / 3 months study.

##### 5.2 ELIGIBILITY CRITERIA

###### Inclusion Criteria:

1. Female subjects, aged 25 - 35 years
2. Body Mass Index 28 - 45

###### Exclusion Criteria:

1. History of hepatorenal, musculoskeletal, autoimmune or neurological disease.
2. History of endocrine disorder like hypothyroidism, Cushing syndrome.
3. On-going therapy with androgenic medications
4. On ergogenic levels of nutritional supplements that may affect muscle mass (e.g. Creatinine, and/or stenedione, DHEA) within six weeks prior to the start of the study
5. Women, who are pregnant, have a desire for pregnancy or are nursing
6. Known Hypertensive and / or Diabetic
7. Anticipated poor compliance with study treatments and any other factor that may jeopardize the follow – up (e.g. no fixed address, long distance to hospital, etc.)



8. Usage of medications like psychotropic drugs, anti-convulsants, steroid hormones.
9. Current enrollment in another clinical trial.

## **6. INFORMED CONSENT**

Informed consent for the study must be obtained prior to enrollment into the study. Informed consent could vary from formal written consent to a verbal and witnessed discussion of the study medication with patients or their relatives. For future references, a record should be made in patient's file about the date, time and the name of the person involved, for any consent procedure.

## **7. STUDY PRODUCT ADMINISTRATION**

### **7.1 Dosage and Administration**

Subjects will be administered 250 mg. of Forslean capsules twice a day (morning and evening) half an hour before Breakfast and Dinner for 3 months.

## **8.0 DATA EVALUATION**

### **Primary Endpoint**

- Percentage Change in the hormonal levels and on the bone mineral density.

### **Secondary Endpoints**

- Percentage of fat loss and weight loss.
- Increase in metabolic rate.

## REPORT OF THE STUDY TITLED

### “Body Composition and Hormonal Adaptations Associated with Forskolin Consumption in Overweight and Obese Women”

#### 1. Introduction:

Causes of obesity are extremely complex and multifaceted; different influences include genetic and environmental elements. Increasingly, obesity is becoming highly resistant to treatment in most individuals because of this myriad of contributing factors. While this concept of energy balance to maintain weight is easy to understand and correct in theory, the application of this in an uncontrolled environment for most individuals, especially those who are already obese, is extremely difficult, if not impossible. Also, because of advances in technology, physical activity of any kind, if not during leisure time, is almost nonexistent. Poor or no adherence to proper diet and decreased physical activity levels can be expected, especially in chronically sedentary individuals. Because of this, some form of pharmacological or supplemental treatment to aid in weight loss and/or positively alter body composition is desperately needed (*Obes Res.* 2005;13:1335–1343).

A potential supplemental aid for obesity is a compound containing the herbal extract forskolin. Forskolin is an extract from the roots of the *Coleus forskohlii* plant. *C. forskohlii* is a perennial herb with fleshy fibrous roots and is a member of the mint family of plants. It grows in the wild in warm subtropical temperate areas such as India, Burma, and Thailand. Research into the medicinal value of extracted forskolin began in the early- to mid-1980s and was primarily used as an agent to help a number of cardiovascular disease conditions, mainly through a vasodilatory effect (*J Clin Invest.* 1984;74:212–23). This effect was accomplished by increasing adenylate cyclase activity within the body.

Before forskolin, most weight loss aids used some form of adrenergic  $\alpha$  - and  $\beta$  -receptor agonists, such as ephedrine. However, compared with ephedrine and even more selective adrenergic receptor agonists, forskolin does not interact with adrenergic receptors and, thus, does not result in excessive stimulation of cardiac tissue and does not raise blood pressure (*Molec Pharmacol.* 1982;22:109 –15). Therefore, forskolin is not a sympathomimetic drug; it exhibits a vasodilatory effect, and a decrease in blood pressure is expected (*Res Qlty Exerc Sport.* 1999; 70: 135– 49). Also as a postreceptor agent, adrenergic receptors should not down-regulate over time; thus, a diminished lipolytic effect should not occur. Therefore, forskolin could potentially be used for long periods of time with no diminished lipolytic effects.

We carried out this study to evaluate effect of Forskolin on increasing lean body mass mainly without affecting any hormonal levels or BMD.

## **2. Study Objective:**

This was a clinical trial to primarily evaluate the effect of Forskolin on the hormonal levels particularly testosterone and the BMD (Bone Mineral Density). A second objective was to observe the effect of Forskolin on Lean body mass and on Weight Loss.

The study was conducted with compliance to Good Clinical Practice guidelines and the Declaration of Helsinki 1964, as modified by the 41<sup>st</sup> World Medical assembly, Hong Kong, 1989.

## **3. Study design and Methods:**

24 obese female subjects, aged 25-35 yrs, and with body mass index ranging from 28 to 45 (I degree to III degree obesity) were enrolled in the study. Exclusion criteria had to be followed as per the norms set in the protocol.

After taking their informed consent, patients were assessed at baseline for demographic and baseline characteristics. A physical examination was done which included recording blood pressure, weight, BMI and % body fat measurement. Body fat measurement was done using a bioelectrical impedance monitor. This measures the percentage of body fat to total body weight. From this value the percentage of lean body mass was calculated which equals to hundred minus % of body fat to total body weight.

Laboratory test like estrogen, progesterone, testosterone, luteinizing hormone (LH) and BMD were recorded and the subject then received the study drug. The medication was advised to be taken half an hour before breakfast and dinner.

The subject was given medication enough to last till next follow up visit. The follow up schedule was as follows - visit 1 (23<sup>rd</sup> day), visit 2 (46<sup>th</sup> day), visit 3 (69<sup>th</sup> day) and visit 4 (92<sup>nd</sup> day) i.e., the final visit.

Physical examination was repeated at all visits. Laboratory tests were repeated at visit 2 and visit 4, except for BMD which was done only at visit 4.

In addition, adherence to trial medication was recorded. Adverse events, patient withdrawals and concomitant illnesses were recorded in accordance with good clinical practice guidelines.

## **4. Results:**

All 24 patients completed the trial with no dropouts.

The demographic and baseline data is presented in Table 1. All subjects fulfilled inclusion criteria with respect to BMI and were in the follicular phase of their menstrual cycle as reflected by the estrogen and LH levels.

**Table 1: Baseline Characteristics**

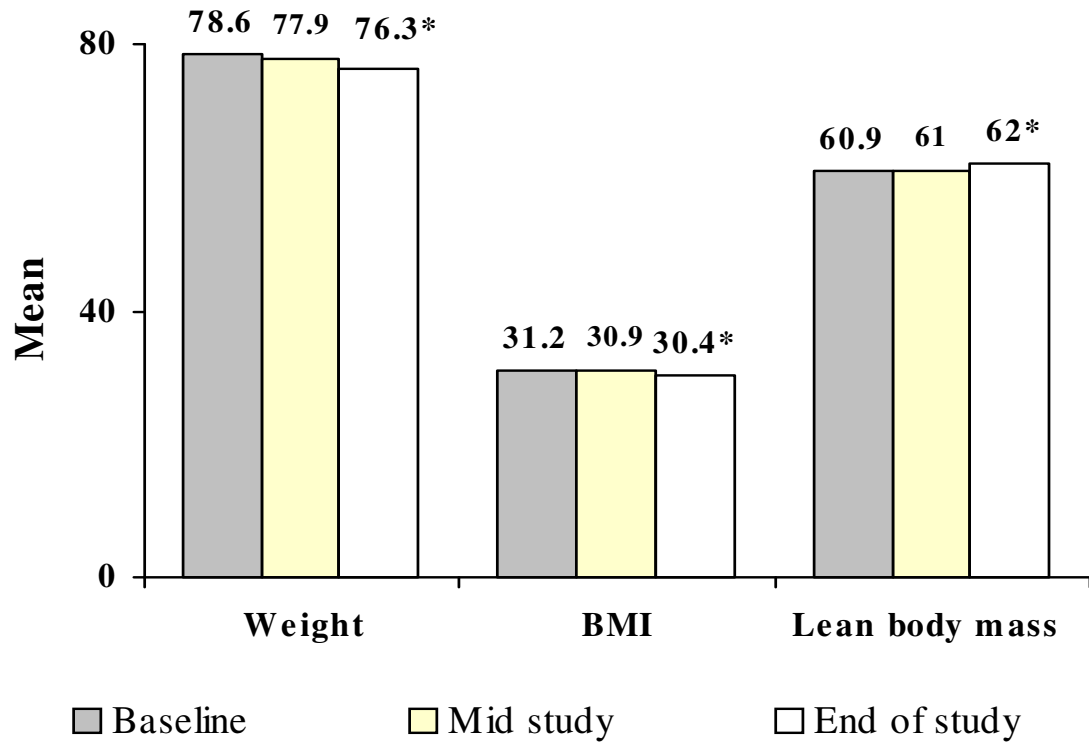
• Characteristic	Forskolin (n=24)
Age (years)	30.9 ± 3.3
Weight (kg)	78.6 ± 7.6
BMI (kg/m <sup>2</sup> )	31.3 ± 3.2
Body fat (%)	39.1 ± 3.9
SBP (mm Hg)	122.2 ± 5.1
DBP(mm Hg)	81.1 ± 4.4
Heart rate (beats/min)	76.8 ± 3.5
Testosterone (ng/ml)	0.65 ± 0.2
Oestrogen (pg/ml)	104.0 ± 33.4
Progesterone (ng/ml)	6.3 ± 4.8
LH (mIU/ml)	12.7 ± 5.1
BMD	0.57 ± 0.01

Plus minus values are mean ± standard deviations.

### ***Body Composition Analysis***

Effect of treatment on weight, BMI and lean body mass (%) is seen in Figure 1. There was a significant decrease in all these parameters. The decrease was seen right from the beginning of the study follow up and continued till the end of the study. Mean (95% CI) decrease in % lean body mass scores was 1.2 (0.8 to 1.5, P < 0.001).

**Figure 1: Effect of Forskolin treatment on weight, BMI and lean body mass (%) in 24 patients**



\* P < 0.05 for difference before and after treatment

**Table 2** shows the effect of treatment on individual body measurements. There was a significant and consistent decrease in all measurements at every follow up visit and this was maintained till the end of the study.

**Table 2: Effect of Forskolin treatment on body measurements (n=24)**

<b>Characteristic</b>	<b>Baseline (n=24)</b>	<b>Mid study (n=24)</b>	<b>Visit 4 (n=24)</b>	<b>Significance</b>
Calf circumference (cm)	38.4 ± 6.0	38.1 ± 5.9	37.3 ± 5.9	P < 0.05
Upper arm (cm)	28.9 ± 4.0	28.6 ± 4.1	27.3 ± 4.0	P < 0.05
Thigh (cm)	50.3 ± 6.0	49.7 ± 5.9	48.6 ± 5.9	P < 0.05
Hip (cm)	114.2 ± 10.2	114.0 ± 10.1	112.6 ± 10.1	P < 0.05
Waist (cm)	93.9 ± 10.7	93.6 ± 10.7	92.7 ± 10.9	P < 0.05

Plus minus values are mean ± standard deviation

### ***Dietary Recall***

The mean daily caloric intake, obtained through dietary recall, was 2133.33 ± 331.9 kcal/d at baseline. The post-values for daily caloric intake were 2112.5 ± 287.9 kcal/d for forskolin. There were no significant differences across time for daily caloric intake as obtained with the dietary recall.

### ***Blood Pressure***

There was no effect on blood pressure or heart rate with Forskolin treatment. Neither the systolic nor the diastolic blood pressure showed any significant difference at baseline or any of the follow up visit. **Table 3** shows the blood pressure measurements at follow up visits.

**Table 3: Effect of Forskolin treatment on blood pressure (n=24)**

Characteristic	Baseline (n=24)	Mid study (n=24)	Visit 4 (n=24)	Significance
SBP (mm Hg)	122.2 ± 5.1	123.5 ± 4.1	121.7 ± 3.9	Not significant
DBP (mm Hg)	81.1 ± 4.4	81.7 ± 4.6	81.7 ± 2.8	Not significant

***Hormonal levels and BMD***

**Table 4** shows the effect of Forskolin treatment on laboratory parameters. There was no significant difference in any of the parameters at any of the follow up measurements.

**Table 4: Effect of Forskolin treatment on laboratory parameters (n=24)**

Characteristic	Baseline (n=24)	Mid study (n=24)	Visit 4 (n=24)	Significance
Testosterone (ng/ml)	0.65 ± 0.2	0.69 ± 0.2	0.69 ± 0.2	Not significant
Oestrogen (pg/ml)	104.0 ± 33.4	119.9 ± 51.4	101.1 ± 34.7	Not significant
Progesterone (ng/ml)	6.3 ± 4.8	11.1 ± 7.5	5.4 ± 6.0	Not significant
LH (mIU/ml)	12.7 ± 5.1	15.7 ± 8.9	12.7 ± 6.6	Not significant
BMD	0.57 ± 0.01	Not done	0.57 ± 0.04	Not significant

Plus minus values are mean ± standard deviation

**5.0 Safety:**

Only 3 patients reported adverse events like diarrhea and sticky stools. However the intensity of these symptoms was mild and did not lead to withdrawal from the study.

**6.0 Conclusion:**

Forskolin demonstrated a significant increase in lean body mass with a corresponding reduction in body weight, BMI and fat content. There was no effect on any hormonal levels or BMD. The good tolerability along with this efficacy makes it an attractive option in the treatment of obesity.