

Randomized, Double blind and Placebo controlled Clinical trial to determine safety and efficacy of i-Slim, an Ayurvedic proprietary daily health reconstituted drink in the management of Obesity

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Abstract: Plant based medicine is still the mainstay of about 75–80% of the world population, mainly in the developing countries, for primary health care because of better cultural acceptability, better compatibility with the human body and lesser side effects. The classical Indian texts of Ayurveda have an armamentarium of medicinal plants used to manage various acute and chronic diseases. They have stood the test of time for their safety, efficacy, cultural acceptability and lesser side effects. Ancient literature also mentions herbal medicines for overweight, obesity, age-related diseases namely memory loss, osteoporosis, diabetic wounds, immune and liver disorders, etc. for which no efficient modern medicine or only palliative therapy is available.¹⁻⁴ The metabolic syndrome refers to the co-occurrence of several known cardiovascular risk factors, including insulin resistance, obesity, atherogenic dyslipidemia and hypertension. Obesity is also considered to be a major risk factor for hypertension. There is a significant correlation between obesity indices and systolic and diastolic blood pressure.⁵⁻⁷ An excessive weight gain falls under the umbrella of Medoroga or Sthoulya in Ayurveda. Management of Medoroga continues to be a challenging problem and the present clinical trial is an effort to find a solution for the holistic management of Medoroga.⁸⁻¹³ Diseases like Hypothyroidism, Cushing syndrome, Polycystic ovarian syndrome and Drugs like steroids, antidepressant can make a person obese. The pathophysiology of obesity usually includes chronic excess of nutrient intake relative to the level of energy expenditure.¹⁴ i-Slim, an Ayurvedic proprietary reconstituted health drink from Indusviva Health Sciences Pvt. Ltd., Bangalore, is an polyherbal formulation in the management of obesity. With its unique combination of anti-obesity herbal active blend and with the goodness of proteins, multi vitamins and enzymes, i-Slim is considered safe and efficacious in obesity management.

Key Words: Ayurveda, Body mass index (BMI), Metabolic syndrome, Obesity, Medoroga, i-Slim.

1. INTRODUCTION:

Metabolic syndrome is not a specific disease. The metabolic syndrome is a constellation of metabolic derangements such as insulin resistance, hyperinsulinemia, abdominal obesity, impaired glucose tolerance, dyslipidemia, coronary heart disease, hypertension, and a proinflammatory and prothrombotic state. It is a common cause of the development of atherosclerotic vascular disease and type 2 diabetes.^{15,16} An early hypothesis was that insulin resistance is the cause of metabolic syndrome. Without question, insulin resistance contributes to hyperglycemia. Another view sees obesity as the main cause as it strongly associates with all metabolic risk factors, its role is plausible. A related view contends that positive caloric balance underlies the metabolic syndrome. Obesity is a useful clinical indicator of a state of overnutrition but this does not necessarily mean that an excess of adipose tissue is the true cause.^{17,18}

Currently, in developed countries and developing countries alike, the food industry is rather successful in the mass production and marketing of calorie-dense foods. Such processed foods are made readily available in grocery stores, shops, schools, restaurants, and homes.^{19,20} Obese people also experience higher rates of depression and anxiety, but it is not clear whether obesity causes or aggravates mental illness, or whether mental illness and medications to treat it confer a propensity toward weight gain and disordered eating.^{21,22}

Epidemiologic studies have identified high body mass index (BMI, the weight in kilograms divided by the square of the height in meters) as a risk factor for an expanding set of chronic diseases, including cardiovascular disease, diabetes mellitus, chronic kidney disease, many cancers, and an array of musculoskeletal disorders.^{23,24} The body mass index (BMI) is the metric currently in use for defining anthropometric height/weight characteristics in adults and for classifying them into groups. The common interpretation is that it represents an index of an individual's fatness. It also is widely used as a risk factor for the development of various health issues.

The body fat distribution is referred to as being "android" if it occurred in the upper body and "gynecoid" when it occurred in the lower segment of the body. This is because men tend to accumulate fat in the abdominal (upper body) area, whereas women tend to accumulate it in the peripelvic (gluteal) area and the thighs.^{25,26}

Anthropometric determination of fat mass directly has been done using skin-fold thickness measured at various sites.²⁷ Skinfold thickness measurements are widely used to assess body fat because the measurements are non-invasive, simple, and less expensive than laboratory-based techniques. The skin fold thickness around the triceps, mid axillary and subscapular regions have been considered in this clinical study as the efficacy parameter to signify reduction in obesity.²⁸

2. AIM:

Randomized, Double-blind and Placebo controlled Clinical trial to determine safety and efficacy of i-Slim, an Ayurvedic proprietary daily health reconstituted drink in the management of obesity.

3. MATERIALS AND METHODS:

Local ethical committee approval was obtained before initiation of the study. Those who opted for treatment were informed of voluntary nature of trial and written consent was obtained from the parent or guardian. They were free from withdrawal of the study.

3.1 INFORMED CONSENT PROCESS

All subjects who were willing to participate in the study were given detailed description about the investigational product, nature and duration of the study. Also, subject's responsibilities after entering, the study were explained. Subjects were pre-screened by the investigators for the inclusion criteria. Only subjects who met the requirements of this section, signed an informed consent form, subjects who were willing to follow instructions given by the investigator and have an updated medical history on file with the investigator were entered in the study.

3.2 STUDY DESIGN

Randomized, Double-blind and Placebo controlled Clinical trial to determine safety and efficacy of i-Slim, an Ayurvedic proprietary daily health reconstituted drink in the management of obesity.

A baseline history will be obtained in order to determine the patient's eligibility for enrolment in the study. The baseline assessment included personal data, a description of symptoms and details of past medical history, history of possible exacerbating factors, etc. All the patients were advised to apply the given product on the affected area for a period of 12 weeks.

1 sachet of i-Slim three times a day with water, shaken properly was administered for group A, and placebo twice day for group B. Every day the subject recorded the actual time when the product is consumed.

3.3 NOTE OF ADVERSE EVENT (AE):

An adverse event is the development of an undesirable medical condition - e.g. symptoms or abnormal results of an investigation - or the deterioration of a pre-existing medical condition (not relevant in this study). Adverse events (AE) were collected by means of a standard questionnaire. Relation of Adverse events (AE) to study medication were classified as 'Unrelated', 'Possible' and 'Probable'.

3.4 INCLUSION CRITERIA

- Male & female subjects of age 18 to 60 years old
- Subjects having metabolic syndrome like pre-obese condition, overweight and high appetite
- BMI between 28-30 and 30-34
- Accepting to return to the centre for the planned visits
- Accepting to follow the investigator's instructions during the entire study period
- Accepting to not change their habits regarding: food, physical activity
- Agreeing to not receive any drug able to change the physical characteristics during the entire duration of the study

3.5 EXCLUSION CRITERIA

- Drug allergy of any known source
- Use of drugs which may influence the test results in the investigators opinion
- Unwilling to sign informed consent
- Pregnant and lactating mother
- Patients with features of other co-morbidity features like stroke, heart disease, insulin dependent Diabetes mellitus
- Cancer and other degenerative diseases
- Patients with addiction of higher levels of alcohol and nicotine

3.6 PRIMARY ENDPOINTS:

- Tolerance (number of participants with adverse events) and subject compliance to the i-Slim formulation.
- Perception of palatability and easiness.
- Reduction in obesity as measured by BMI and Skin fold thickness parameters

3.7 SECONDARY ENDPOINTS:

Short-term safety as assessed by incidence of adverse events, and compliance to the drug therapy.

4. STATISTICS:

Descriptive statistics was used to describe variables and comparison with baseline. No statistical method will be used for determination of level of significance.

4.1 EVALUATION OF SAFETY PARAMETERS

Table 1. EVALUATION OF i-SLIM ON SAFETY AND TOLERANCE PARAMETERS		
PARAMETERS	Day 1	Day 90
Erythema	0	0
Edema	0	0
Vomiting	0	0
Pruritus and Urticaria	0	0
Burning micturition	0	0
Hypopigmentation	0	0
Hyperpigmentation	0	0

All the scores are expressed as Nil- 0, mild-1, moderate-2 and severe-3.

A baseline history was obtained in order to determine the patient’s eligibility for enrolment in the study. The baseline assessment included personal data, a description of symptoms and details of past medical history, history of possible exacerbating factor/s, etc. All the patients were advised to consume the given product for a period of 12 weeks.

Follow up visits and observation:

Subjects were assessed at entry, and at the end of 30 days and 90 days (12 weeks). At each visit, the subjects were evaluated for Body mass index (BMI) and Skin fold thickness (SFT) which included triceps, subscapular and mid axillary. The overall clinical assessment was defined as cured, improved and unchanged.

4.2 EVALUATION OF EFFICACY PARAMETERS

Table 2. CHARACTERISTICS OF THE TREATMENT AND PLACEBO GROUPS WITH SPECIAL REFERENCE TO BODY MASS INDEX (BMI) AND SKIN FOLD THICKNESS (SFT)								
Parameters	Day 0	Day 30	Day 60	Day 90	Day 0	Day 30	Day 60	Day 90
i-Slim powder				Placebo				
Body mass index (BMI)	30±2.30	28±2.80	27.05±2.30	30±2.90	30.50±2.40	30±2.80	29.05±2.60	29.2±2.90
Skin fold thickness (SFT)								
Triceps	29.99±9.01	28.6±8.80	27.05±7.30	26.10±6.90	29.92±8.01	29.6±7.80	28.95±6.30	29.10±6.90
Subscapular	33.04±8.01	32.69±8.60	32.05±7.10	31.59±6.99	33.92±8.08	33.056±7.89	33.02±8.30	32.78±7.90
Mid axillary	33.24±9.01	31.69±8.80	30.75±8.10	29.59±7.29	32.12±7.1	32.056±8.19	32.01±8.20	31.78±8.30

5. RESULTS:

THE SAFETY AND TOLERABILITY OF I-SLIM ARE SHOWN IN TABLE.1: i-Slim is seen to be safe and tolerable. None of the subjects complained about erythema, oedema, vomiting, pruritic, urticaria, burning micturition, hypopigmentation and hyperpigmentation. I-Slim was observed to be safe from baseline till the end of the study.

CHARACTERISTICS OF TREATMENT IN BOTH TRIAL AND PLACEBO GROUPS WITH SPECIAL REFERENCE TO BMI AND SFT PARAMETERS ARE DESCRIBED IN TABLE.2: It is observed that the

parameters like Body mass index (BMI) and Skin fold thickness (SFT) significantly reduced in treatment group as compared to the placebo.

5.1 BODY MASS INDEX (BMI)

Treatment group: Pre-treatment, BMI was recorded at 30 ± 2.30 at baseline. Post treatment, at the end of 30 days (1 month), the BMI was noted at 28 ± 2.80 . At the end of 60 days (2 months), the BMI was recorded at 27.05 ± 2.30 . At the end of 90 days (3 months/end of study), the BMI was recorded at 30 ± 2.90 .

Placebo group: Pre-treatment, BMI was recorded at 30.50 ± 2.40 at baseline. Post treatment, at the end of 30 days (1 month), the BMI was recorded to 30 ± 2.80 . At the end of 60 days (2 months), the BMI was recorded at 29.05 ± 2.60 . At the end of 90 days (3 months/end of study), the BMI was recorded at 29.2 ± 2.90 .

5.2 SKIN FOLD THICKNESS (SFT)

A) TRICEPS

Treatment group: Pre-treatment, skin fold thickness (SFT) at Triceps area was recorded at 29.99 ± 9.01 at baseline. Post treatment, at the end of 30 days (1 month), the SFT at Triceps area was noted at 28.6 ± 8.80 . At the end of 60 days (2 months), the SFT at Triceps area was recorded at 27.05 ± 7.30 . At the end of 90 days (3 months/end of study), the SFT at Triceps area was recorded at 26.10 ± 6.90 .

Placebo group: Pre-treatment, skin fold thickness (SFT) at Triceps area was recorded at 29.92 ± 8.01 at baseline. Post treatment, at the end of 30 days (1 month), the SFT at Triceps area was noted at 29.6 ± 7.80 . At the end of 60 days (2 months), the SFT at Triceps area was recorded at 28.95 ± 6.30 . At the end of 90 days (3 months/end of study), the SFT at Triceps area was recorded at 29.10 ± 6.90 .

B) SUBSCAPULAR

Treatment group: Pre-treatment, skin fold thickness (SFT) at Subscapular area was recorded at 33.04 ± 8.01 at baseline. Post treatment, at the end of 30 days (1 month), the SFT at Subscapular area was noted at 32.69 ± 8.60 . At the end of 60 days (2 months), the SFT at Subscapular area was recorded at 32.05 ± 7.10 . At the end of 90 days (3 months/end of study), the SFT at Subscapular area was recorded at 31.59 ± 6.99 .

Placebo group: Pre-treatment, skin fold thickness (SFT) at Subscapular area was recorded at 33.92 ± 8.08 at baseline. Post treatment, at the end of 30 days (1 month), the SFT at Subscapular area was noted at 33.056 ± 7.89 . At the end of 60 days (2 months), the SFT at Subscapular area was recorded at 33.02 ± 8.30 . At the end of 90 days (3 months/end of study), the SFT at Subscapular area was recorded at 32.78 ± 7.90 .

C) MID AXILLARY

Treatment group: Pre-treatment, skin fold thickness (SFT) at Mid axillary area was recorded at 33.24 ± 9.01 at baseline. Post treatment, at the end of 30 days (1 month), the SFT at Mid axillary area was noted at 31.69 ± 8.80 . At the end of 60 days (2 months), the SFT at Mid axillary area was recorded at 30.75 ± 8.10 . At the end of 90 days (3 months/end of study), the SFT at Mid axillary area was recorded at 29.59 ± 7.29 .

Placebo group: Pre-treatment, skin fold thickness (SFT) at Mid axillary area was recorded at 32.12 ± 7.1 at baseline. Post treatment, at the end of 30 days (1 month), the SFT at Mid axillary area was noted at 32.056 ± 8.19 . At the end of 60 days (2 months), the SFT at Mid axillary area was recorded at 32.01 ± 8.20 . At the end of 90 days (3 months/end of study), the SFT at Mid axillary area was recorded at 31.78 ± 8.30 .

The present clinical study reveals the safety, efficacy and tolerability of i-Slim in obese subjects. The efficacy parameters included the Body mass index (BMI) and Skin fold thickness (SFT) which reduced significantly in obese subjects in the treatment group when compared to the placebo. No clinically significant adverse reactions were either reported or observed, during the entire study period of 12 weeks (90 days) and overall compliance to the safety and efficacy was excellent.

6. DISCUSSION:

Overweight and obesity are common in many countries throughout the world, and their prevalence is increasing not just in developed countries but also in developing countries as they become more affluent.²⁹ For the patients with a BMI between 28 and 34, especially those with metabolic complications, medical therapy is effective. A comprehensive lifestyle based weight loss programme with the use of wellness supplements can initiate and maintain weight loss. In addition to this, use of very low-calorie diet can support effective weight loss.^{30,31} Currently there are several classes of drugs available to help weight loss. The available drugs can be divided into centrally acting (phentermine and sibutramine) and peripherally acting (orlistat). All these drugs are active and can produce weight loss but pose lots of side effects.³²

However, it is important to eat less, therefore the diet should be mildly hypocaloric based on the individual's size. An energy deficit of 500 to 600 kcals seems to be accepted and tolerated by most patients. The prescribed diet should start from the patient's habitual macronutrient intake and make small changes. Some changes that can be recommended are less total fat and less saturated fat, possibly an increase in mono-unsaturated fats and lower

glycaemic index carbohydrates.³³ Activity helps maintain lean mass and promotes weight and fat loss (because it adds to the energy deficit). However, the type of exercise/activity done may vary, but it is necessary to be active every day. Whilst walking is a usual activity prescribed, it is important to realise that variety in exercise is important and that the exercise chosen is one with which the patient is happy and can comply.³⁴

The concept of metabolic syndrome may be classified under the broad heading of *Medoroga* in Ayurveda. *Atisthaulya* or *Medoroga* or *Medobahulyata* (Obesity) is considered as one of the eight despicable condition as described in *Charaka samhita*. Increased fat is accountable for several serious consequences like decrease of life span, decrease in enthusiasm and activity, difficulty in sexual act, bad odour, excess perspiration and excessive hunger and thirst.³⁵ Ayurveda has an armamentarium of *Medohara* and *Lekhaniya* (Anti-obesity and Hypolipidemic) drugs mentioned in which helps us in understanding of prevention and management of obesity. *Charaka Samhita* has given *Lekhaniya Gana* of 10 herbs, while *Sushruta* and *Vagbhata* have mentioned 8 and 10 *Ganas* respectively.³⁶

i-Slim is an effective Ayurvedic proprietary health formula specifically formulated with weight reducing poly herbal blend with inherent milk solids, natural proteins, multi vitamins and minerals. It is safe and efficacious in managing over weight and obesity. I-Slim supports overall holistic management of metabolic syndrome.

6.1 COMPOSITION OF i-SLIM

30 gms of i-Slim contains:

Table 3. Ingredients of i-Slim				
Form	Sanskrit name	Botanical name	Part used	Quantity
Exts.	Vrikshamla	<i>Garcinia indica</i>	Fruit	500 mg
	Gandhira	<i>Coleus forskohlii</i>	Root	125 mg
	Bahunetra	<i>Ananas comosus</i>	Fruit	45 mg
	Tila	<i>Sesamum indicum</i>	Seed	40 mg
	Saptaranga	<i>Salacia chinensis</i>	Root	30 mg
	Godugdha	NA	NA	7.8 mg

Vrikshamla fruits (*Garcinia indica*) are considered cardiogenic and are used as appetiser and carminative. It also possesses weight reducing properties.³⁷ *Garcinia indica* fruits contains garcinol, hydroxycitric acid which has been shown to significantly reduce body weight. Hydroxycitric acid (HCA) has gained much attention in recent years for its pivotal role in fat/lipid metabolism, with implications for use in weight loss.³⁸

Gandhira (*Coleus forskohlii*) is traditionally known to have anthelmintic properties. It is used in the management of pains, inflammatory conditions, skin disorders, haemorrhoids and acid peptic disorders.³⁹ *Coleus forskohlii* is being used exclusively for weight management and hypotension. It is exclusively known as a fat burner and is one of the commercially important herbal ingredients for weight loss dietary supplements in the global market.⁴⁰⁻⁴²

Bahunetra (*Ananas comosus*) fruits are traditionally used as diuretic, appetiser and carminative. It is also a known anthelmintic.⁴³ *Ananas comosus* fruits contains an enzyme known as Bromelain. It breaks down excess proteins in the body into essential amino acids which helps in maintaining energy during the weight management process.⁴⁴

Tila (*Sesamum indicum*) is traditionally known for its unctuousness and its use as a carminative, galactagogue, diuretic, anabolic and aphrodisiac is documented.⁴⁵ Sesame (*Sesamum indicum*) contains proteins, carbohydrates, antioxidants, lignans, tocopherols and other micronutrients. In recent times it has gained importance to lower or regulate cholesterol levels. It is found to be very effective in the management of obesity.⁴⁶

Saptaranga (*Salacia chinensis*) is traditionally used in Indian system of Medicine for its sugar and fat lowering properties.⁴⁷ *Salacia chinensis* roots possesses Salacinol and Mangiferin as major phytochemicals. These alpha-glucosidase inhibitors decrease the absorption of carbohydrates from the intestine, resulting in a slower and lower rise in blood glucose throughout the day, especially right after food and helps manage obesity.⁴⁸

Godugdha (Milk solids/Whey) has rejuvenating and refreshing properties.⁴⁹

The synergistic combination of herbal ingredients with their inherent vitamins, proteins and enzymes in i-Slim is responsible for its effectiveness in the management of metabolic syndrome. The composition of i-Slim effectively inhibit pancreatic lipase enzyme, resulting in weight loss and management of obesity. The inherent nutrients in i-Slim exerts antioxidant activity and rejuvenates the body during the period of weight management.

7. CONCLUSION:

The present clinical trial clearly indicates the safety and efficacy of i-Slim, an Ayurvedic proprietary daily health reconstituted drink in the holistic management of obesity. i-Slim is an effective fat blocker. It slows the

conversion of carbohydrates into fats, halts fat storage. It further has hunger-suppressing quality which is an important way that this product supports weight loss. i-Slim has the ability create a more efficient metabolism and produces a feeling of satiety. I-Slim is also known to improve immune function and thus it rejuvenates the body. This clinical study has demonstrated that i-Slim is very safe and effective in subjects as it reducing the Body mass index (BMI) and Skin fold thickness (SFT) in comparison with the placebo group. Overall patient compliance was good and no adverse drug reactions were reported with both trial and placebo health drink groups during the period of study. I-Slim is regarded safe for short term and long-term use as a weight management health supplement. There is further scope of clinical studies on i-Slim with reference to various therapeutic segments associated with the obesity pandemic.

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