TABLE OF CONTENTS

TITLE PAGE

A Study to evaluate the Safety and Efficacy of AirLite™ in patients with Obesity.

Protocol No.:	TCR/REE/17/010
Version No.:	Version No.: 1.0 Date: 30.08.2017
Investigational Product:	AirLite™
Indication:	Obesity
Development Phase:	Post Marketing Survey
Sponsor:	Ree Veda (A division of Ree Labs Pvt. Ltd.)
CRO:	Taiyo Clinical Research
Name of Investigator	Name of Site
Dr. Mahesh Padsalge	Diabecare, Nerul (East)
Dr. Sanjay Bhadada	PGIMER, Chandigarh
	The study, including the archiving of essential documents has been conducted as per the protocol, GCP, Declaration of Helsinki, Indian Council of Medical Research (ICMR), SOPs and applicable regulatory requirements. We accept the responsibility for the correctness of the project and validity of the data produced in this clinical study report.

SYNOPSIS

Name of Sponsor/ Company: Ree Veda (A Division of Ree Labs Pvt. Ltd.)	
Name of Finished Product: **AirLite™**	**Volume:** 01
Name of Active Ingredient:	
Title of Study: A Survey to evaluate the Safety and Efficacy of AirLite™ in patients with obesity	
Treatment period (months/Days): **3 Months**	**Phase of development:** Post Marketing Survey

Objectives:

Primary Study Objective

To evaluate the effect of AirLite™ in the following symptoms in patients with Obesity.

- Controlling Appetite
- To observe the change in patient's BMI from baseline to end of treatment.

Secondary Study Objective

- To Evaluate Safety and Tolerability of AirLite™.
- To evaluate the patients Quality of Life
- Global Assessment for overall improvement by the Subject.
- Global Assessment for overall improvement by the Investigator.

Methodology:

This was an open label, randomized, multi-centric study.

The study was conducted in 50 patients with the compliant of obesity in an outpatient setting. The Subjects were otherwise in good health or with controlled diabetes and/or hypertension and who had a desire to lose weight

In this study, subjects who are currently on treatment for Obesity were approached and upon receiving signed informed consent form from the patient or his/ her legally acceptable representative (LAR), he/

she underwent the screening procedure for the assessment of eligibility.

On the screening visit Day -5, all the subjects meeting the inclusion criteria were enrolled in the study. On the Baseline visit Day 0, the enrolled patients were randomized. One group were asked to stop their current medication and start taking AirLite™ daily as prescribed along with diet and exercise. The other group was asked to continue only with diet and exercise. Both groups were asked to follow a standardized diet and exercise plan.

The data were collected on paper CRF. The data analysis was performed for predefined parameters to correspond with the outcome measures.

The subjects were excluded for safety analysis unless there was consent withdrawal/termination pertaining to adverse event.

Number of Patients: (Planned & analyzed)

1. Planned for inclusion: 50
2. Screened: 50
3. Screen failed: 00
4. Enrolled: 50
5. Completed the study and used for analysis: 50

Diagnosis and main criteria for inclusion: Patients with BMI ranging from 25 kg/m2 to 35 kg/m2 who were otherwise in good health or with controlled diabetes and/or hypertension and those with a desire to lose weight.

Test product, dose, mode of administration and batch number:

AirLite™

Manufacturer: Ree Veda (A Division of Ree Labs Pvt. Ltd.)

Duration of treatment: 3 months

Criteria for evaluation:

Efficacy:

1. Appetite Control (Using a questionnaire to measure appetite)
2. Fat reduction and Fat Measurement
3. Cholesterol Estimations
4. Weight and Body Measurements
5. BMI Measurements
6. Quality of Life Questionnaire
7. Global Assessments by Patient and Investigator
8. Incidences of any Adverse Events

Safety:

a. Proportion of patients with adverse event associated with the drug.

Statistical Methods: Statistical analysis was done using Microsoft Excel.

Summary: Conclusion **Efficacy Results**	1. Appetite Control (Using a questionnaire to measure appetite) 2. BMI Measurements 3. Quality of Life Questionnaire 4. Global Assessments by Patient and Investigator
Safety Results	Safety and tolerability of the test product were assessed depending on the outcome from this clinical study. Incidences of any Adverse Events
Conclusion	It was concluded that patients who had Airlite daily were found to be more energetic, lost comparatively more weight as compared to the arm that did not have Airlite and had their appetite controlled more better then the comparator arm.
Publications	Ongoing
Date of Report	Ongoing

LIST OF ABBREVIATIONS

AE	Adverse Event
ADR	Adverse Drug Reaction
ALP	Alkaline Phosphatase
BP	Blood Pressure
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
CDSCO	Central Drugs Standard Control Organization
CRF	Case Report Form
CHD	Coronary Heart Disease
CBC	Complete Blood Count
CRA	Clinical Research Associate
CRO	Contract Research Organization
DLC	Differential Leukocyte count
EC	Ethics Committee
ESR	Erythrocyte Sedimentation Rate
HR	Heart Rate
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HBsAg	Hepatitis B Surface Antigen
Hb	Hemoglobin
ICF	Informed Consent Form
IEC	Institutional/ Independent Ethics Committee
IRB	Institutional/ Independent Review Board
ICH GCP	International Conference on Harmonization – Good Clinical Practices
ICMR	Indian Council of Medical Research

IP	Investigational Product
LAR	Legally Acceptable Representative
LCD	Low Calorie Diet
LFT	Liver Function Test
PI	Principal Investigator
RBC	Red Blood Count
RR	Resting Rate
RFT	Renal Function Test
SGPT	Serum Glutamic Pyruvic Transaminase
SGOT	Serum Glutamic Oxaloacetic Transaminase
SAE	Serious Adverse Event
TCR	Taiyo Clinical Research
TLC	Total Leukocyte Count
UPT	Urine Pregnancy Test
VDRL	Venereal Disease Research Laboratory

ETHICS

This was an Open label, randomized, multi-centric study requiring Ethics Committee Approval.

Ethics Committee

Sites Name	Ethics Committee	EC Registration Number
Diabecare, Nerul East	Royal Pune Ethics Committee	ECR/45/Inst/MH/2013/RR-16
PGIMER, Chandigarh	Institutional Ethics Committee, PGIMER, Chandigarh	ECR/25/Inst/CH/2013/RR-16

List of Administrative Personnel

Sr. No.	Role and Name	Signature
1	**Sponsor: Dr. Rohit Kulkarni**	
2	**Clinical Operations CRO:**	
3	**Documentation Writer / Reporting author:**	
4	**Reviewed and Quality Check:**	

INTRODUCTION & RATIONALE

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. [1.1]

Body mass index (BMI) is a simple index of weight-for-height that is commonly used to classify overweight and obesity in adults. It is defined as a person's weight in kilograms divided by the square of his height in meters (kg/m2).

A BMI over 25 kg/m2 is defined as overweight, and a BMI of over 30 kg/m2 as obese [1.1]. These markers provide common benchmarks for assessment, but the risks of disease in all populations can increase progressively from lower BMI levels.

The worldwide prevalence of obesity nearly has tripled between 1975 and 2016. In 2016, more than 1.9 billion adults aged 18 years and older were overweight. Of these over 650 million adults were obese. Also, 39% of adults aged 18 years and over (39% of men and 40% of women) were overweight. Overall, about 13% of the world's adult population (11% of men and 15% of women) were obese in 2016. [1.7]1.8]

In 2016, an estimated 41 million children under the age of 5 years were overweight or obese. 1.6]

Obese patients are often at increased risk for several conditions that require detection and appropriate management, but generally do not lead to widespread or life-threatening consequences. These include gynecological abnormalities, Osteoarthritis, Gallstones and their complications, Stress incontinence.

Childhood obesity is associated with a higher chance of obesity, premature death and disability in adulthood. But in addition to increased future risks, obese children experience breathing difficulties, increased risk of fractures, hypertension, early markers of cardiovascular disease, insulin resistance and psychological effects.

The general goals of weight loss and management are:

1. To reduce body weight.

2. To maintain a lower body weight over the long term.

3. To prevent further weight gain.

AirLite™ is a unique Nutraceutical formulation of scientifically chosen ingredients derived from food which help in supplementing the normal diet to manage weight without affecting the benefits derived from normal food. It increases fat metabolism, controls appetite and hinders absorption of fat. It is a complement to weight control and weight management program.

AirLite has been created by highly qualified doctors and scientists keeping in mind healthy weight loss. It is a unique formulation containing 23 active health ingredients including essential vitamins and minerals. It consists of Fenugreek, Gudmar and Inulin.

Potential Risks / Benefits

There are no Potential risks in taking AirLite^{TM}.

STUDY OBJECTIVES

Objectives

Primary Study Objective

To evaluate the effect of AirLite™ in the following symptoms in patients with Obesity.

- Controlling Appetite
- To observe the change in patient's BMI from baseline to end of treatment.

Secondary Study Objective

- To Evaluate Safety and Tolerability of AirLite™.
- To evaluate the patients Quality of Life
- Global Assessment for overall improvement by the Subject.
- Global Assessment for overall improvement by the Investigator.

Study Outcome Measures

1. Appetite Control (Using a questionnaire to measure appetite)
2. BMI Measurements
3. Quality of Life Questionnaire
4. Global Assessments by Patient and Investigator
5. Incidences of any Adverse Events

INVESTIGATIONAL PLAN

Overall Study Design and Plan Description

This was a multi-centric, open label randomized study to **evaluate the safety and efficacy of AirLite™ in Patients with Obesity.** The study was conducted at 02 centers in India.

The Study was conducted in an out-patient setting. Total 50 subjects were enrolled in the study. Duration of patient participation of each patient was planned to be not more than 3 months.

The subjects were randomized to either of the groups on Day 0. The treatment phase started on Baseline day (Day 0).

a. Group 1: Subjects who used AirLite™ along with an exercise and diet plan for their weight loss.

b. Group 2: Subjects who continued their existing treatment for their weight loss, along with an exercise and diet plan.

STUDY FLOW CHART (To be Added)

Discussion of Study Design

This was a multi-centric, open label randomized study to **evaluate the Safety and Efficacy of AirLite™ in patients with obesity.** The study was conducted at 02 centers in India.

Total 50 subjects were enrolled in the study. Data from both the sites was pooled and then used for statistical analysis.

Study Period

The observation period in the study was not more than 3 months.

Selection of study population

Inclusion Criteria

Subjects meeting all of the following criteria were recruited for the Study:

1. Male or Female adults aged between 45 and 60 years (both inclusive)
2. Patients with BMI ranging from 25 kg/m2 to 35 kg/m2
3. Patients who were otherwise in good health or with controlled diabetes and/or hypertension
4. Patients with a desire to lose weight.
5. Readiness and ability to complete the 3-month study, according to the Investigators judgement, following the screening visit.
6. Patients who were accustomed to regular daily consumption of 3 main meals (breakfast, lunch, dinner)
7. Consistent and stable body weight in the last 3 months, prior to the screening visit (less than 5% self-reported change)
8. Subjects agreement to comply with study procedures:
    a. To take the IP as recommended
    b. For patients in the test group, to avoid the use of other weight loss and/ or management

products/ programs apart from the study plan.

c. To adhere to diet and exercise regimen during the study
d. To complete the patient diary and study questionnaires

9. Women of childbearing potential:
    a. Agreeing to use contraception measures
    b. Negative Urine Pregnancy Test at Screening
10. Patients willing to give written consent for participation
11. Patients who were willing to comply with the study procedures

Exclusion criteria

Subjects were excluded if ANY of the following conditions apply:

1. Pregnant women or women with potential for pregnancy and lactating patients
2. Patients with history of severe renal dysfunction
3. Patients with history of severe hepatic impairment
4. Patients with a history of hypersensitivity to the ingredients of the study drug.
5. Patients who were inappropriate for research participation for medical reasons (at discretion of treating physician).
6. Patients who had received any study medication or participated in any type of clinical study within 30 days prior to screening
7. Subjects suffering from malabsorption syndrome
8. Alcoholics or drug abusers
9. Untreated or unstable thyroid gland disorder or hypertension
10. Acute or chronic gastrointestinal disease or digestion/ absorption disorders (e.g.: inflammatory bowel disease, celiac disease, pancreatitis, etc.)
11. Type 1 Diabetes Mellitus or Untreated/ Unstable Type 2 Diabetes Mellitus.
12. GI surgery or liposuction 4 months before screening visit
13. History of eating disorders such as anorexia nervosa, bulimia, binge eating within the past 12 months prior to screening.
14. Patients who were unwilling to comply with study procedures

Treatment

Treatments Administered

Each subject in Group 1 was prescribed AirLite™ for no more than 3 months. The contents of the sachet had to be mixed thoroughly in water and taken once daily 10-15 minutes post breakfast. Apart from this the patients had to follow a standard diet and exercise.

Subjects in Group 2 had to continue with their ongoing treatment for obesity and a standard diet and exercise.

Table: Overall Subject Disposition by Treatment Group - All Participants	
	Total
	(N=100)
Total Patients Screened	50
Completed participants	100 (100.0%)

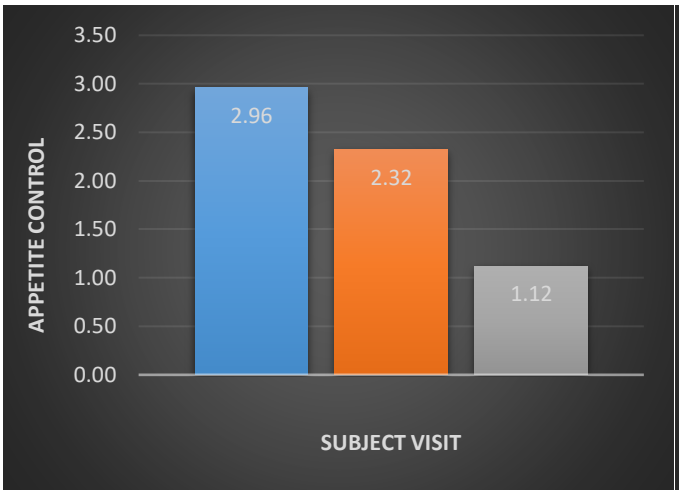
Note: Percentages were based on all randomized subjects.

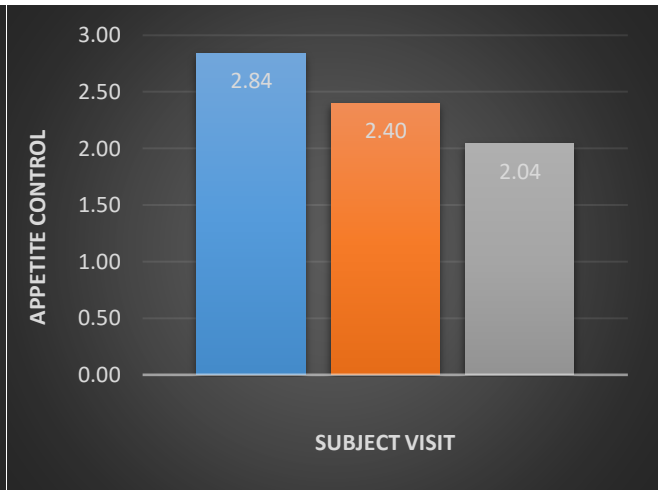
EFFICACY EVALUATION

Appetite Assessment

One of the key parameter for the study was to see the appetite control that was achieved by patients who were on Airlite, which was assessed on a scale of 0=Absent, 1= A little, 2= Moderate, 3=Strong, 4=Very Strong. The average score for appetite assessment at the baseline was 2.96 for patients with Airlite as compared to 2.84 for patients in the comparator group without Airlite, which meant that the baseline scores of the subjects from both the arms were comparable and both had a moderate to strong urge to eat food post their meals.

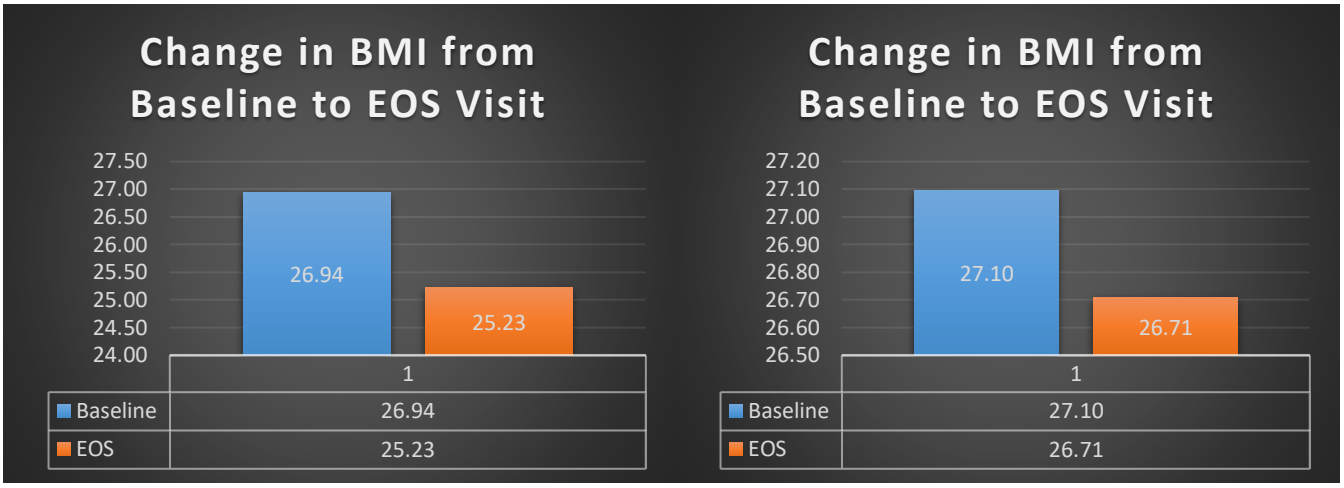
Post starting Airlite, at the end of 45 days there was a mild reduction of score to 2.32 in the Airlite group as compared to 2.40 in the comparator group, while it showed a drastic reduction to 1.12 in the Airlite group as against to 2.04 in the comparator group, which helps conclude that patients who were on Airlite had a much more better control over their appetite as compared to ones who did not had Airlite on a daily basis.





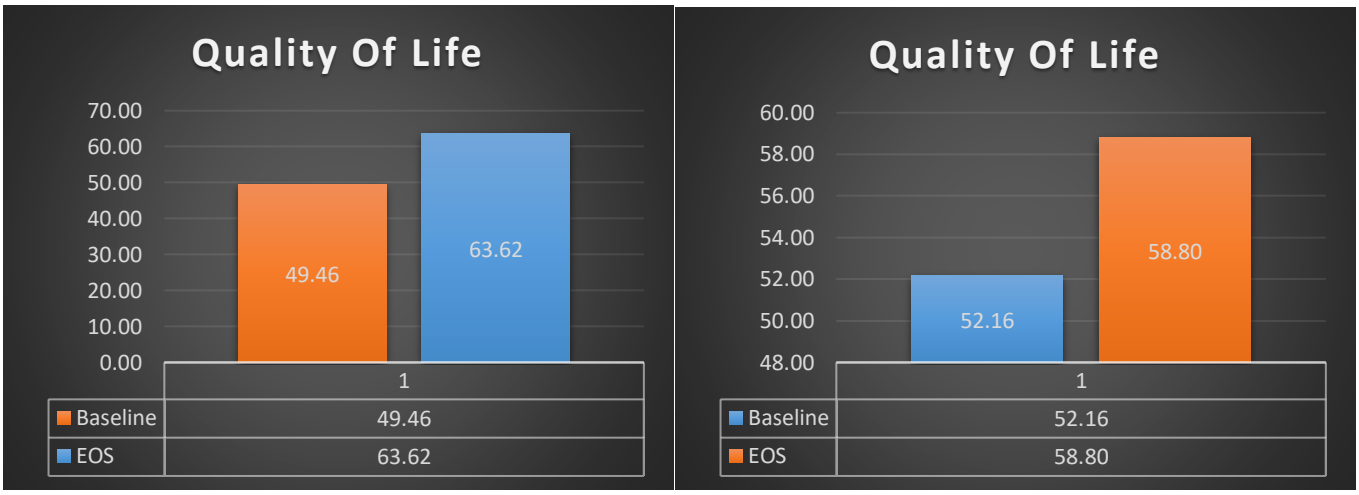
Change in Body Mass Index (BMI)

There was a distinct reduction in the average BMI of the Airlite group as compared to the comparator group. It was observed that there was a reduction of 6.34% in the BMI from 26.94 to 25.23 in the Airlite arm as compared to a reduction of 1.14% from 27.10 to 26.71 in the comparator arm.

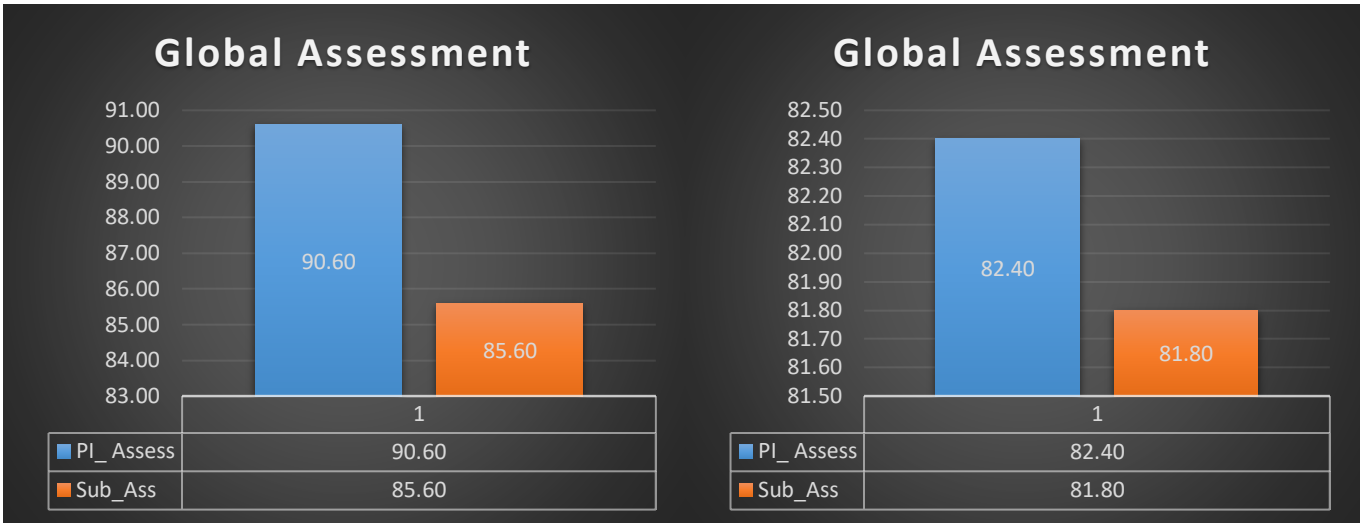


Quality of Life

Quality of life was assessed by the treating doctor at the baseline and at the end of the study. It was observed that patients in the Airlite group showed an overall improvement of 22.25% as compared to 11.29% in the group without Airlite. Patients in Airlite group reported feeling fresh, less lethargic and having more stamina to finish their daily routines as compared to the other group.



Global Assessment



The subjects and the treating doctor were asked their feedback on the overall satisfaction level in regard to the treatment and the outcomes noted for each of the patients. It was seen that in the Airlite group the treating doctor feedback was 9.05% higher as compared to the non – Airlite group. Whereas the patient feedback was 4.40% higher in the Airlite group as compared to the non – Airlite group at the end of the study.

SAFETY EVALUATION

AirLite™ is a Nutraceutical formulation. There were no major side effects observed or reported during the 3 months of observation period. During the entire observation period none of the participants reported any side effect.

DISCUSSION AND OVERALL CONCLUSIONS:

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health.

Causes of Obesity [1.5]

The fundamental cause of obesity and overweight is an energy imbalance between calories consumed and calories expended. Globally, there has been:

- an increased intake of energy-dense foods that are high in fat; and
- an increase in physical inactivity due to the increasingly sedentary nature of many forms of work, changing modes of transportation, and increasing urbanization.

Common health consequences of Overweight and Obesity [1.3],[1.4]

Raised BMI is a major risk factor for noncommunicable diseases such as:

- cardiovascular diseases (mainly heart disease and stroke), which were the leading cause of death in 2012;
- diabetes;
- musculoskeletal disorders (especially osteoarthritis – a highly disabling degenerative disease of the joints);
- some cancers (including endometrial, breast, ovarian, prostate, liver, gallbladder, kidney, and colon).

Reducing Overweight and Obesity

Overweight and obesity, as well as their related noncommunicable diseases, are largely preventable. Supportive environments and communities are fundamental in shaping people's choices, by making the choice of healthier foods and regular physical activity the easiest choice (the choice that is the most accessible, available and affordable), and therefore preventing overweight and obesity.

At the individual level, people can:

- limit energy intake from total fats and sugars;
- increase consumption of fruit and vegetables, as well as legumes, whole grains and nuts; and
- engage in regular physical activity (60 minutes a day for children and 150 minutes spread through the week for adults).

Goals of Weight Loss and Weight Management

The general goals of weight loss and management are:

1. To reduce body weight.
2. To maintain a lower body weight over the long term.
3. To prevent further weight gain.

Strategies for Weight Loss and Weight Maintenance [1.2]

Dietary Therapy: In majority of overweight and obese patients, adjustment of the diet to reduce caloric intake is required.

Physical Activity: An increase in physical activity is an important component of weight loss therapy since it leads to increased expenditure of energy.

Self-monitoring of both eating habits and physical activity: Objectifying one's own behavior through observation and recording is a key step in behavior therapy. Patients should be taught to record the amount and types of food they eat, the caloric values, and nutrient composition. Keeping a record of the frequency, intensity, and type of physical activity likewise will add insight to personal behavior

Stress management: Stress can trigger dysfunctional eating patterns, and stress management can defuse situations leading to overeating.

Stimulus Control: Identifying stimuli that may encourage incidental eating enables individuals to limit their exposure to high-risk situations

Problem Solving: Self-corrections of problem areas related to eating and physical activity. Approaches to problem solving include identifying weight-related problems, generating or brainstorming possible solutions and choosing one, planning and implementing the healthier alternative, and evaluating the outcome of possible changes in behavior.

Contingency management: Behavior can be changed by use of rewards for specific actions, such as increasing time spent walking or reducing consumption of specific foods Rewards can come from either the professional team or from the patients themselves

Cognitive Restructuring: Unrealistic goals and inaccurate beliefs about weight loss and body image need to be modified to help change self-defeating thoughts and feelings that undermine weight loss efforts.

Social Support: A strong system of social support can facilitate weight reduction.

Obesity is a chronic disease, and both the patient and the practitioner need to understand that successful treatment requires a life-long effort.

AirLite™ is a unique Nutraceutical formulation of scientifically chosen ingredients derived from food which help in supplementing the normal diet to manage weight without affecting the benefits derived from normal food. It increases fat metabolism, controls appetite and hinders absorption of fat. It is a complement to weight control and weight management program.

AirLite has been created by highly qualified doctors and scientists keeping in mind healthy weight loss. It is a unique formulation containing 23 active health ingredients including essential vitamins and minerals. It contains:

i. Fenugreek (Trigonella Foenum Graecum) contains saponins which stimulates insulin production, thereby controlling blood glucose
ii. Gudmar (Gymnema Sylvestre) helps reduce triglycerides, cholesterol and lower blood glucose
iii. Inulin is a fructooligosaccharide source of soluble fibers and hence helps in reduction of cholesterol absorption. It also suppresses cholesterol synthesis and stimulates bile acid synthesis

The synergy of the above ingredients enables AirLite™ to help in controlling appetite, fat reduction and fat control in the body.

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