Clinical Study Reports

(Uncontrolled studies)

Clinical Study Report

Study 1

Study Title

Clinical Evaluation of Efficacy and Safety of Kilose Capsule on Obesity: An Open Clinical Trial

Test Facility

M.S. Ramaiah Medical College Hospital, Bangalore, India.

Investigators

Prasanna Kumar KM

Sponsored by

THE HIMALAYA DRUG COMPANY
MAKALI, BANGALORE
INDIA

GCP-COMPLIANCE CERTIFICATE /DECLARATION

The study titled "Clinical Evaluation Of Efficacy And Safety Of Kilose Capsule On Obesity: An Open Clinical Trial''was conducted to prove the efficacy and safety of the formulation 'Kilose capsules'' in the year 2007 under the investigatorship of Prasanna Kumar KM and sponsorship of The Himalaya Drug Company. These studies were carried out around one to two decades back; when the principles of Good Clinical Practices were not officially established. However, We, The principal sponsor for the trial, would like to ensure that the trials were performed under good ethical considerations, existing and prevalent during the time as per the declaration of Helsinki and suitable ethical safety and precautionary measures were practised during the trial; safeguarding the rights and well-being of the trial subjects.

Study title:	Clinical Evaluation of Efficacy and Safety of Kilose Capsule on Obesity: An Open Clinical Trial
Name of the test drug/investigational product:	Kilose capsules
Indication studied:	Obesity
Design:	An open clinical study
Duration:	6 months
Dose and patient population:	Kilose 2-3 capsules twice daily before meals; 50 patients were selected for the study
Name and Address of the sponsor:	The Himalaya Drug Company, Makali, Bangalore – 562123, India.
Development phase of study:	Phase IV
Study initiation date (first patient enrolled or any other verifiable definition):	March 2007
Date of early study termination, if any:	None
Study completion date (last patient completed):	August 2007
Name and affiliation of principal or coordinating investigator(s) or sponsor's responsible medical officer):	Prasanna Kumar KM M.S. Ramaiah Medical College Hospital M.S.R.I.T. Post, Bangalore
Name and complete postal address of the company/sponsor signatory (the person responsible for the study report within the company/sponsor:	The Himalaya Drug Company, Makali, Bangalore – 562123, India.
Statement in compliance with Good Clinical Practices (GCP), including the archiving of essential documents:	Trial was carried out according to the protocol design and declaration of Helsinki principles. All final approved case record forms and a copy of all records (informed consent documents, laboratory data slips, source documents, test article dispensing records, etc.) which support the case report forms of the study was retained in the files of the responsible investigator for a period of 3 years.
Date of the report (identify any earlier reports from the same study by title and date):	This clinical study was conducted between March 2007 - August 2007. It is under publication. Clinical study report was generated as per ICH-E3 guidelines.

Synopsis

Name of sponsor/Company The Himalaya Drug Company, Makali, Bangalore – 562123, India.	**Individual study table referring to part of the dossier:** **Part:** Clinical documentation	***(For national authority use only)***
Name of finished product Kilose capsules		
Name of active ingredient Herbal formulation		

Title of study:	Clinical Evaluation of Efficacy and Safety of Kilose Capsule on Obesity: An Open Clinical Trial
Investigators:	Prasanna Kumar KM
Study centers:	M.S. Ramaiah Medical College Hospital M.S.R.I.T. Post, Bangalore
Publication (Reference):	Data on file
Studied period (Years): **(Date of first enrolment):** **(Date of last completed):**	6 months March 2007 - August 2007
Phase of development	Phase IV
Objectives:	To evaluate the safety and efficacy of Kilose on obesity
Methodology:	A fifty subjects, who were 20% more than the desirable body weight in the age group of 20-45 years, who were willing to give informed written consent were included in the study. All subjects were advised to take 2-3 capsules twice daily preferably before meals for 6 months. The response to therapy was evaluated initially, at 3 months and at the end of the study. The patients were statistically analysed using "Paired 't' Test".
Number of patients (Planned and analysed):	50/48
Diagnosis and main criteria for inclusion:	Obesity
Test product, **product dose** **mode of administration,** **batch number:**	Kilose 2-3 capsules twice daily before meals Oral
Duration of treatment:	6 months
Reference therapy, **dose and** **mode of administration,** **batch number:**	No reference therapy used.

Name of sponsor/Company The Himalaya Drug Company, Makali, Bangalore – 562123, India.	**Individual study table referring to part of the dossier:** **Part:** Clinical documentation	***(For national authority use only)***
Name of finished product Kilose capsules		
Name of active ingredient Herbal formulation		

Criteria for evaluation	
Efficacy:	Reduction in body weight, lipid profile and skin fold thickness
Safety:	Incidence of adverse effects
Statistical methods:	Statistical analysis was performed by "Paired 't' Test" using GraphPad Prism, Version 4.03 for windows, Graphpad Software, San Diego, California, USA.
Summary-conclusions	
Efficacy Results:	Among the 50 subjects enrolled in the study, 48 subjects completed the study. The subjects treated with Kilose showed significant reduction in body weight and in patients treated with placebo there was a minimal reduction which was not significant. The clinical parameters like high body weight, lipid profile and skin fold thickness showed clinical improvement from the 3rd month onwards, which further improved with the treatment of Kilose showing significance of p<0.001 at the end of the study. Almost all the patients treated with Kilose showed good overall response.
Safety Results:	No adverse effect were observed during study
Conclusion:	The efficacy of Kilose was studied in patients who were obese. At the end of the study, Kilose was associated with a significant reduction in Obesity of the patients. The weight loss was directly proportional to the initial weight. There were no clinically significant adverse reactions, either reported or observed, during the entire study period and overall compliance to the treatment was excellent. Therefore, it may be concluded that, "Kilose" is effective and safe in reduction of Obesity.
Date of the report (identify any earlier reports from the same study by title and date):	This clinical study was conducted between March 2007 - August 2007. It is under publication. clinical study report was generated as per ICH-E3 guidelines.

Investigator's statement

PRINCIPAL OR CO-ORDINATING INVESTIGATOR(S) SIGNATURE(S)

OR SPONSOR'S RESPONSIBLE MEDICAL OFFICER

STUDY TITLE: Clinical Evaluation of Efficacy and Safety of Kilose Capsule on Obesity: An Open Clinical Trial

STUDY AUTHOR (S): Prasanna Kumar KM

The above titled study was conducted by Prasanna Kumar KM at M.S. Ramaiah Medical College Hospital M.S.R.I.T. Post, Bangalore. under the direct sponsorship of The Himalaya Drug Company, between March 2007 - August 2007.This study is under publication. Since the applicant, The Himalaya Drug Company is seeking market authorization for 'Kilose capsules under the well established Use category '' of Herbal medicines, It become inevitable to upgrade the existing report in the old format to a CTD version. We, the Sponsor of the study [Now applicant for Market Authorization] herby affirm the overall responsibility of the upgradation of documents to the current Herbal CTD Format. We also assure that the present report judiciously represents the parent report in terms of its quality, integrity and content & No circumstances have been left unreported which may have affected the quality or integrity of the data or have a potential bearing on the validity and reproducibility of the study.

INVESTIGATOR/ OR SPONSORS RESPONSIBLE MEDICAL OFFICER

TABLE OF CONTENTS

List of Abbreviations and Terms

CRF – Case Record Form

Ethical considerations

The study protocol and related documents like informed consent form, case report form were reviewed by an Institutional Review Board (M.S. Ramaiah Medical College Hospital M.S.R.I.T. Post, Bangalore).

All study procedures including screening, informed consent procedures, subject recruitment, dosing, efficacy and safety assessment procedures and end of the study procedures were conducted in accordance with the ethical principles that have their origins in the declaration of Helsinki.

LISTING OF INVESTIGATORS

Sl. No.	Principal/Co-investigator	Designation	Institutional Affiliation
1.	Prasanna Kumar KM	Prof. & Head Dept. of Endocrinology	M.S. Ramaiah Medical College Hospital M.S.R.I.T. Post, Bangalore

INTRODUCTION

Rationale for the study: Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy and/or increased health problems. Obesity is associated with many hazards and is recognized as a risk factor in the aetiology of premature death, diabetes mellitus, hypertension, atherosclerosis, gall bladder problems and certain types of cancer. Inactivity leads to obesity and vice-versa, thus forming a vicious circle. A number of agents have been evaluated for their efficacy and safety in the management of obesity. Amphetamines have a well defined abuse potential and drugs like diethylpropion and fenfluramine cause appreciable undesirable symptoms related to depression and pulmonary hypertension.

Aims and objectives: To evaluate the effect of Kilose on obesity.

Target population: Fifty patients having body weight more than 20% of the desired weight.

Treatment duration: 6 months

Primary end points:

- Reduction in the body weight

Secondary end points:

- To assess the safety profile of Kilose capsules
- To find out, incidence of adverse events during the study period, and overall compliance to the drug treatment.

Trial was carried out according to the protocol design and declaration of Helsinki principles. All final approved case record forms and a copy of all records (informed consent documents, laboratory data slips, source documents, test article dispensing records, etc.) which support the case report forms of the study was retained in the files of the responsible investigator for a period of 3 years.

INVESTIGATIONAL PLAN

The study was undertaken in 50 cases having body weight more than 20% than the desired weight

Inclusion Criteria:

- Patients having body weight 20% more than the desired
- Patients of either sex
- Patients Aged more than 18 years
- Willing to sign inform consent document

Exclusion criteria:

- Pregnant patients, patients with hormonal and other systemic disorders
- Patients unwilling to provide informed consent or abide by the requirements of the study

Methodology

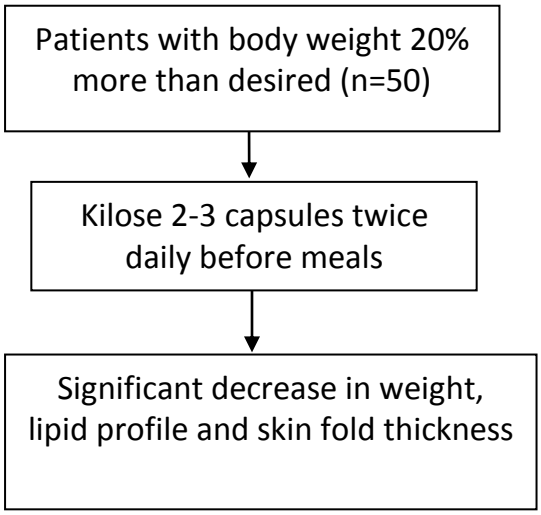
A fifty subjects aged between 25 to 48 years, with 20% more body weight than the desired, who were willing to give informed written consent were included in the study. All subjects were advised to use take either Kilose or similar looking placebo and advised to take 2-3 capsules twice daily preferably 30 minutes before meals for 6 months. Patients were told to restrict themselves to the "Kilose" as the only treatment and resort to no other active treatment intervention during the study period was allowed. The response to therapy was evaluated initially, at 3 months and at the end of the study. The criterion for evaluation was the signs and symptoms like reduction in body weight, decrease in skin fold thickness and lipid profile.

Trial was carried out according to the protocol design & declaration of Helsinki principles. Investigators followed the procedure as mentioned in the protocol at each stage of the study by taking subject's proper consent, screening assessment, recruitment of only those subjects who fulfilled all the criteria, follow-up of subjects on their scheduled visit, assessment of all the parameters at all visits, maintaining the investigational reports of all the subjects, maintaining Investigational product, proper filling up of CRF's, giving proper instructions to the subjects about use of Investigational product and their schedule visits. Any of the subjects deviating from the protocol was not considered as completed case. In case of occurrence of Adverse Event and/or Serious Adverse Event, Investigator reported the same to the sponsor and Institutional Review Board within 24 hrs from the time of occurrence of the Adverse Event and/or Serious Adverse Event. Investigators at site as per the declaration of Helsinki principles maintained source documents. At each study site, site related documents declaration of Helsinki principles, Institutional Review Board Approval Letter, Confidentiality Agreement,

Clinical Trial Agreement, Financial Agreement, CV of Site Personnel, Study protocol, Case Report Form, Investigator's Brochure, Subject Protocol, Consent Form (Language- English), Screening Log, Subject Enrollment Log, Sample Accountability Record, Monitoring Log Record, Trial Supply Record documents, Signature Sheet was maintained in site record file.

STUDY DESIGN AND PATIENTS

Open label study of 50 patients.



Dosage

The dose to start was: Kilose 2-3 capsules twice daily before meals for 6 months

At the monitoring visits, the monitor checked whether the study is being conducted as per protocol and that there are no unacceptable protocol deviations. The monitor ensured that the investigator is maintaining accurate, timely, and complete records and makes them available to the monitor for checking. Various steps was taken depending on the follow up discipline maintained by the subjects, to ensure that the subject follow up as per the specified schedule. Monitoring Log Record was maintained at site as well as with monitor to ensure the regular monitoring visits to the sites.

DATA QUALITY ASSURANCE

1. Prior to the enrollment of any subject at the site the investigator and the monitor reviewed the protocol and all study related procedures, information of Investigational product, Procedures for reporting adverse events, Procedure for completing the CRFs.

2. The monitor on a regular basis visited the study site. During these visits, information recorded in the CRFs was verified for accuracy completion and legibility.
3. The monitor reviewed the informed consent, IP accountability, storage and study progress.
4. The monitor verified that investigator followed the approved protocol and the study procedures.
5. Study subject data was kept confidential. CRFs or any other documents identified a subject by initial and numbers only.
6. The investigator kept in investigator file a subject identification list and Screening / enrolment log (including name, age, address)

EFFICACY AND SAFETY EVALUATION

The efficacy was assessed based on the symptomatic reduction in weight, lipid profile and skin fold thickness.

In case of occurrence of Adverse Event and/or Serious Adverse Event, Investigator reported the same to the sponsor and Institutional Review Board within 24 hrs from the time of occurrence of the Adverse Event and/or Serious Adverse Event. Investigators at site as per the declaration of Helsinki principles maintained source documents.

Application of various statistical tests depended on availability of the quality and complete data, care for which was taken during data collection.

1. The final analysis was done at the end of completion of study.
2. There was reporting & descriptive analysis of withdrawn, drop out & protocol deviation cases. The missing, unused & spurious data was identified & appropriately taken care of during the final analysis.
3. Statistical analysis of the final data was done.

RESULTS

Among the 50 subjects enrolled in the study, 48 subjects completed the study. The subjects treated with Kilose showed significant reduction in body weight and in patients treated with placebo there was a minimal reduction which was not significant (Table 1). The clinical parameters like high body weight, lipid profile and skin fold thickness showed clinical improvement from the 3rd month onwards, which further improved with the treatment of Kilose showing significance of $p<0.001$ at the end of the study. Almost all the patients treated with Kilose showed good overall response (Table 2, 3).

There were no clinically significant adverse reactions, either reported or observed, during the entire study period and overall compliance to the treatment was excellent.

DISCUSSION

Obesity has become a major public health problem mainly due to improper eating habits and physical inactivity. It has been recognized as a heterogenous group of disorders rather than a single disorder that is accompanied by an increased risk of morbidity and mortality. By definition, obesity exists when adipose tissue comprises a greater-than-normal fraction of total body weight. It can be assessed in terms of height and weight, and weight can be related to height and age. An alternative method of estimating obesity is the body mass index or BMI (optimum BMI 19-25). The degree of adiposity can be assessed by skin fold thickness in various areas of the body together with height, weight and age. Certain patterns of obesity are less desirable from the health point of view, such as fat deposits around the waist and flank as evidenced by a high ratio of waist-to-hip circumference, which is associated with a greater health risk than fat deposition at the hips. The Framingham study demonstrated that a 20% excess over desirable weight clearly imparted a health risk. When energy intake exceeds expenditure, the excess calories are stored in adipose tissue and this net positive balance results in obesity.

Kilose Capsule is a herbal formulation that ensures favorable effect on weight reduction and normalization of lipid profile. It is a researched Ayurvedic product and can be safely used without any side effects. Kilose contains *Achyranthes aspera, Balsamodendron mukul, Garcinia cambogia and* Triphala and the effect of the formulation is due to the synergistic action of the herbs.

CONCLUSION

The efficacy of Kilose was studied in patients who were obese. At the end of the study, Kilose was associated with a significant reduction in Obesity of the patients. The weight loss was directly proportional to the initial weight. There were no clinically significant adverse reactions, either reported or observed, during the entire study period and overall compliance to the treatment was excellent. Therefore, it may be concluded that, “Kilose” is effective and safe in reduction of Obesity.

TABLES

Table 1: Effect of Kilose on Obesity			
Parameter	**Baseline**	**At the end of study**	***p* value**
Mean body weight (kg)	76.6 ± 6.2	67.2 ± 2.4	0.01

Table 2: Effect of Kilose on skin fold thickness (mm)			
Skin fold	**Baseline**	**At the end of study**	***p* value**
Triceps	28.33 ± 2.36	25.80 ± 2.87	0.01
Subscapular	33.22 ± 9.90	32.11 ± 9.77	NS
Mid axillary	32.52 ± 10.83	31.33 ± 10.29	NS

Table 3: Effect of Kilose on lipid profile (mg %)			
Parameter	**Baseline**	**At the end of study**	***p* value**
Serum cholesterol	285.31 ± 29.81	179.89 ± 37.19	0.01
Serum triglyceride	232.73 ± 97.41	111.35 ± 43.86	0.01
HDL	39.94 ± 7.97	40.57 ± 7.63	NS
LDL	166.89 ± 47.50	102.74 ± 41.29	NS