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# Evaluation of plant based formulation on adolescent obesity and its associated bio-markers: A randomized, double blind, placebo controlled study

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**Summary**

*Objective:* Obesity and overweight are the fifth most fatal diseases leading to an increased rate of morbidity and mortality in global population, with its incidence increasing drastically. Taking this into consideration we have conducted the present study in order to explore the efficacy of plant based formulation in the management of adolescent obesity and its associated biomarkers.

*Design:* Randomized, double blind, placebo controlled trial was conducted in 130 obese adolescent of both sexes, with BMI above 25 kg/m$^2$. The subjects were randomly assigned into test formulation group (TFG) and placebo group (PG). TFG received two 500 mg capsule containing test formulation whereas, the PG received two 500 mg of cellulose powder containing capsule daily for 3 months. The parameters such as blood pressure, inflammatory cytokines, adipokines and lipid profile were assessed in all subjects pre and post treatment.

*Results:* There was a considerable improvement in the levels of lipid profile, inflammatory cytokines, adipokines and blood pressure after treatment in TFG compared to PG. The statistical difference obtained between the groups after three months of treatment for the various biomarkers are given as mean with 95% CI for BMI ($-1.4 \pm 0.6$ ($-2.5$ to $-0.7$)), total cholesterol mg/dl ($-20.9 \pm 5.0$ ($-30.8$ to $-11.0$)), triglyceride mg/dl ($-12.9 \pm 5.7$ ($-23.9$ to $-1.2$)), HDL-c mg/dl ($7.2 \pm 0.8$ (5.6–8.8)), IL-6 ($-0.7 \pm 0.1$ ($-0.9$ to $-0.6$)), hs C-reactive protein (CRP) mg/l($-1.0 \pm 0.01$ ($-1.2$ to $-0.8$)), adiponectin μg/ml($4.9 \pm 0.4$ (4.2–5.7)), leptin ng/ml ($-8.0 \pm 1.4$ ($-10.7$ to $-5.3$)), diastolic blood pressure (DBP) mmHg ($-10.4 \pm 0.8$ ($-12.0$ to $-8.7$)) and systolic blood pressure (SBP) mmHg ($-6.7 \pm 0.7$ ($-8.1$ to $-5.3$)). Also, there was a statistical significance within group TFG.

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*Conclusion:* The study concludes that the test formulation may prevent the future cardio vascular risk incidence in obese adolescents by reducing inflammation, overweight, lipid profile and by regulating adipokines. Thus it may help to improve the health pattern in obese patients with least side effects.


## Introduction

Conventional drug's Orlistat, Sibutramine, Tesofensine, etc., though efficient, have many side effects leading to cardiovascular risks, hypertension, depression, anxiety, on their long term use. Traditional medicine has evolved since Vedic period, i.e. 6000 years before Christian era. Ayurveda has drugs for many diseases and one among them is obesity or ''Medoroga.'' It is quoted in ayurveda that it is comparatively easy to help an underweight person, rather than an overweight.[1] Thus taking the lead form ayurvedic system of medicine we have formulated a test formulation that might act on obesity and its associated complications.

### Rational for selection of plants

Plants considered for the preparation of test formulation in the present study are *Hippophae rhamnoides*, *Dioscorea bulbifera* and *Terminalia chebula*. These plants have a good literature back up on its pharmacological action and its administration has been recorded since ancient times. Obesity is a metabolic disorder with multi targeted biomarkers such as body mass, lipid profile, circulating blood pressure, adipokines and inflammatory cytokines. A single plant may not be sufficient to act on all the above targets; hence, there is a need for combination of plants showing anti-inflammatory, anti-obesity, hypotensive and anti-oxidant properties. Preclinical study had been conducted for the test formulation, according to the results obtained human effective dose was determined.

The pharmacological literatures quoted on these plants are, *H. rhamnoides* leaf tea has potential anti-obesity and antioxidant effects, which mediates the regulation of lipid and antioxidant metabolism in high-fat diet-induced obese mice.[2] Leaves of *H. rhamnoides* are prospective in the management of obesity and related disorders.[3] It is known from ayurvedic literature that several species of *Terminalia* are used for obesity therapy.[4] The tree bark powder of *Terminalia sp*, possess antioxidant function comparable to vitamin-E and besides it has hypocholesterolemic effect. Aqueous extract of *D. bulbifera* bulbs posses anti-hyperglycaemic and anti-dyslipidemic activity in the high fat diet induced mice.[5] The presence of phytoestrogen in *D. bulbifera* can prevent the early estrogen deficiency which leads to dyslipidemia, atherosclerosis and cardiovascular events among women.[6,7]

### Adolescent obesity and associated complication

Obesity is defined as abnormal or excessive fat accumulation. It is the risk factor for a number of chronic diseases including diabetes, cardiovascular diseases and cancer, leading to high mortality and morbidity.[8]

Positive correlation exists between adipose tissue and expression of TNF (tumor necrosis factor) alpha gene in obese patients.[9] Obese patients have increased level of plasma pro-inflammatory cytokines, including hsCRP (high sensitive C-reactive protein).[10] Hypoadiponectinemia contribute to a low-grade systemic chronic inflammatory state and impaired glucose tolerance, which leads to obesity. Dysfunction of adipose tissues is responsible for excess release of interleukin-6 (IL-6) and ignorable production of adiponectin.[11,12] The effect of adiponectin is also assessed in relation to glucose tolerance as well as lipid metabolism.[13,14] It also plays an important role in cardiovascular disorders[15,16] and is inversely associated with markers such as TNF-$\alpha$ and CRP.[17] Researchers have also found that obese and overweight children have 3 fold more risk of developing hypertension in comparison to non-obese.[18–22]

In the light of the above facts, a randomized, double blind, placebo-controlled trial was designed to investigate the anti-obesity effect of plant-based formulation, by analyzing its efficacy in regulating the biomarkers associated with obesity.

## Materials and method

### Test formulation preparation

The plants were collected from the forests of north east part of India; it was then identified by Dr. N.K. Dubey, Plant Taxonomist, Department of Botany, Banaras Hindu University, Varanasi, India. The voucher specimens were maintained in the Institute.

The test formulation was a hydroalcoholic extract of all three plants, and each 500 mg capsule contains *D. bulbifera* (175 mg/kg), *T. chebula* (160 mg/kg) and *H. rhamnoides* (137 mg/kg) and remaining was additive (calcium carbonate 90% and starch 10%). Both test formulation and placebo capsules were manufactured by Varanasi Bioscience Pvt Ltd, UP, India, and was administered twice a day (BID).

The test formulation contained chief biomarkers such as chebulic acid from *T. chebula*, quercetin and isorhamnetin from *H. rhamnoides*, and diosgenin from *D. bulbifera*, etc., which were isolated and quantified for their active concentration in each batch. There was no difference in the odor and appearance of both placebo and test formulation capsules.

### Study design

The study was a randomized, double bind, placebo controlled, in which 130 obese adolescent were included after screening. Using SAS software the subjects were randomly