PIONEERING ZERONA TREATMENT IN INDIA.

Dr.Deepak V. Chaturvedi,

M.B.B.S; M.D.(Medicine)
Metabolic Physician, Diabetologist,
Antiaging, Obesity & Hormones Specialist.

" Increased waist circumference is the single most important predictor of Metabolic Syndrome"

The Zerona low level LASER device has been clinically validated and FDA cleared to reduce the circumference of the waist, hips, and thighs.

A double blind, randomized, placebo controlled trial of a 2 weeks non invasive laser (Zerona) treatment conducted from May 2007 to June 2008 across multiple private practice sites in United States of America. Sixty Seven volunteers between the ages of 18-65 years with BMI between 25-30 kg/m². Participants were randomly assigned to receive low level laser treatments or a matching sham treatment three times per week for two weeks. Results of the study are as follows:

Table 1: Pre-procedure BMI measurements for treatment groups (n=67)

BMI (kg/m^2)	Test group (n• 35)	Control group (n• 32)	Difference
Mean	25.74	26.05	0.31

BMI, body mass index.

Table 2: Mean Change in Total Combined Circumference measurement s from baseline to endpoint for treatment groups (n=67):

	Test group (n• 35)	Control group (n• 32)
Mean reduction in total circumference (in.)	• 3.521	• 0.684

In., inches.

Figure 1: Total circumference measurements across study duration for all participants (n=67):

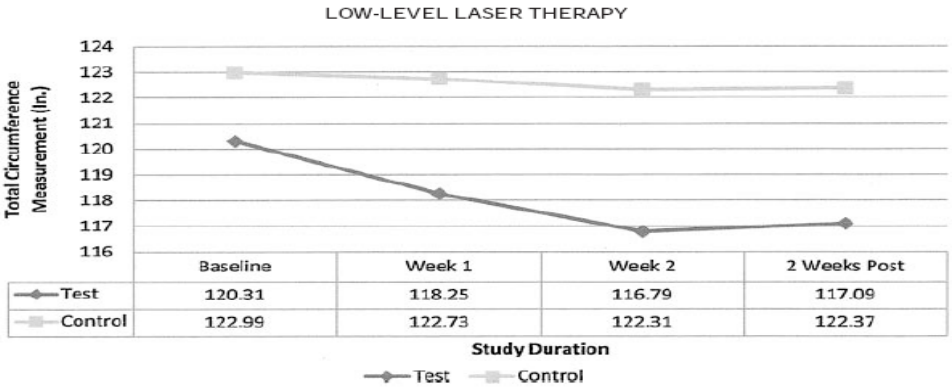


Table 3 : The difference in change in total circumference measurements between evaluation time points between treatment groups (n=67):

Mean reduction (in.)	Test group (n• 35)	Control group (n• 32)	Difference between groups
Baseline—week 1	• 2.06	• 0.27	• 1.794
Baseline—week 2	• 3.52	• 0.68	• 2.838
Baseline—2 weeks post	• 3.21	• 0.62	• 2.953
Week 1—week 2	• 1.46	• 0.42	• 1.044
Week 1—2 weeks post	• 1.15	• 0.36	• 0.799
Week 2—week 4	• 0.31	• 0.06	• 0.245

In., inches.

Figure 2: Circumferential measurements of the waist at each evaluation point for all participants (n=67)

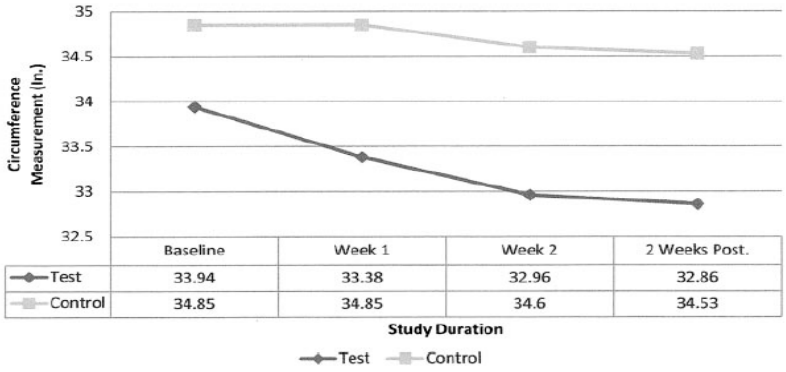


Figure3: Circumferential measurements of the hip at each evaluation point for all participants (n=67):

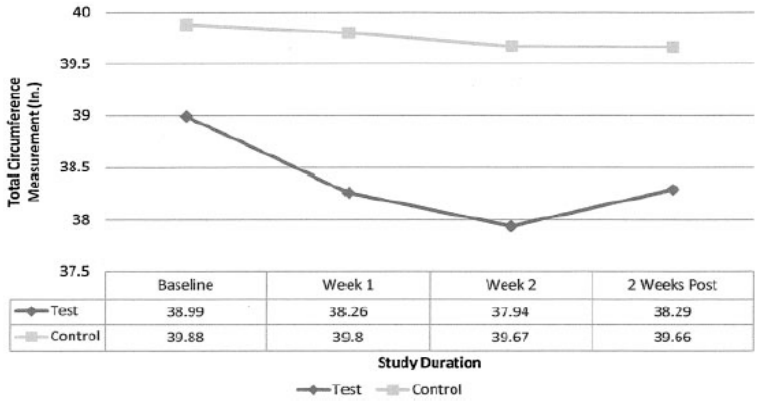


Figure4: Circumferential measurements of right thigh at each evaluation point for all participants (n=67):

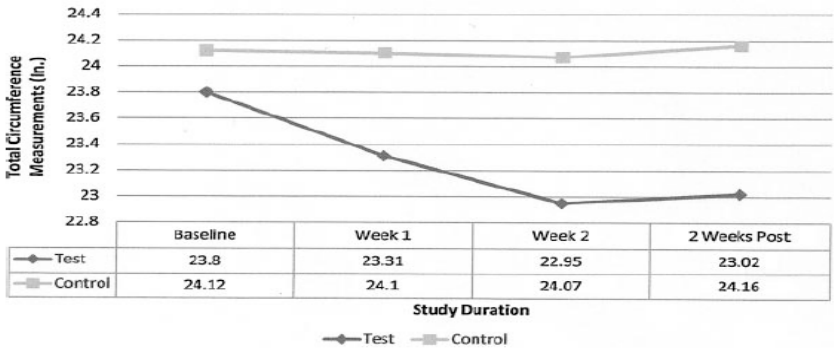
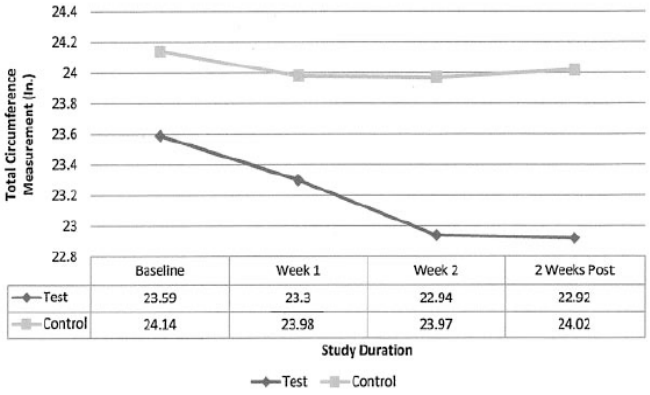
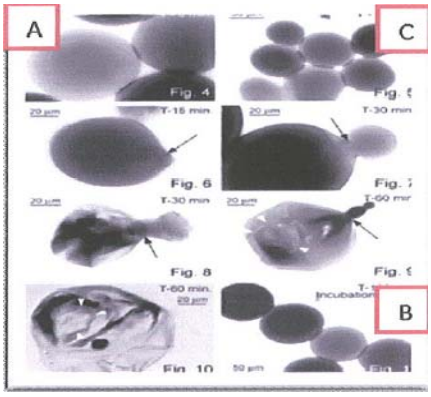


Figure 5: Circumferential measurements of left thigh at each evaluation point for all participants (n=67):

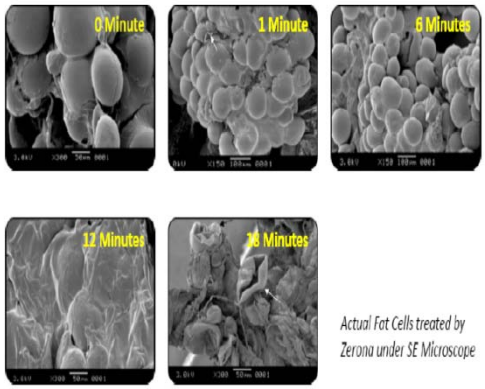


Histological evidence elucidates that Zerona modulates subcutaneous fat adipocytes causing the release of stored intracellular fatty material resulting in the reduction of adipocyte mass. Subsequent to fatty material release, the debris is safely absorbed and mobilized by the lymphatics and circulatory system yielding a statistically significant decrease in the overall circumferential measurements in two weeks.

Figure 6: Zerona induced release of noxious stored fatty material:

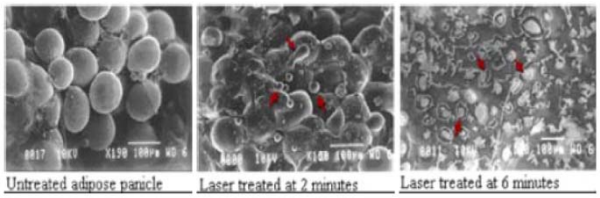


A: Non-treated cells. B: Bottom right image illustrates control sample. C: Middle sequence of images received Zerona illustrates release of stored fatty material.



Actual Fat Cells treated by Zerona under SE Microscope

Emulsification of adipose particles subsequent to laser irradiation



Untreated adipose panicle | Laser treated at 2 minutes | Laser treated at 6 minutes

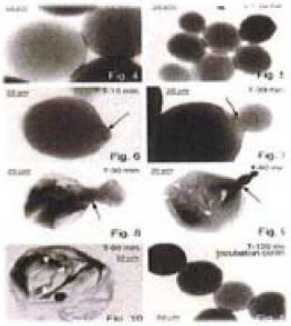
The Zerona Effect On Fat Cells

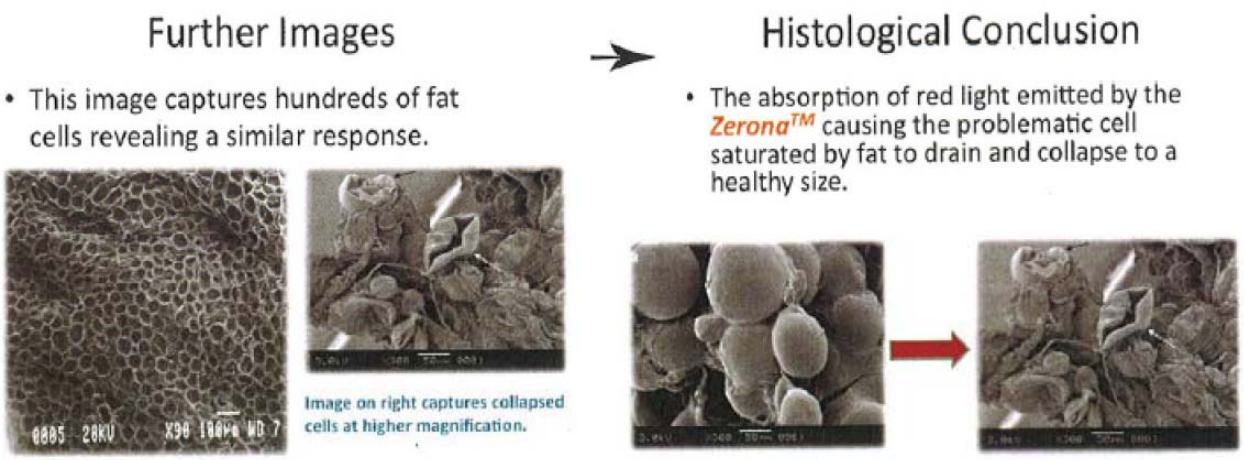
- The absorption of light and consequential secondary reaction cause an opening or pore to form within the cell's protective barrier.
- Weakening the structual support of the cell

The blue arrow identifies the protective barrier of the cell.
The red arrow reveals the deterioration of the protective barrier of the cell.
This image was taken 6 minutes after **Zerona** simulation at x60,000 magnification

The Result of the Pore

- The once voluminous fat cell collapses because of the laser induced opening.
- Similar to if a gap was created in a dam, the water would rush out.





Coupled with the placebo controlled, double blind, randomized, multicentered clinical investigation which determined the efficacy of the application was a study to assess fasting lipid levels in nineteen patients. Results indicated a statistically significant reduction in both triglyceride and total cholesterol serum levels (Table 4):

Table 4: Reduction in serum total cholesterol levels (n=19)

Total cholesterol (n=19)	Baseline (mg/dL)	Study end (mg/dL)
Average	191.11	178.79*
Std. dev.	43.34	36.46

*Statistically significant $p<0.01$

The effect on serum lipid levels reinforces an underlying health benefit associated with the application of Zerona.

Adipose tissue (AT) is defined as an endocrine organ responsible for the synthesis of bioactive peptides which participate in autocrine, paracrine, and endocrine pathways. Furthermore, AT is composed of a vibrant collection of cells including fibroblast, pre-adipocytes, adipocytes, immune cells, and a variety of other cells all embedded within the framework of connective tissue. It is believed that several adipose derived bioactive substances are released through a coordinated fashion with other cells located in AT utilizing paracrine or autocrine pathways.

The diverse collection of cytokines and bioactive molecules (adipokines) released by AT have been shown to modulate lipid metabolism and homeostasis, energy consumption and expenditure, immunity, insulin sensitivity, and blood pressure. As the largest organ in the body, the orchestra of adipokines secreted and their direct participation in an extensive communication network involving multiple tissue systems delineates function far greater than as a simple reservoir for metabolic components.

An individual classified as overweight or Obese possesses adipocytes that have undergone structural modifications subsequent to excessive nutrient consumption. The expansion in adipose mass and volume increase of adipocyte induces macrophage infiltration altering adipocyte behavior resulting in the release noxious adipokines that can contribute to the onset of diabetes, hypertension and cardiovascular diseases. Adipocyte function and behavior is directly related to its mass. Following period of excessive nutrient consumption, adipocytes become hypertrophic (enlarged).Adipocyte expansion is believed to interrupt the cell yielding pathological consequences. Adipocyte hypertrophy has been shown to directly disrupt angiogenesis, adipogenesis, ECM dissolution and reformation, lipogenesis, Growth factor production, Glucose metabolism, Lipid metabolism, Enzyme production, Immune response and hormone reduction. Furthermore, studies have illustrated an alteration in gene expression reporting an up regulation in pro-inflammatory factors including classic cytokines and complement factors promoting the onset of metabolic disorders like atherosclerosis. Participating in paracrine and autocrine signaling, adipocyte impairment may account for metabolic dysfunction as AT communicates with multiple body systems including nervous, Immune, skeletal, cardiovascular and gastro-intestinal.

Adipocyte hypertrophy affects AT function increasing the patient's risk of developing serious metabolic disorders. An important therapeutic strategy for overweight or obese patients is to significantly reduce adipocyte volume to prevent the onset of obesity related co-morbidities. In a lean state, adipocyte release beneficial hormones and bio active substances that can prevent insulin resistance, diabetes and atherosclerosis. Immediate reduction of the adipocyte mass is necessary to restore proper cell function and behavior. The Zerona, FDA cleared for the reduction of subcutaneous fat volume, as measured by circumferential measurement serves as a viable therapy for adipocyte volume reduction without destruction.

The adipocyte destructive procedures are not advisable as these procedures devoid the body from physiological/endocrine/regulatory roles of adipocytes. It's not the adipocyte tissue but its increased size due to excessive accumulation of fat which is required to reverse the deleterious effects of obesity.

Reduction in adipocyte cell volume can potentially reestablish proper adipocyte function triggering production of valuable bioactive substances. A series of blood analysis were conducted to elucidate the medical utility of Zerona. Investigations included the assessment of post therapy levels of serum Cholesterol, Triglycerides, LDL, HDL and Leptin.

Leptin represents an adipocyte derived cytokine whose role has been well documented and illustrates the importance of adipocyte function. Leptin is believed to function as a "Starvation signal" mitigating hyperphagia, slowing the metabolic rate and modulating hormone levels. Plasma Leptin levels are found elevated in patients with larger fat mass compared to patients to the patients with the smaller mass. Although elevated levels of Leptin have been shown to reduce body weight and food consumption in rodents, levels are found to be elevated in obese humans with limited functionality, illustrating "Leptin Resistance". Loss of Leptin sensitivity dampens mechanisms that regulate hunger and metabolic metabolism increasing the risk of obesity related co morbidities. Following a 2 weeks series of 6 Zerona treatments, patients Leptin levels were significantly lower compare to baseline, evidence that Zerona modulates adipocyte functions (Table 5).

Table 5: Leptin levels following a 2 week Zerona treatment:

Leptin (n=22)	Baseline	Study end (6/1/09)
Average	29.49	14.60*
Std. dev.	16.54	11.53

*p<0.0001. Zerona patients participated in Ketosis (zero-sugar) diet

Performing an equally important role is Adiponectin, a hormone solely produced by adipocytes. Similar to Leptin, synthesis of Adiponectin is tightly coupled with AT fat mass, demonstrating a negative relationship with larger masses. Individuals who are classified as Obese display a lower plasma Adiponectin concentration when compared to non obese group. Furthermore, a direct correlation between low Adiponectin levels and the onset of type 2 Diabetes has been reported. Numerous articles have reported anti-atherosclerotic effects of Adiponectin when adipocyte mass is maintained at lean levels. Adipocyte hypertrophy reduces the synthesis of Adiponectin resulting in the up regulation of TNF-α, Insulin resistance and hyperlipidemia.

Excessive adipose tissue mass deregulates AT function having deleterious endocrinologic and immunologic effects. Zerona has earned FDA clearance as safe and effective therapeutic device for the reduction of adipose mass of the waist, hips and thighs. The cosmetic slimming induced by Zerona represents a limited benefit as the device may serve as an effective means for promoting the release of anti-diabetic and anti-atherosclerotic adipokines.