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### **Studies on the anti obesity activity of ethanolic extract of Centella Asiatica in Triton-X, High fat diet and Progesterone induced obesity**

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#### ABSTRACT

Our aim in the present study was to evaluate the anti-obesity activity of Centella asiatica in high fat diet (HFD), Triton-X and Progesterone induced obese rats and mice. Ethanolic extract of centella asiatica was prepared and the extract is tested with different doses (100mg/kg, 200mg/kg, 400mg/kg) and the efficiency of EECA is comparable to that of orlistat (20mg/kg b.wt), a standard anti-obesity drug. Although food consumption was moderately increased in HFD-fed rats, EECA administration significantly reduced weight gain in them. Serum total cholesterol (TC), triglycerides (TG), low density lipoproteins (LDL) and very low density lipoproteins (VLDL) levels were significantly ( $P < 0.05$ ) lowered, while high density lipoproteins (HDL) increased in EECA administered with different (HFD, Triton-X, Progesterone). Based on our results we demonstrate that EECA has potential anti-obesity activity.

**Keywords:** Centella asiatica, HFD (high fat diet), progesterone, lipid levels.

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## INTRODUCTION

Obesity has turned up as one of the major health concerns in the 21st century and is one of the leading causes of preventable death. Obesity is a term applied to excess body weight with an abnormally high proportion of body fat. Thermodynamically speaking, imbalance between energy intake (feeding) and energy expenditure (physical activity) leads to obesity<sup>(1)</sup> Development of obesity is, however, more complicated due to; sedentary life style, genetic factors, medical illness, microbiological aspects, social factors and neurobiological mechanisms are also involved<sup>(2)</sup>.

A growing public health concern is that the prevalence of obesity among children aged 6–19 is up to 16.5% in the USA and has also increased in Europe, Asia, Africa and South American countries Despite increased attention given to overweight and obesity by virtually every major body concerned with public health, including the National Institutes of Health (NIH) the Centers for Disease Control the United States Department of Agriculture<sup>(3)</sup> and the World Health Organization primary and secondary prevention efforts have generally been disappointing. Obesity impacts many facets of society. For example, it is economically costly to society (World Health Organization, 1998) increases mortality rate reduces quality of life (Fontaine, Bartlett &Barofsky,2000) and increases the risk of various morbidities<sup>(4)</sup> Extreme obesity has been estimated to truncate the lifespan of young adults by 5–20 years

The medical problems caused by obesity begin at the head and end at the toes and involve almost every organ in between. Several of these problems contribute to the earlier mortality associated with obesity and include coronary artery disease, severe hypertension that may be refractory to medical management, impaired cardiac function, adult-onset (type 2) diabetes mellitus, obesity hypoventilation and sleep apnea syndromes, cirrhosis, venous stasis and hypercoagulability with an increased risk of pulmonary embolism, and necrotizing panniculitis. Ayurvedic system of medicines is one of the oldest system of medicine having a history of more than 3000 years. Several prototype derived from these herbal medicines are in use for various kind of disease and disorders. It not only gives new molecule but also with newer mechanism of action, hence is called Gold mine. Several infusions or decoctions of plants used in traditional medicine to reduce obesity could be utilized to delete the clinical side effects of the current chemically formulated antiobesity agents.

A large study of literature indicates that substantial progress has been made concerning our knowledge of bioactive components in plant foods and their links to obesity. For the present research protocol we have chosen *Centella asiatica* to evaluate its anti-obesity activity. As per the

literature survey<sup>(5)</sup> it was found that flavonoides, sitosterols, tannins and saponines have shown the anti-obesity activity by various mechanisms, the selected plant have shown the presence of some common phytoconstituents in their extracts like sitosterols, triterpenoids, flavonoids etc. Moreover traditional system of Indian medicine also claims for its anti-obesity activity. With this back ground we have selected these plants for its phytochemical analysis, screening its anti-obesity activity.

Pre-clinical evaluatory study of the plant extract was done by using three animal models i.e. high fat diet induced obesity, triton x-100, progesterone induced obesity, in rodents(rats and mice).

### **Plant Introduction:**

*Centella asiatica* (CA) is a very important medicinal herb used in the orient<sup>(6)</sup>, which is also becoming popular in the West<sup>(7)</sup>. Commonly known as mandukparni or Indian pennywort or jalbrahmi, it has been used as a medicine in the Ayurvedic tradition of India for thousands of years and listed in the historic 'Sushruta Samhita', an ancient Indian medical text<sup>(8,9)</sup>.

### **Distribution of plant:**

The plant is found throughout India growing in moist places up to an altitude of 1800 m. It is found in most tropical and subtropical countries growing in swampy areas, including parts of India, Pakistan, Sri Lanka, Madagascar, and South Africa and South pacific and Eastern Europe.

### **Description of plant:**

*Centella asiatica* (CA), a clonal, perennial herbaceous creeper belonging to the family *Umbellifere* (*Apiceae*) It is a tasteless, odourless plant that thrives in and around water. It has small fan-shaped green leaves with white or light purple-to-pink or white flowers and it bears small oval fruit. The whole plant is used for medicinal purposes<sup>(10)</sup>.

### **Centella asiatica herb:**



## **MATERIALS AND METHOD**

### **Materials:**

**Standard drug:** Orlistat (20 mg/kg)

**Solvents used for plant extraction:** Hexane, Methanol, Ethanol.

**Chemicals used for induction:**

Triton X-100, Progesterone.

Other Equipments: Centrifuge, Soxhlet extractor,

UV – visible spectrophotometer, auto analyser.

**Methods:**

**Collection and authentication of plant:**

The plant was collected during the April 2014 from Tirumalla forest area of Chittoor district India. The plant was authenticated by Dr. Madhava Chetty, Department of Botany, Sri Venkateshwara University, Tirupati and voucher specimen of the plant were preserved at institute herbarium library.

**Preparation of extracts:**

The dry 40 # powder of the leaves, (2.5 kg) of *Centella asiatica* were macerated at room temperature, in Hexane for 24 h. The Extract was suctioned and filtered using Whatmann filter paper. This was repeated for two more days and similar extracts were pooled together and concentrated at 40°C under reduced pressure using Buchi R-153 Rotavapour. The residual plant material was extracted successively with chloroform and methanol, ethanol in the same manner as followed for hexane. The ethanolic extract which was used for further studies is designated as EECA. Qualitative phytochemical screening is done with the Ethanolic extract.

**Animals:**

Wistar albino adult male rats weighing 200-250g were obtained from the animal house. The animals were grouped and housed in polyacrylic cages (38x 23x 10 cm) with not more than five animals per cage and maintained under standard laboratory conditions (temperature 25±2°C) with dark and light cycle (14/10 hour). They were allowed free access to standard dry pellet diet (Hindustan Lever, Kolkata, India) and water ad libitum. The mice were acclimatized to laboratory condition for 10 days before commencement of experiment.

**Acute toxicity studies:**

The acute oral toxicity study of the extract was carried out by using Wistar rats of either sex weighing between 150-200 g per revised OECD (Organization for Economic Cooperation and Development) guidelines 423. The ethanol extract of whole aerial part from *Centella asiatica* was administered orally to overnight fasted animals at the dose of 250 mg/kg, 500 mg/kg, 1000 mg/kg and 2000 mg/kg of body weight. After administration of the extracts, the animals were observed continuously for the first two hours, for any toxic manifestation. Thereafter, observations were

made at regular intervals for 48 h. Further the animals were under investigation up to a period of 2 week for mortality and general behaviour

### **In vivo screening of anti obesity activity:**

#### **1.TritonX-100 induced obesity:**

Obesity was induced in Wistar rats by single intraperitoneal injection of freshly prepared solution of Triton-X-100 (100mg/kg) in physiological saline solution after overnight fasting for 18 h The animals were divided into four groups of five rats each. The first group was given standard pellet diet, water and orally administered with 5% CMC. The second group was given a single dose of triton administered at a dose of 100mg/kg, i.p. After 72 hours of triton injection, this group received a daily dose of 5% CMC (p.o) for 7 days. The third group was administered a daily dose of 0.5g/day Centella asiatica suspended in 5%CMC, p.o., for 7 days, after inducing hyperlipidemia. Fourth group was administered with the standard Orlistat 20mg/kg, p.o. for 7 days On the 8thday, blood was collected by retero orbital sinus puncture, under mild ether anaesthesia. The collected samples were centrifuged for 10 minutes. Then serum samples were collected and used for various biochemical experiments. The animals were then sacrificed and the liver collected (11).

#### **Liver lipid extraction**

The liver was homogenized in cold 0.15M KCl and extracted with CHCl<sub>3</sub> CH<sub>3</sub>OH (2% v/v). This lipid extract was used for the estimation of lipid parameters.

#### **Evaluation of parameters:**

The various parameters like Body weight, lipids <sup>(12,13,14,15)</sup> and SGOT, SGPT and Glucose were estimated.

**Statistical analysis:** The results are expressed as mean  $\pm$  SEM. Comparisons between the treatment groups and positive control; positive control and control were performed by one-way analysis of variance (ANOVA) followed by Dunnet-t-test. In all tests the criterion for statistical significance was

P < 0.05 (95% level). The analysis was performed by using GraphPad Prism 4.

P value P<0.05 is considered as significant \*P<0.05, \*\*P<0.01,\*\*\*P<0.001.

#### **2.High Fat Diet induced obesity:**

36(06 x 6) Wistar albino rats (180-250 g) were used in this model. The animals were maintained under standard nutritional and environmental conditions throughout the experiment.

#### **Animal grouping:**

The animals were randomly divided into following 6 groups; each group consists of six animals.

Animal grouping and their treatment is as follows:

Group- I : Normal (Normal Diet)

Group- II : Control (High fat diet)

Group- III : Orlistat 20mg/kg + HFD

Group- IV : EECA (100mg/kg) + HFD

Group- V : EECA (200mg/kg) +HFD

Group- VI : EECA (400mg/kg) + HFD

### **Procedure:**

Animals were divided in to 6 groups each group having 6 animals, first group (lean Rat) had free access to standard pelleted chow which provided 76.8% of energy as carbohydrates, 19.2% as protein, and 4.3% as fat. Remaining 30 rats were fed with a high fat diet providing 60% of energy as fat, 20% as protein and 20% as carbohydrates to the animals. Experimental obesity and other metabolic changes were induced by dietary manipulation (by proving HFD) for 48 days to remaining groups. After 48 days rats were found to be obese, change in body weight during this period was recorded.

### **Estimation of parameters:**

Body weight , different lipid levels and Glucose, SGOT and SGPT were estimated . Statistical analysis: The results are expressed as mean  $\pm$  SEM. Comparisons between the treatment groups and positive control; positive control and control were performed by one way analysis of variance (ANOVA) followed by Dunnett test. In all tests the criterion for statistical significance was  $P < 0.05$  (95% level). The analysis was performed by using Graph Pad Prism 4.

P value  $P < 0.05$  is considered as significant \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

### **3.Progesterone induced obesity:**

The neuroactive steroid progesterone is a female reproductive hormone. Its level increases during the second part of the menstrual cycle and control the secretory phase of endometrium. Some reports suggest that use of progesterone containing preparation as contraceptive or for hormonal replacement therapy to cause significant weight gain by increasing fat deposition. Progesterone also exerts antiestrogenic effects, which also been shown to increase in food intake. FurthMRBore, progesterone has been reported as the most fattening of steroids hormone that promotes synthesis and storage of fats. Therefore, progesterone induced hyperphagia causes weight gain and fat deposition is useful as animal model of drug induced obesity.

### **Animal selection:**

36 (06 x 6) female albino mice (20-25 g) were used in this first model. They were housed six per cage under standard laboratory conditions at a room temperature at  $22 \pm 2^{\circ}\text{C}$  with 12h light/dark cycle. The animals were maintained under standard nutritional and environmental conditions throughout the experiment. The experiment was carried out between 9:00–16:00 hours at ambient temperature. All the pharmacological experimental protocols were approved by the Institutional Animals Ethics Committee (Ref: CPCSEA/769/2010) of Sigma Institute of Clinical Research and Administration Pvt. Ltd, Hyderabad, India.

### **Animal grouping:**

The animals were randomly divided into following 6 groups; each group consists of six animals. Animal grouping and their treatment is as follows:

Group- I: Normal (Effect of arachis oil on mice)

Group- II: Control ( Progesterone)

Group- III: EECA (100mg/kg) + Progesterone

Group- IV: EECA(200mg/kg) + Progesterone

Group- V: EECA (400mg/kg) + Progesterone

Group- VI: Orlistat20 mg/kg + Progesterone

Progesterone vial contents were dissolved in arachis oil and dose of 10 mg/ kg was administered subcutaneously in the dorsal neck region to mice for 28 days, control group received the vehicle. All drugs were given at a dose of 0.4 ml/100 gm body weight. The test drugs were injected 30 minutes before to progesterone administration.

Estimation of parameters:

The parameters like change in body weight, lipid parameters and glucose levels and SGOT and SGPT were estimated.

### **Statistical analysis:**

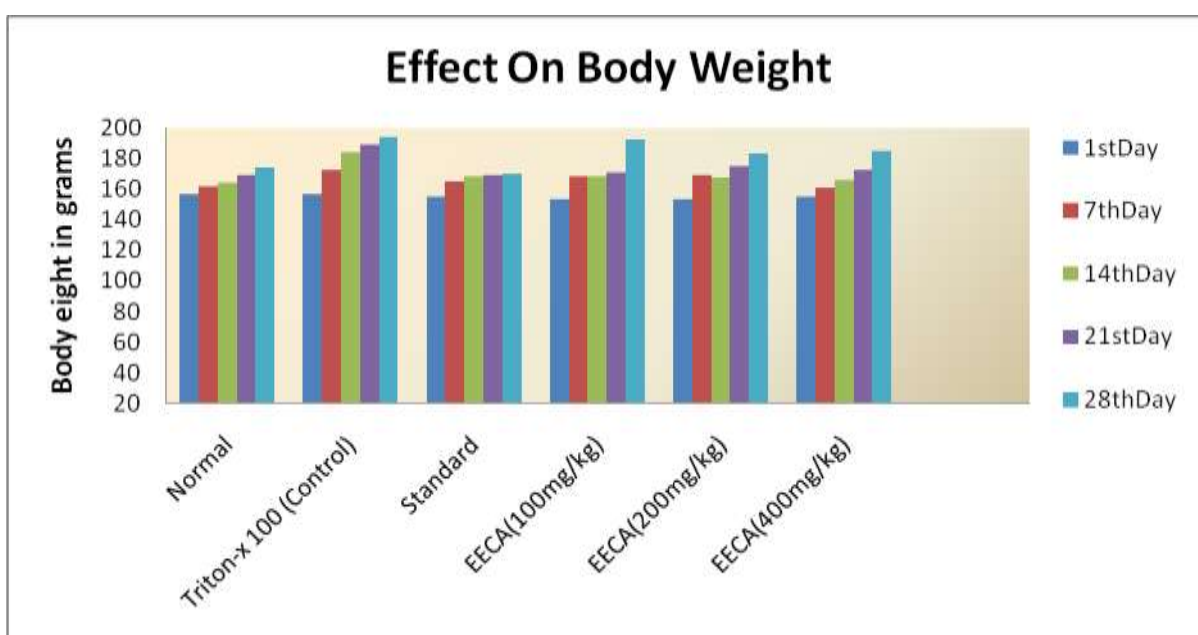
The results are expressed as mean  $\pm$  SEM. Comparisons between the treatment groups and positive control; positive control and control were performed by one way analysis of variance (ANOVA) followed by Dunnett test. In all tests the criterion for statistical significance was  $P < 0.05$  (95% level). The analysis was performed by using GraphPad Prism 4. P value  $P < 0.05$  is considered as significant \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

## RESULTS AND DISCUSSION

**Table 1: Effect of Ethanolic extract of Centella asiatica on body weight in Triton-x induced obesity in rats.**

Treatment groups	1 <sup>st</sup> Day	7 <sup>th</sup> Day	14 <sup>th</sup> Day	21 <sup>st</sup> Day	28 <sup>th</sup> Day
Normal	157.5±2.08	162.5±2.19	164.3±2.03	169.8±1.69	174.5±1.23
Triton-x 100 (Control)	157.5±2.81	172.5±2.14	184.3±2.36	189.8±1.662	194.5±1.258
Standard (orlistat20mg/kg)	155.0±1.82	165.2±3.13	168.5±3.05*	169.8±1.83***	170.2±2.19***
EECA(100mg/kg)	153.3±3.07	168.2±0.79	168.8±2.77*	171.0±4.25***	192.0±4.50***
EECA(200mg/kg)	153.3±3.05	169.0±1.52	167.5±0.84***	175.0±0.81***	183.2±2.72***
EECA(400mg/kg)	155.2±2.89	161.3±1.56	166.8±1.77**	172.8±1.68***	185.3±5.10***

The effect of EECA on body weight was showed in the below graph.

**Figure 1: EECA on body weight****Table 3: Effect of Ethanolic extract of Centella asiatica on glucose, SGOT and SGPT levels on Triton-x induced obesity in rats.**

Treatment Groups	Glucose mg/dl	SGOT mg/dl	SGPT mg/dl
Sham operated (Normal)	77.83±4.42	12.84±0.82	34.12±2.35
Triton-X -100( Control)	87.5±2.81	25.50±2.14	44.31 ±2.36
Standard (Orlistat 20mg/kg)	64.00±1.39***	12.70±0.87***	28.97±1.45***
EECA (100mg/kg)	85.17±1.24***	23.44±1.12ns	59.53±3.50**
EECA (200mg/kg)	82.17±4.28***	21.02±1.29ns	45.35±4.37***
EECA (400mg/kg)	63.83±1.49***	13.59±1.35***	38.98±4.26***

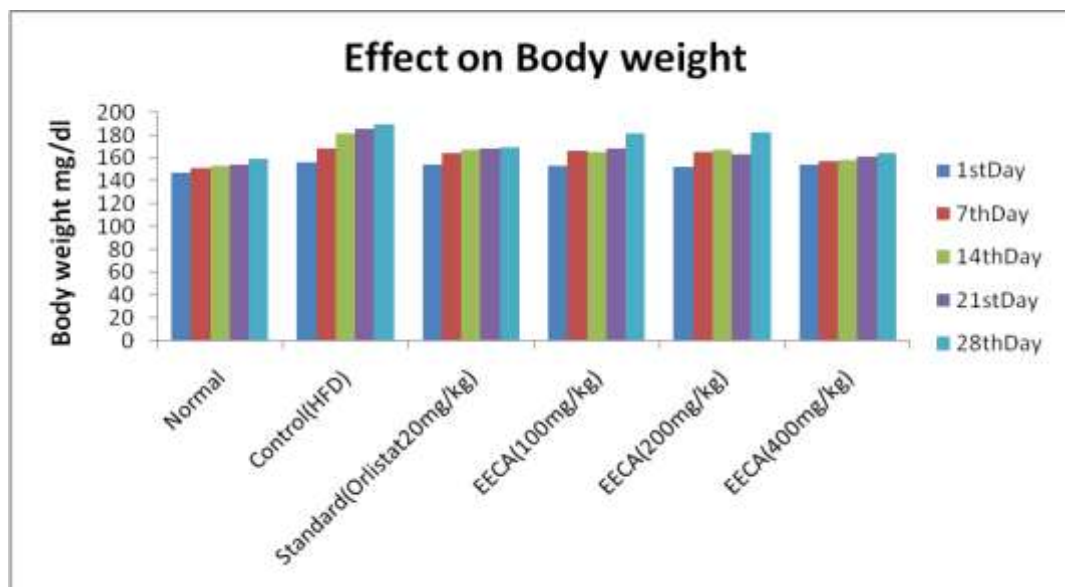


**Table 4: Effect of Ethanolic extract of centella asiatica on lipid levels on Triton-x induced obesity in rats.**

Treatment Groups	TC (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)
Normal	125.7±1.45	66.84±0.58	40.05±0.52	72.33±1.61	13.37±0.05
Triton-X-100 (control)	184.6±2.55	76.84±0.48	68.15±0.66	92.33±1.53	18.37±0.09
Standard(Orlist at 20mg/kg)	142.2±2.10** *	68.00±1.77** *	47.89±1.20** *	80.40±3.28** *	13.89±0.22** *
EECA (100mg/kg)	185.7±2.96** *	72.17±1.88** *	39.34±1.67** *	131.9±3.35ns	14.43±0.37** *
EECA (200mg/kg)	172.1±1.23** *	70.24±1.58** *	54.15±1.08** *	118.4±0.80ns	14.04±0.31** *
EECA (400mg/kg)	162.7±1.03** *	63.70±1.08** *	56.31±1.52** *	103.9±2.11*	12.73±0.21** *

**Table 4: Effect of Ethanolic extract of Centella asiatica on body weight in HFD induced obesity in rats.**

Treatment groups	1 <sup>st</sup> Day	7 <sup>th</sup> Day	14 <sup>th</sup> Day	21 <sup>st</sup> Day	28 <sup>th</sup> Day
Normal	147.5±2.75	152.5±2.08	154.3±2.07	155.8±1.66	160.5±1.25
HFD (Control)	157.5±2.81	169.5±2.14	182.3±2.36	186.8±1.78	190.5±1.18
Standard (orlistat20mg/kg)	155.0±1.82	165.2±3.13	168.5±3.05*	169.5±1.83***	170.2±2.19***
EECA(100mg/kg)	154.3±3.07	167.2±0.79	166.8±2.77*	169.0±4.25***	182.0±4.50***
EECA(200mg/kg)	153.3±3.07	166.0±1.52	168.5±0.84**	164.0±0.81***	183.2±2.72***
EECA(400mg/kg)	155.2±2.89	158.3±1.56	159.8±1.77**	162.8±1.68***	165.3±5.10***

**Figure 2: Effect of EECA on Body weight in HFD induced obese rats showed in the following graph.**

**Table 6: Effect of Ethanolic extract of Centella asiatica on Glucose, SGOT and SGPT levels on HFD induced obesity in rats.**

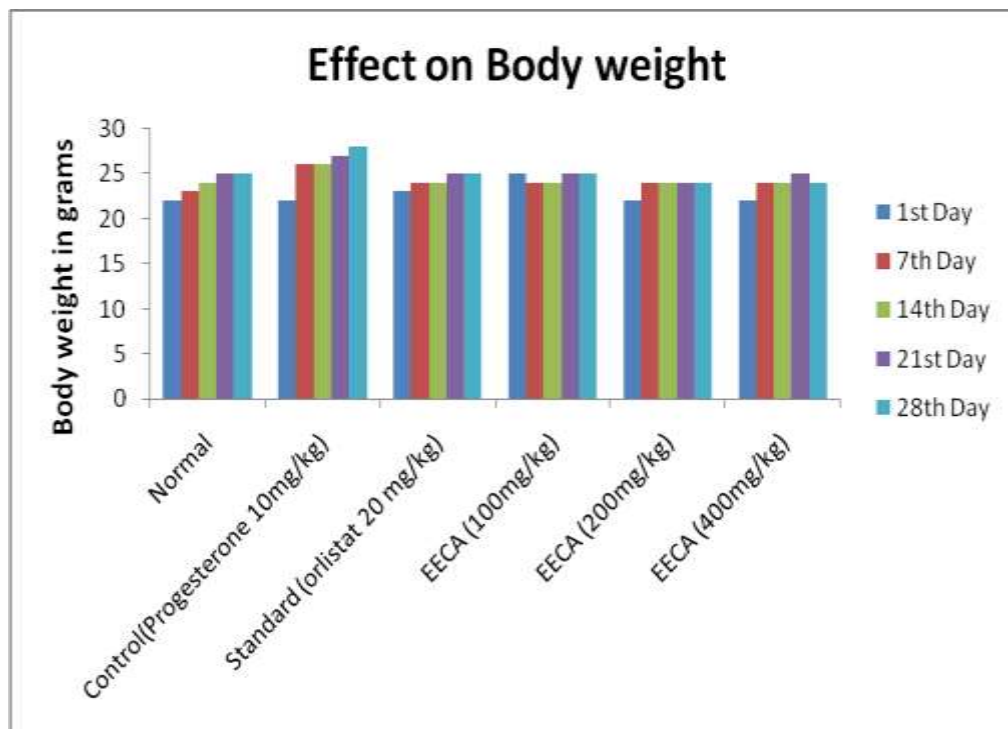
Treatment groups	Glucose mg/dl	SGOT mg/dl	SGPT mg/dl
Normal	75.83±4.42	24.3±1.03	41±1.12
HFD (control)	85.5±2.81	43.52±0.63a	63.5±1.09a
Standard (Orlistat 20mg/kg)	63.00±1.39***	34.5±1.02**	52±1.04*
EECA(100mg/kg)	74.17±1.24***	44.5±1.02**	58.2±1.04*
EECA(200mg/kg)	71.17±4.28***	39.4±1.23*	59.9±1.43*
EECA(400mg/kg)	62.83±1.49***	37.6±1.26*	56.2±1.32**

**Table 7: Effect of Ethanolic extract of Centella asiatica on lipid levels on HFD induced obesity in rats.**

Treatment Groups	TC (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)
Shamoperated (normal)	65.45±1.69	51.7±2.98	29.38±0.98	25.26±1.63	10.34±0.59
HFD (control)	106.93±3.09 <sup>b</sup>	95.74±2.83 <sup>b</sup>	24.28±0.85 <sup>a</sup>	66.31±3.52 <sup>b</sup>	18.99±0.57 <sup>b</sup>
Standard (Orlistat 20 mg/kg)	84.46±4.43*	61.90±7.39**	34.6±1.99**	37.59±1.89*	12.38±1.48**
EECA (100 mg/kg)	81.5±5.27*	70.18±5.42*	35.38±1.02*	44.91±5.48**	12.78±1.08*
EECA (200 mg/kg)	82.7±5.16*	72.88±5.22*	30.88±1.32*	41.91±5.68**	14.98±1.08*
EECA (400 mg/kg)	69.53±0.66**	56.77±2.47**	32.28±2.11*	24.9±2.44**	10.38±0.49*

**Table 8: Effect of Ethanolic extract of Centella asiatica on Body weight on progesterone induced obesity in mice.**

Treatment Groups	1 <sup>st</sup> Day	7 <sup>th</sup> Day	14 <sup>th</sup> Day	21 <sup>st</sup> Day	28 <sup>th</sup> Day
Sham operated (Normal)	22.93±0.85	23.24±0.43	24.36±0.30	25.56±0.23	25.95±0.25
Control (Progesterone 10mg/kg)	22.15±0.72	26.11±0.50 <sup>b</sup>	26.77±0.27 <sup>a</sup>	27.67±0.32 <sup>c</sup>	28.04±0.36 <sup>b</sup>
Standard (Orlistat 20mg/kg)	23.92±0.60 <sup>ns</sup>	24.12±0.52*	24.87±0.43*	25.42±0.43**	25.80±0.16**
EECA (100mg/kg)	25.06±0.45*	24.78±0.73 <sup>ns</sup>	24.73±0.17**	25.17±0.36**	25.00±0.46***
EECA (200mg/kg)	22.18±0.58 <sup>ns</sup>	24.79±0.28 <sup>ns</sup>	24.23±0.37***	24.32±0.64***	24.67±0.51***
EECA (400mg/kg)	22.67±0.43 <sup>ns</sup>	24.12±0.62*	24.58±0.61**	25.67±0.66*	24.98±0.64***



**Figure 3: Effect of EECA on Body weight in Progesterone induced obesity in mice.**

**Table 9: Effect of Ethanolic extract of Centella asiatica on Glucose, SGOT and SGPT levels on Progesterone induced obesity in albino mice.**

Treatment Groups	Glucose(mg/dl)	SGOT (mg/dl)	SGPT (mg/dl)
Sham operated ( Normal)	75.83±4.42	13.84±0.82	33.12±2.35
Control(Progesterone 10mg/kg)	84.5±2.81	23.50±2.14	43.31 ±2.36
Standard (Orlistat 20mg/kg)	63.00±1.29***	11.70±0.87***	25.77±1.45***
EECA (100mg/kg)	84.17±1.24***	22.44±1.12ns	57.53±3.50**
EECA (200mg/kg)	90.17±4.28***	20.02±1.29ns	43.35±4.37***
EECA (400mg/kg)	61.53±1.39***	13.49±1.35***	40.98±4.26***

**Table 10: Effect of Ethanolic extract of Centella asiatica on lipid levels on Progesterone induced obesity in mice.**

Treatment Groups	TC (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)
Sham operated (Normal)	123.7±1.45	65.84±0.48	39.05±0.74	70.33±0.53	12.56±0.19
Control (Progesterone 10mg/kg)	183.6±2.55	76.84±0.93	65.15±0.66	90.33±1.53	17.37±0.09
Standard (Orlistat 20mg/kg)	141.2±2.10***	68.00±1.77***	43.59±1.20***	80.40±3.28***	12.89±0.22***
EECA(100mg/kg)	183.7±2.96***	70.17±1.88***	35.34±1.67***	129.9±3.35ns	13.43±0.37***
EECA(200mg/kg)	170.1±1.23***	70.24±0.58***	54.15±1.08***	118.4±0.80ns	13.04±0.31***
EECA (400mg/kg)	160.7±1.03***	62.70±0.38***	56.31±1.52***	103.9±2.11*	12.73±0.21***

## DISCUSSIONS:

Obesity is a chronic metabolic disorder that results from the imbalance between energy intake and energy expenditure. Among the multiple factors contributing to its etiology, the sedentary life styles, white collar jobs, lack of exercise, psychological factors and the consumption of energy rich diets are the major ones. It is characterized by enlarged fat mass and elevated lipid concentration in blood.

Globally, more than 1.1 billion adults worldwide are overweight and 312 million of them are obese. In addition, at least 155 million children worldwide are overweight or obese, according to the International Obesity Task Force. This task force and the World Health Organization (WHO) have revised the definition of obesity to adjust for ethnic differences, and this broader definition may reflect an even higher prevalence with 1.7 billion people classified as overweight worldwide.

*C. asiatica* has been shown the effect on total cholesterol and high density lipoprotein cholesterol values. The extraction of plant is done with the several solvents based on polarity and solubility. ethanol was selected for the phytochemical screening of the plant *Centella asiatica*.

The Phytochemical tests with the ethanol extract of *C. asiatica* indicated the presence of carbohydrates, alkaloids, Tannins, terpenoids, saponins, proteins and amino acids. Hyperlipidemia is associated with heart disease, which is the leading cause of death in the world. The lowering of the levels of harmful lipids to satisfactory values has been confirmed by several experimental animal and interventional studies indicating lowered morbidity and mortality in coronary heart diseases. The results are discussed under the lipid profile in serum. Lipid profile in serum with high triglyceride (TG) and cholesterol levels were significantly reduced by treatment of *C. asiatica*. The acute toxicity studies of the ethanolic extract of *Centella asiatica* was found to be non-lethal up to the dose of 2000 mg/kg body weight of the animals so that 1/5<sup>th</sup> and 1/10<sup>th</sup> was selected for the further investigations.

### **Effect on body weight:**

When compared to normal and control groups the body weight observed was higher in High fat diet, Triton X-100 and progesterone induced obese animals. EECA treated group exhibited significant activity by reducing the body weight as mention in the table 2,5 and 8. And the values are comparable to the standard drug.

### **Effect on Glucose, SGOT and SGPT levels:**

The Glucose and SGOT and SGPT levels were increased after Triton X-100, High fat diet and Progesterone and the values are mentioned in the table 3,6 and 9. When the animals treated with

ethanolic extract with 100mg/kg,200mg/kg and 400mg/kg shown the significant reduction of glucose levels & SGPT levels . SGOT levels reduced mostly with the 400mg/kg of EECA as shown in the table3,6 &9. The values are comparable with the standard drug Orlistat 20mg/kg.

#### **Effect on lipid profile:**

Total cholesterol, Triglycerides, LDL and VLDL levels were significantly increased in triton-injected ,High fat diet induced and Progesterone induced animals to control rats. The results are shown in Tables 4,7,and 10. and 10. The *C.asiatica* markedly lowers the levels of serum cholesterol and other serum lipids. The decrease in cholesterol may indicate increased oxidation of mobilized fatty acids of inhibition or lipolysis. The present investigation shows that all triton induced, High fat diet induced and progesterone induced animals displayed hyperlipidemia as shown by their elevated levels of serum and liver cholesterol, triglyceride, VLDL, LDL level. It can be concluded that *C.asiatica* treatment was effective in reduction of cholesterol, TG, VLDL, LDL in a dose dependent manner.(mentioned in the table 4,7 and 10).

Histopathological studies revealed that control group showing normal architecture; (b) hyperlipidemic group showing fatty infiltration and granular degeneration; (c) Fenofibrate group showing negligible cytoplasmic fatty infiltration and granular degeneration; (d) group treated with 200mg/kg extract showing mild cytoplasmic fatty infiltration and mild granular degeneration; (e) group treated with 400mg/kg extract showing mild cytoplasmic fatty infiltration and mild to moderate granular degeneration.

#### **CONCLUSION:**

By the present study it can be concluded that *Cetella asiatica* has the beneficial effect of lipid lowering capacity and it can be useful in the prevention of cardiovascular diseases. It decreases plasma lipid concentrations , especially triglycerides and low density lipoproteins. With the treatment of EECA (200mg/kg and 400mg/kg) the lipid levels are decreased in the HFD induced obese rats and TritonX-100 induced obese rats and in progesterone induced albino mice Histopathological studies revealed that group treated with 200mg/kg extract and 400mg/kg extract of *Centella asiatica* showed mild cytoplasmic fatty infiltration and mild granular degeneration as compared to normal and control groups. So it can be concluded that 200mg/kg and 400mg/kg extract of *Centella asiatica* treatment will be effective in reduction of cholesterol, TG, VLDL, LDL in a dose dependent manner. Further detailed studies on this herb will be required to know

the exact mechanism of action of this plant extract, and it will become very useful in the treatment of obesity and hyperlipidemia which are the risk factors for several diseases

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