

## EVALUATION OF ANTI OBESITY ACTIVITY OF GCCr-Ob FORMULATION

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### ABSTRACT

Obesity is a very common problem worldwide; more than 5% population of the world is suffering from it. Obesity is a condition of abnormal body weight resulting from an accumulation of extra adipose tissue, generally in response to a state of positive energy balance that occurs when energy intake exceeds energy expenditure. This Study prompted us to undertake a study to examine the possible antiobesity and antihyperlipidemic activities of GCCr-Ob formulation in triton and atherogenic diet induced hyperlipidemia in rats. Clofibrate (100mg/kg) and GCCr-Ob (200mg/kg), (400mg/kg) treated animals significantly decreased body weight and serum lipid profile in all experimental models compared to obese control animals. Result indicates the GCCr-Ob formulation (400mg/kg) showed significant ( $P < 0.05$ ) results with Clofibrate.

**KEYWORDS:** Obesity, Clofibrate, TritonWR1339, Atherogenic diet, Serum lipid profile.

### INTRODUCTION

Obesity increases susceptibility to a wide range of both cardiovascular and metabolic diseases including hypertension, non-insulin-dependent diabetes mellitus and hyperlipidemia. Obesity is characterized by an elevated body mass index (BMI), which is defined as the weight of an individual in kilograms divided by the square of the height in meters<sup>1</sup>. Obesity is a growing health problem in many of the richest nations of the world and should now be considered as a chronic disease that is reaching epidemic proportion<sup>2</sup>. The consumption of synthetic drugs leads to hyperuricemia, diarrhoea, nausea, myositis, gastric irritation, flushing, dry skin and abnormal liver function<sup>3</sup>. Thus, there is considerable interest on development of lipid lowering drugs from natural products. Plant-based pharmaceuticals have been employed in the management of various diseases affecting human<sup>4</sup>. Various herbs are used in curbing obesity like guggul - Resiti guggulu, Ephedra (Ephedra sinica), nomame herba, galega, laxatives, caffeine, tobacco and fibers (Psyllium, Plantago, Guar fibers) etc<sup>1</sup>. All the ingredients of present formulation GCCr-Ob namely Garcinia cambogia, Chitosan and Chromium Picolinate were found to be helpful in treating obesity. However, little scientific information is available regarding their use in combination.

The aim of the present on Garcenia cambogia is claimed to lower body weight and reduce fat mass in

humans<sup>5</sup>. Chitosan acts as a 'fat sponge' by significantly binding fat in the digestive tract<sup>6</sup>. The action of Chitosan in cholesterol management may be explained by the theory that ingested Chitosan salts react with fatty acids and bind lipids because of hydrophobic interactions; these bound lipids are extracted rather than absorbed<sup>7</sup>. Chromium ion is an insulin sensitizer and Picolinate acts as a chromium chelator<sup>8</sup>. Chromium Picolinate supplementation enhances insulin sensitivity and glucose disappearance, and improves lipids in male obese hyperinsulinemic rat<sup>9</sup>. Hence the present study was undertaken to evaluate the effect of GCCr-Ob formulation on atherogenic diet induced obesity and hyperlipidemia in rats and Triton induced hyperlipidemia in rats.

### MATERIALS AND METHODS

#### Drugs and Chemicals

Clofibrate was obtained from Torrent Pharma, Ahmedabad. Garcinia Cambogia was obtained from Jay Radhe Sales, Ahmedabad. Chitosan and Chromium Picolinate were obtained from Himedia Chemical, Mumbai. All other chemicals and reagent were of pure analytical grade and obtained from local suppliers.

The formulation GCCr-Ob contains Garcinia Cambogia (71.325%), Chitosan (28.53%) and Chromium picolinate (0.143%). All the drug solutions were prepared using 1% v/v Tween 80 as emulsifying agent and given at volume of 0.2 ml/ 20g for mice & 0.2ml/200g for rats orally.

## Animals

Wistar albino rats (140 to 160 g) of either sex procured from Indian Institute of Sciences were used for this study. They were maintained under standard conditions (temperature  $22 \pm 2^\circ\text{C}$ , relative humidity  $60 \pm 5\%$  and 12 h light/dark cycle). The animals were housed in sanitized polypropylene cages containing sterile paddy husk as bedding. They were having free access to standard pellet diet and water ad libitum. The Institutional Animal Ethics Committee approved the experimental protocol. All the animals received humane care according to the criteria outlined in the "Guide for the Care and Use of Laboratory Animals" prepared by the "National Academy of Sciences" and published by the "National Institute of Health".

### Triton induced Hyperlipidemia in rats

The rats were divided into 5 groups of 6 each and assigned as follows.

Group 1: Vehicle control (1% Tween 80, p.o)

Group 2: Triton WR 1339 (100mg/kg, ip.)

Group 3: Triton WR 1339 (100mg/kg, ip.) + Clofibrate (100mg/kg, p.o)

Group 4: Triton WR 1339 (100mg/kg, ip.) + Formulation GCCr- Ob (200mg/kg, p.o)

Group 5: Triton WR 1339 (100mg/kg, ip.) + Formulation GCCr- Ob (400mg/kg, p.o).

The treatment was given 6hr after intraperitoneal injection of Triton WR 1339. The blood was collected after 24 hour of Triton WR 1339 injection and analyzed for various biochemical parameters.<sup>10</sup>

### Atherogenic diet induced obesity in rats:

The Wistar rats were randomly divided into 5 groups of 6 each. From group II to V animals were fed with atherogenic diet instead of normal diet for 7 days. All the animals were treated once daily for 7 days. The group I will be served as normal control. Atherogenic diet contains 79% standard diet+ 0.5% cholesterol+ 20% butter fat

Group 1: normal control (1% Tween 80)

Group 2: Atherogenic control (atherogenic diet)

Group 3: Clofibrate (100mg/kg) + atherogenic diet

Group 4: Formulation GCCr-Ob (200mg/kg) + atherogenic diet

Group 5: Formulation GCCr-Ob (400mg/kg) + atherogenic diet

Body weigh was measured on 0<sup>th</sup> day and on 8<sup>th</sup> day. On 8<sup>th</sup> day the blood was collected by retro orbital sinus puncture, under mild ether anaesthesia in heparinised tubes. Serum separated by immediate centrifugation of blood samples using semi ultra cooling centrifuge at 3000 rpm for 5 minutes at room temperature and used for

estimating various biochemical parameters. The serum triglyceride and total cholesterol were measured using GPO-POD method.<sup>12,13</sup>

### Statistical Analysis

The results are expressed as mean  $\pm$  SEM. Comparison between the treatment groups and control were performed by one-way analysis of variance (ANOVA) followed by Dunnet's t-test using Graph Pad Prism 5.01. In all tests the criterion for statistical significance was  $p < 0.05$ .

## RESULTS

There was significant increase in serum TG and TC level of triton induced hyperlipidemic animals compared to control animals ( $P < 0.05$ ). Clofibrate (100mg/kg) and GCCr-Ob (200mg/kg), (400mg/kg) treated animals significantly decreased serum TG and TC level compared to Triton induced obese animals as shown in (table 1).

There was significant increase in the body weight of atherogenic diet induced hyperlipidemic animals compared to control animals ( $P < 0.05$ ) on 8<sup>th</sup> day. Clofibrate (100mg/kg) and both GCCr-Ob (200mg/kg), (400mg/kg) treated animals significantly reduced body weight compared to atherogenic diet induced obese animals as shown in (table 2).

Serum triglyceride and total cholesterol level significantly increased in the atherogenic diet induced hyperlipidemic animals compared to control animals ( $P < 0.05$ ) on 8<sup>th</sup> day. Both Clofibrate (100mg/kg) and GCCr-Ob (200mg/kg), (400mg/kg) treated animals significantly decreased serum triglyceride and total Cholesterol level compared to atherogenic diet induced obese animals as shown in (table 2).

## DISCUSSION

The presence of obesity needs to be regarded in the context of other risk factors. Hyperlipidemia is characterized by high levels of cholesterol and high triglycerides important risk factor in the initiation and progression of atherosclerosis, and ischemic heart diseases<sup>14</sup>. Hyperlipidemia associated disorders are also not free from toxic side effects<sup>15</sup>. The consumption of synthetic drugs leads to hyperuricemia, diarrhoea, nausea, myositis, gastric irritation, flushing, dry skin and abnormal liver function<sup>3</sup>.

Thus, there is considerable interest on development of lipid lowering drugs from natural products. The weight reducing effect of the Polyherbal formulation may be attributed to *Garcinia cambogia* reported to inhibit lipogenesis<sup>16</sup>. All the ingredients of the formulation possessed thermogenic property. Since obesity is associated with defective thermogenesis.

Triton model is used as acute model for induction of hyperlipidemia. The systemic administration of the surfactant triton to mice or rats results in a biphasic elevation of plasma cholesterol and triglycerides. The method employing Triton hypercholesterolemia is rather simple and rapid for detection of compounds interfering with the synthesis and excretion of cholesterol<sup>10</sup>.

In atherogenic diet induced hyperlipidemia rats showed elevated levels of serum triglyceride and total cholesterol compared to normal control rats. Cholesterol feeding has been often used to elevate serum or tissue cholesterol levels to assess the hypercholesterolemia related metabolic disturbances in animals<sup>17,18</sup>. In the models treatment with GCCr- Ob significantly opposed it which is comparable to standard antihyperlipidemic drug Clofibrate.

The GCCr-Ob formulation has also seems have potent antiobesity activity which has been seen in all the models. The reason for antiobesity and antihyperlipidemic action of the formulation was found to be the combination and complementary actions of the individual components of the polyherbal formulation.

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**Table 1: Effect of GCCR-OB on serum lipid profile in triton induced Hyperlipidemia**

Groups	Serum Triglyceride	Serum Total Cholesterol
Control	69.44±1.42	82.84±1.86
Obese Control	156.3±1.04*	151.7±0.78*
Clofibrate (200mg/kg)	108.1±2.66 <sup>##</sup>	121.15±2.25 <sup>##</sup>
GCCr-Ob (200mg/kg)	127.2±2.10 <sup>#</sup>	139.8±0.70 <sup>#</sup>
GCCr-OB (400mg/kg)	106.1±1.05 <sup>##</sup>	124.0±2.50 <sup>##</sup>
Values are expressed as mean ±SEM; n=6 animals in each group; *P<0.05 when compared to control. <sup>#</sup> P<0.05 and <sup>##</sup> P<0.01 when compared to obese control.		

Table 2: Effect of GCCR-OB on body weight and serum lipid profile in rats fed with Atherogenic diet.

Groups	Difference in Body weight	Serum Triglyceride	Serum Total Cholesterol
Control	8.5±0.56	69.54±1.42	82.94±1.86
Obese Control	34.5±2.23*	98.0±1.38*	134.3±0.58*
Clofibrate (200mg/kg)	26.17±1.13*	72.52±1.36 <sup>##</sup>	83.9±0.51 <sup>##</sup>
GCCr-Ob (200mg/kg)	22.67±2.45*	85.10±1.41 <sup>#</sup>	97.19±0.43 <sup>#</sup>
GCCr-Ob (400mg/kg)	25.33±2.83*	76.22±1.57 <sup>##</sup>	87.7±0.98 <sup>##</sup>

Values are expressed as mean ±SEM; n=6 animals in each group; \*P<0.05 when compared to control. <sup>#</sup>P<0.05 and <sup>##</sup>P<0.01 when compared to obese control.

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