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Research Article

**“Antiobesity Effect Of *Gymnema Sylvestre* In High Fat Diet Induced Obesity Model Of Wistar Rats”**

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ABSTRACT

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The prevalence of obesity and overweight has risen to such an extent that it has become a matter of concern. *Gymnema sylvestre* is popular in indigenous system of medicine. Present study was planned to explore the antiobesity property of extract of leaves of *Gymnema sylvestre* in rat model of obesity. Adult wistar rats weighing around 150-200g were used. Obesity was induced by feeding with high fat diet (HFD) for four weeks. *Gymnema sylvestre* leaves extract was used in a dose of 100mg/kg and 200mg/kg. Body weights, body mass index, locomotor activities (ambulatory activity and frequency of rearing) were recorded. At the end of 8<sup>th</sup> week rats were sacrificed, their internal organs (kidney, liver, spleen and heart) and fat pads (perirenal, mesenteric and gonadal) were identified, removed and weighed. On giving test drug all the parameters of obesity improved significantly. GS 100 mg/kg caused around 33% weight reduction while GS 200mg/kg caused around 38% weight reduction when compared to the disease control group. Significant improvement was also observed for BMI and locomotor activities. Weight of internal organs and fat pads also decreased significantly as compared to the disease control group. Present study concludes that leaf extract of *Gymnema sylvestre* possess significant dose dependent antiobesity activity. The drug acts in a dose dependent manner with 200 mg/kg being more effective than 100mg/kg.

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## INTRODUCTION:

Modernization has changed the lives of people in various ways. People are shifting toward unhealthy dietary habits along with adopting the sedentary lifestyle. This has led to rise in the incidence and prevalence of many non-communicable diseases, one of them being obesity, the modern epidemic. According to the reports of World Health Organization (WHO) there are around 2.3 billion overweight and 700 million obese people worldwide by 2015. [1] Obesity, in general, can be defined as the accumulation of excess body fat to an extent that health is adversely affected. [2,3] It increases the risk of other diseases like insulin resistance, type II diabetes mellitus, dyslipidaemia, cardiovascular diseases, osteoarthritis, some cancers and many others. [4, 5] Among the various anthropometric indices that are used for assessing obesity BMI is considered the most useful measure of obesity and overweight. [6, 7]

Diet, exercise and behavioural modification are some of the non-pharmacological measures to curb the problem. Various drugs are also available in the market but these are indicated only in limited cases besides having their own risks. [8,9] Despite so many advances made in the medical field we are still far apart from successful treatment of obesity.

*Gymnema sylvestre* is an indigenous herb of family Asclepiadaceae. [10] The extract of leaves has shown to possess antidiabetic, antimicrobial, anti-inflammatory, antiarthritic and various other medicinal properties. [11- 14] The present study was planned to explore the antiobesity effect of this valuable herb.

## MATERIAL AND METHODS

Experiment was started after the ethical clearance of Institutional Animal Ethics Committee of King George's Medical University. The work was carried out from January 2016 to March 2016.

### Experimental Procedure

Adult healthy female wistar rats 24 in number weighing around 150-200g were procured from Indian Institute of Toxicology Research, Lucknow. They were kept in the institutional animal house and divided into 4 groups with 6 rats in each group. All the guidelines of CPCSEA were followed and standard conditions of temperature ( $25 \pm 2^\circ$  C), humidity ( $55 \pm 5\%$ ) and twelve hour light- dark cycle were maintained during the work.

On day 0 body weight, Body mass index (BMI) and locomotor activity (ambulatory activity & rearing) was measured. Group 1 was given normal chow while rest of the

groups (2, 3, 4) were kept on high fat diet (HFD) provided by Bharat Science Solution Company, Lok Nagar, Unnao, Uttar Pradesh. Composition of HFD was such that it contained carbohydrate 44%, crude fat 25%, crude protein 18%, fiber 13%, moisture 8 %, vitamins, minerals and other ingredients in appropriate quantity.

At the end of 4<sup>th</sup> week, all the parameters were measured again. During phase II of the study group 1 was given only normal chow, group 2 was provided with HFD, group 3 was put on HFD plus *Gymnema sylvestre* 100mg/kg while group 4 was given HFD along with *Gymnema sylvestre* 200mg/kg. Drugs were given as a suspension using distilled water by oral route. Finally at the end of 8<sup>th</sup> week all the parameters were measured. After that all the rats were sacrificed and their internal organs (kidney, liver, spleen and heart) and fat pad (perirenal, mesenteric and gonadal) were removed and weighed.

**Test drugs:** Dried powdered extract of leaves of *Gymnema sylvestre* was obtained from Ekgaon Company, New Delhi. The drug was administered in a dose of 100 and 200 mg/kg.

**Measurement of Body Weight and Body Mass Index (BMI):** Digital weighing machine was used to measure the body weight of rats and BMI was calculated as follows:

**Measurement of Locomotor Activity (Ambulatory Activity & Rearing):** Open field behaviour test apparatus (68×68×45 cm) was used to calculate locomotor activity (ambulatory activity and the frequency of rearing) for a period of 5 minutes.

**Removal of different organs and fat pads:** Rats were sacrificed by using sodium pentobarbital (150mg/kg i.p.). Different organs (kidney, liver, spleen and heart) and fat pads (perirenal, mesenteric and gonadal) were identified, removed and weighed.

**Statistical Analysis:** Done by using SPSS Statistics 20 software. Data were expressed as mean  $\pm$  standard error of mean (S.E.M.). Analysis of variance (ANOVA) followed by Dunnett's post hoc test and paired t test were used as statistical tests. p-value < 0.05 was considered statistically significant.

## RESULTS

At day 0 all the groups were found comparable with no significant difference among the groups in terms of body weight, BMI and Locomotor activity. At the end of 4<sup>th</sup> week and 8<sup>th</sup> week all the parameters were measured again.

### Effect on body weight

High fat diet for 4 weeks increased the body weight significantly while there was no such change in the group 1. At 8<sup>th</sup> week body weight of group 3 (GS 100 mg/kg) & 4

(GS 200mg/kg) decreased significantly as compared to their values at week 4 (table 1). At the end of 8<sup>th</sup> week Dunnett's post hoc test showed that group 3 & 4 were not significantly different from group 1 thus GS reduced body weight significantly.

#### Effect on Body mass index (BMI)

When given HFD for 4 weeks BMI of all the groups on HFD increased significantly (p value <0.01). After starting drug treatment the value of BMI reduced significantly in drug groups 3 & 4 as compared to their previous values at week 4 (Table 2). At the end of 8<sup>th</sup> week there was no significant difference when group 3 & 4 were compared with normal control group 1. GS at both the doses reduced the BMI to such an extent that it was comparable to the normal control group.

#### Effect on Body Locomotor activity

Due to obesity ambulatory activity of all the groups on HFD reduced significantly (p value <0.05) while frequency of rearing increased in group 3 & 4 (Table 3 & 4). After giving

GS to group 3 & 4 there was significant increase in their ambulatory activity. GS also significantly decreased the frequency of rearing of both the groups. At the end of 8<sup>th</sup> week Group 3 & 4 were found comparable to normal control (dunnett's post hoc test) while they were significantly different from disease control (group 2).

#### Effect on weight of internal organs

At the end of 8<sup>th</sup> week rats were sacrificed and their internal organs (kidney, liver, spleen and heart) were removed and weighed. Significant differences were found in the weight of internal organs of different groups and when compared to the values of disease control group 2 the values of weight of internal organs differed significantly.

#### Effect on weight of different fat pads

Different fat pads (perirenal, gonadal & mesenteric) were removed and weighed. GS at both the doses reduced the weight of internal fat pads significantly (p value <0.05) when compared to the disease control group (ANOVA followed by dunnett's post hoc test).

Table 1: Pre and Post treatment body weight (g) of all the groups (mean  $\pm$  SEM, n=6)

Body Weight				
GROUPS	DAY 0	WEEK 4	WEEK 8	% change as compared to Group 2 at 8 <sup>th</sup> week
Group 1	196.6 $\pm$ 3.1	198.2 $\pm$ 4.2	203.3 $\pm$ 2.7	38.7
Group 2	197.1 $\pm$ 7.5	292.0 $\pm$ 3.7*	331.8 $\pm$ 5.0 <sup>#</sup> <sup>§</sup>	-
Group 3	188.2 $\pm$ 8.6	284.9 $\pm$ 7.4*	222.7 $\pm$ 3.3 <sup>#</sup> <sup>§</sup>	32.9
Group 4	188.4 $\pm$ 11.7	283.8 $\pm$ 9.2*	205.5 $\pm$ 9.0 <sup>#</sup> <sup>§</sup>	38.1

\*Significant as compared to day 0

<sup>#</sup>Significant as compared to week 4

<sup>§</sup>Significant as compared to day 0

Table 2: Pre and Post treatment BMI of all the groups (mean  $\pm$  SEM, n=6)

BMI				
GROUPS	DAY 0	WEEK 4	WEEK 8	% change as compared to Group 2 at 8 <sup>th</sup> week
Group 1	5.6 $\pm$ 0.28	5.6 $\pm$ 0.25	5.8 $\pm$ 0.27	38.9
Group 2	5.7 $\pm$ 0.33	8.4 $\pm$ 0.63*	9.5 $\pm$ 0.78 <sup>#</sup> <sup>§</sup>	-
Group 3	5.2 $\pm$ 0.41	7.9 $\pm$ 0.59*	6.2 $\pm$ 0.52 <sup>#</sup> <sup>§</sup>	34.7
Group 4	5.1 $\pm$ 0.18	7.7 $\pm$ 0.31*	5.5 $\pm$ 0.18 <sup>#</sup>	42.1

\*Significant as compared to day 0

<sup>#</sup>Significant as compared to week 4

<sup>§</sup>Significant as compared to day 0

Table 3: Pre and Post treatment ambulatory activity of all the groups (mean  $\pm$  SEM, n=6)

Ambulatory Activity (AA)				
GROUPS	DAY 0	WEEK 4	WEEK 8	% change as compared to Group 2 at 8 <sup>th</sup> week
Group 1	61.7 $\pm$ 1.9	60.3 $\pm$ 0.8	60.5 $\pm$ 1.3	-41.4
Group 2	64.2 $\pm$ 2.6	48.7 $\pm$ 2.4*	42.8 $\pm$ 2.2 <sup>#</sup> <sup>§</sup>	-
Group 3	66.8 $\pm$ 2.0	50.0 $\pm$ 1.6*	59.2 $\pm$ 1.2 <sup>#</sup>	38.3
Group 4	65.7 $\pm$ 2.3	52.7 $\pm$ 2.6*	62.7 $\pm$ 2.1 <sup>#</sup> <sup>§</sup>	46.5

\*Significant as compared to day 0

<sup>#</sup>Significant as compared to week 4<sup>§</sup>Significant as compared to day 0Table 4: Pre and Post treatment frequency of rearing of all the groups (mean  $\pm$  SEM, n=6)

Frequency of Rearing				
GROUPS	DAY 0	WEEK 4	WEEK 8	% change as compared to Group 2 at 8 <sup>th</sup> week
Group 1	15.0 $\pm$ 0.9	15.3 $\pm$ 1.0	15.3 $\pm$ 1.3	39.3
Group 2	16.3 $\pm$ 1.3	22.6 $\pm$ 1.3	25.2 $\pm$ 1.1	-
Group 3	16.5 $\pm$ 1.3	23.0 $\pm$ 1.2	19.5 $\pm$ 1.0	22.6
Group 4	16.8 $\pm$ 1.1	23.3 $\pm$ 1.3	18.6 $\pm$ 1.2	26.2

\*Significant as compared to day 0

<sup>#</sup>Significant as compared to week 4<sup>§</sup>Significant as compared to day 0

## DISCUSSION

The prevalence of obesity and overweight has risen to such an extent that it has become a matter of concern. Present study was conducted to evaluate the antiobesity effect of leaf extract of *Gymnema sylvestre*. Parameters which were considered to evaluate the obesity were weight, BMI, Locomotor activity (Ambulatory activity and frequency of rearing). To induce obesity rats were fed with high fat diet for 4 weeks. All the parameters of obesity were found to be changed significantly after 4 weeks of HFD feeding. The body weight, BMI and ambulatory activity of the groups fed on HFD increased significantly while the frequency of rearing decreased. It is thought that diet rich in fat are responsible for increase in adiposity and it can be helpful in developing murine model of obesity. Fat rich diets have been used to induce obesity in rats and mice as such diets are more palatable as well as more energy dense. [15, 16, 17]

After treatment with *Gymnema sylvestre* leaves extract for 4 weeks all the parameters changed significantly when compared to their previous values as well as to the disease control group. GS at 100 mg/kg and 200mg/kg caused around 33% & 38% weight reduction respectively when compared to the disease control group. GS 100mg/kg caused 34.7% while GS 200mg/kg caused 42.1% reduction in BMI as compared to disease control. Ambulatory activity also improved significantly. Compared to group 2 the percentage increase in AA by GS 100mg/kg and 200mg/kg

was 38.3% & 46.5% respectively while rearing decreased by 22.6% and 26.2% respectively.

Due to HFD weight of internal organs (kidney, liver, spleen and heart) and internal fat pad (perirenal, gonadal and mesenteric) increased significantly. *Gymnema sylvestre* treatment at both the doses decreased the weight of internal organs and fat pad significantly. Weight of liver, kidney, spleen and heart decreased remarkably as compared to the disease control group. In a similar way weight of perirenal, gonadal and mesenteric fat pad also decreased significantly. *Gymnema sylvestre* is a valuable herb of Indian medicinal system. Extract of leaves of this herb is being tried for various diseases. Active constituents that are considered responsible for its medicinal properties are gymnemic acids. In present study we found that the plant has got an excellent antiobesity effect. The possible mechanism for weight reduction could be its ability to reduce craving for food. It also increases the fecal excretion of neutral steroids and bile acids. [18, 19] Besides the extract of plant also causes reduction of serum insulin, leptin and oxidative stress which directly or indirectly contributes to its weight reducing effect. [20, 21]

## CONCLUSION

Present study concludes that the leaf extract of *Gymnema sylvestre* possess ample amount of weight reducing and antiobesity properties. However this should further be

confirmed on higher animals and humans on a larger scale so that it can be used as a potential antiobesity agent in future.

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