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Effect of anti-obesity activity of *Setaria italica* on rats by using food induced obesity method

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Abstract
The aim of the present investigation is to evaluate the effect of anti-obesity activity of *Sataria italica* on rats by using food induced obesity method. To prepare the extract of *Sataria italic* **(**Fox-Tail millets), using ethanol as solvent & to study the anti-obesity activity of extract of *Sataria italica* using food induced obesity method. In this study checked the anti-obesity parameters like Low density protein cholesterol (LDL), High density protein cholesterol (HDL), Percentage of fat (PF), Waist circumference (WC), Body mass index (BMI), Total cholesterol level. In The present study whole grain extract of *Setaria italica* has shown promising results in experimental anti-obesity. The extract of *Setaria italica* showed the results for increased that the standard Orlistat drug, it indicates the test extract posses anti-obesity activity. The investigations of whole grain extract of *Setaria italica* (150 mg/kg and 300 mg/kg) in both FST and TST models in rats were showed *in vivo* anti-obesity activity. In this study the results were obtained increased such as orlistat. So it is concluded that whole grain extract of *Setaria italica* should possessed the anti-obesity activity.

Keywords: Anti-obesity activity, *Sataria italic*, low density protein cholesterol (LDL), high density protein cholesterol (HDL), percentage of fat (PF), waist circumference (WC), Body mass index (BMI)

Introduction
The World Health Organization (WHO) estimates that 4 billion people, 80% of the world population, presently use herbal medicine for some aspect of primary health care. Herbal medicine is a major component in all indigenous people's traditional medicine and a common element in Ayurveda, homeopathic, naturopathic, traditional oriental and Native American Indian Medicine. WHO notes that of 119 plant-derived pharmaceutical medicines, about 74% are used in modern medicine in ways that correlated directly with their traditional uses as plant medicines by native cultures. Major pharmaceutical companies are currently conducting extensive research on plant materials gathered from the rain forests and other places for their potential medicinal value [1]. Obesity is a pathological condition in with excess body fat. It is a chronic disorder with complex interaction between genetic and environmental factors. It is being characterized by high cholesterol, fatty acid levels, Insulin desensitization; high blood pressure; and excessive adipose mass accumulation. Currently more than 1 billion adults are overweight and at least 300 million of them are clinically obese. It is defined by body mass index and further evaluated by both percentage body fat and total body fat. Obesity is a risk to many secondary conditions like cardiovascular disorder, insulin pathological resistance, retinopathy, neuropathy and cancer. Various factors modulating the development of obesity are age, sex, smoking, growth hormone level, skeletal muscle metabolism. Experimental models used to evaluate obesity are high fat diet, high cafeteria diet, hypothalamic lesions, goldthioglucose induced obesity, monosodium glutamate induced obesity. Non-human primates, Spontaneously obese rats, Obesity due to natural allele defects in mice, V-Genetic variants in the human Uncoupled Protein-1 gene and Viral induce obesity are also preferred [1, 2].

Table 1: BMI classification

Classification	BMI(kg/m2)(principal cut-off points)
Under weight	<18.50
Severe thinness	<16.00
Moderate thinness	16.00-16.99
Mild thinness	17.00-18.49
Normal range	18.50-24.99
Over weight	≥25.00
Pre-obese	25.00-29.99
Obese	≥30.00
Obese class-1	30.00-34.99
Obese class-2	35.00-39.99
Obese class-3	≥40.00

Plant Profile

Setaria italica

The name is derived from the Latin word seta, meaning "bristle" or "hair", which refers to the bristly spikelets. *Setaria* having dense silky or bristly brushlike flowering spikes.

Scientific Name or Botanical Name

Setaria italica

Family: Poaceae-Grass family

Anti-Lipase Activity: In a search of a new pancreatic lipase inhibitor from natural sources, 75 medicinal plants were screened for anti-lipase activity. Three plants exhibited strong in vitro anti-lipase activity (>80%): *Eriochloa villosa*, *Orixa japonica* and *Setaria italica.*

Antioxidant / Anti-inflammatory: Administration of an ethanolic extract of S. italica in acute carrageen-induced rheumatoid female rats significantly reduced the levels of cathepsin, uric acid, LDH, ALT and AST as well as increased the levels of antioxidants in serum, liver and kidney tissue. Results showed effective control of scavenging free radicals and potent antioxidant promoting ability probably due to the presence of flavonoids and alkaloids.

Glucose Lowering / Lipid Benefits: Study showed the supplementation of low GI foxtail millet biscuits cause a significant reduction of baseline serum glucose, serum cholesterol and LDL with a 19.68% reduction of glycosylated hemoglobin. Results suggest the millets have a potential protective role in the management of diabetes.

Medicinal Properties

Considered diuretic, astringent, emollient, appetizer, digestive, stomachic and refrigerant. Studies have suggest alpha-amylase inhibiting, anti-lipase, anti-inflammatory, antioxidant, antihyperglycemic, hypolipidemic, antimicrobial, hepatotoxic properties [4-6].

Medicinal Uses

The germinated seed of yellow-seeded cultivars is astringent, digestive, emollient and stomachic. It is used in the treatment of dyspepsia, poor digestion and food stagnancy in the abdomen. White seeds are refrigerant and used in the treatment of cholera and fever. Green seeds are diuretic and strengthening to virility [7-9].

Materials and Methods

Animals

Male Sprague Dawley rats are housed in individual wire-bottom suspended cages in rooms maintained at 22–23 °C with 12 h light-dark cycles. At the age of 6months (body weight about 450 g) the animals are divided in 2 groups: group I is fed ordinary Rodent Chow, group II a special diet containing Rodent Chow, corn oil and condensed milk, resulting in a composition of 14.7% protein, 44.2% carbohydrate, 15.8% lipid, 2.5% fiber, 1.2% vitamin mixture, and 19% water. Body weight and food intakes are measured, and diet replaced, every 3 to 4 days and had a free access to commercial pellet diet (Lipton rat feed Ltd, Pune, Maharashtra) and tap water *ad libitum*.

Drugs Used: Orlistat

Phytochemical Investigation of *Setaria italica*

Phytochemical investigation of the plant material involves the following:

- Extraction of the plant material.
- Phytochemical evaluation of the extract.

Preparation for Method of Extraction

- In this method, 250gms of the seeds of the plant foxtail millet (*Setaria italica*) were taken.
- They were soaked in distilled water for 3 days.
- Later the total soaked mixture was pulverized into smooth powder/paste.
- Now, the paste was filtered by using filter papers.
- The obtained filterate is extracted.
- The extracted filterate was further used to perform the phytochemical tests.

Experimental design

Male sprague Dawley rats of male sex were randomly divided into 2 groups and treated as follows:

Table 2: GROUPS

Groups	Treatment(Mg/Kg Body Weight)
1	Control
2	High-Fat Diet (HFD)
3	Standard Group (Orlistat-25mg/Kg,P.O)
4	HFD+SI (150mg/Kg,P.O)
5	HFD+ SI (300mg/Kg,P.O)

Table 3: Details of anti-obesity studies

S. No	Groups, route of administration – oral	No. of Animals
I	Normal control (NC)	6
II	Obese control (HFD)	6
III	HFD + Orlistat std (25 mg/kg), (STD)	6
IV	HFD + SI(Low dose), 150 mg/kg	6
V	HFD +SI(High dose),300mg/kg	6

Where, n=Number of rats; NC=Normal control; HFD=High fat diet; STD=Orlistat; SML=Human equivalent dose of 5 g; SMM= Human equivalent dose of 7.5 g; SMH= Human equivalent dose of 10 g; *SI=Setaria italic.*

Results

Table 4: Preliminary Phyto-chemical screening

Phytochemical Tests	Result
Carbohydrates	+
Alkaloids	+
Proteins	+
Fixed oils and fats	+
Terpenoids	+
Cardiac glycosides	+

Table 5: Treatment Groups

Groups	Treatment (Mg/Kg Body Weight)
1	Control
2	High-Fat Diet (HFD)
3	Standard Group (Orlistat-25mg/Kg,P.O)
4	HFD+SI (150mg/Kg,P.O)
5	HFD+ SI (300mg/Kg,P.O)

Table 6: Effect of SI on liver parameters and blood glucose in obese rats

Parameter	Normal Control	HFD	STD(25mg/Kg)	SI(150mg/Kg)	SI(300mg/Kg)
Total cholesterol	77.180±0.847	118.2±0.271$^{###}$	87.861±0.461^{a***}	100.16±0.529^{a**}	89.620±0.543^{a*b*}
Triglycerides	219.68±2.4	265.0±4.69$^{###}$	240.58±2.64^{a***}	248.5±8.65^{a***}	244.92±6.58^{a***bns}
HDL(mg/dL)	71.6±2.9	36.51±2.20$^{###}$	47.18±0.41^{a***}	37.76±1.31^{a***}	48.71±2.381^{a***}
LDL(mg/dL	48.71±2.381	63.68±2.94$^{###}$	46.5±4.8^{a***}	50.4±5.5^{a***}	47.25±5.2^{a***}
VLDL (mg/dL)	17.03±0.169	41.22±4.6$^{###}$	19.172±0.092^{a***}	25.5±6.6^{a**}	21.6±0.105^{a**}
SGOT(U/L)	33.4±0.050	69.2±1.9$^{###}$	49.8±2.9^{a***}	59.2±2.25^{a***}	38.1±4.6^{a***}
SGPT(U/L)	39.7±0.6	78.2±2.02$^{###}$	47.6±1.5^{a**}	56.3±3.7^{a**}	44.8±5.4^{a***}
Total bilirubin	2.5±0.04	3.9±0.08$^{###}$	3.17±0.9^{a***}	2.99±0.12^{a***bns}	2.73±0.19^{a***b**}
Blood glucose	81.9±3.4	96.1±4.9$^{###}$	88.0±6.0^{a*}	83.3±3.3^{a**}	75.2±5.2^{a***b**}

All values are expressed as Mean ± SEM, (n = 10), ###P<0.001 when compared with the normal control group, ∗P<0.05; ∗∗∗P<0.001; ∗∗P<0.01; ns P>0.05. a versus high fat diet-induced obesity; b versus standard control (one- way ANOVA, Tukey's post hoc test, n = 10 per group).

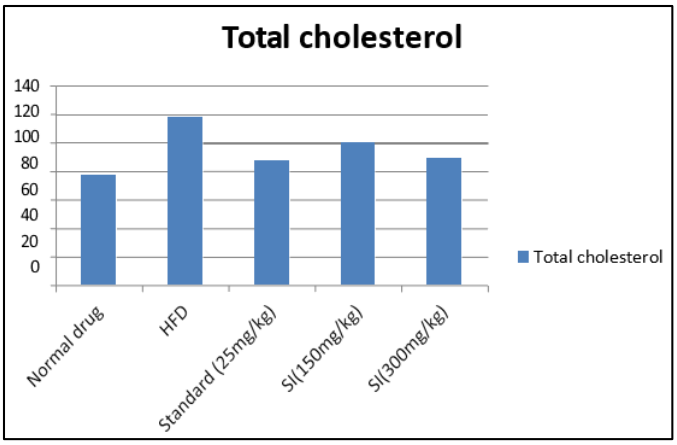


Fig 1: Effect of treatment on total cholesterol

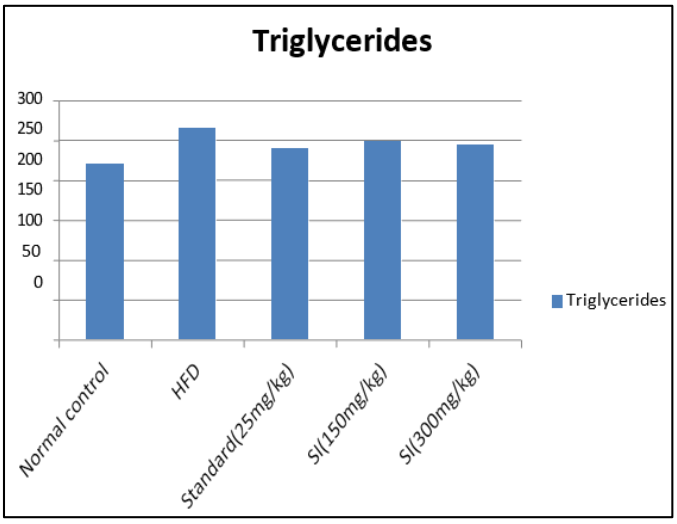


Fig 2: Effect of Treatment on Triglycerides

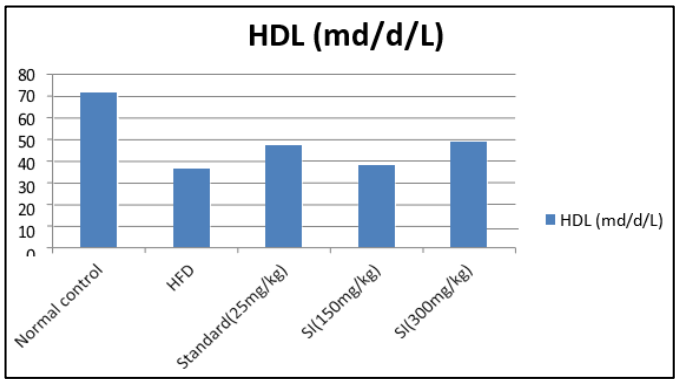


Fig 3: Effect of Treatment On HDL

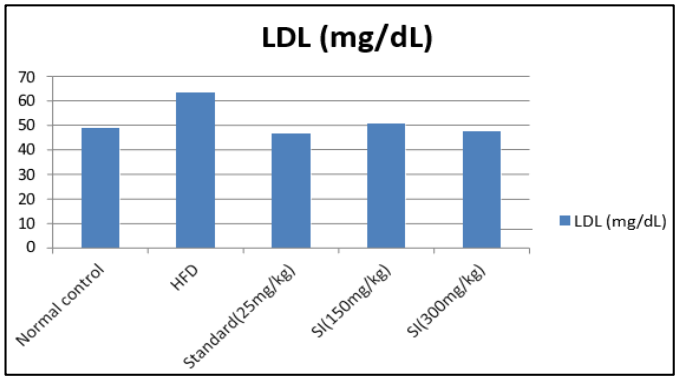


Fig 4: Effect of Treatment On LDL

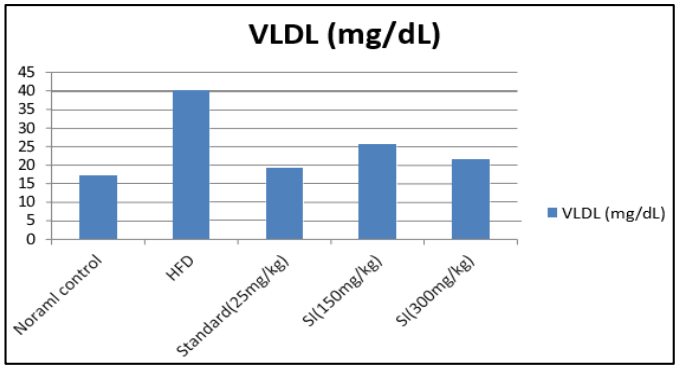


Fig 5: Effect of Treatment on VLDL

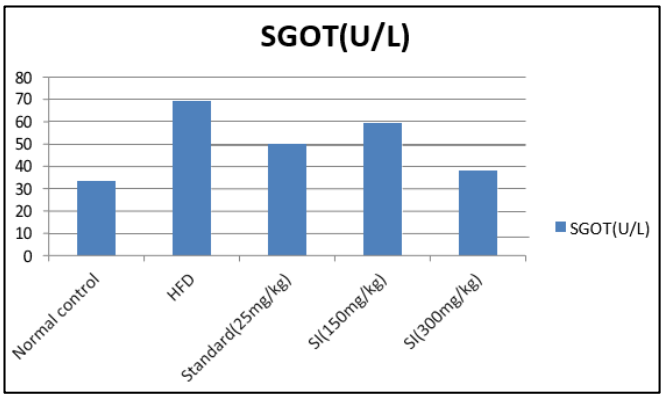


Fig 6: Effect of Treatment on SGOT

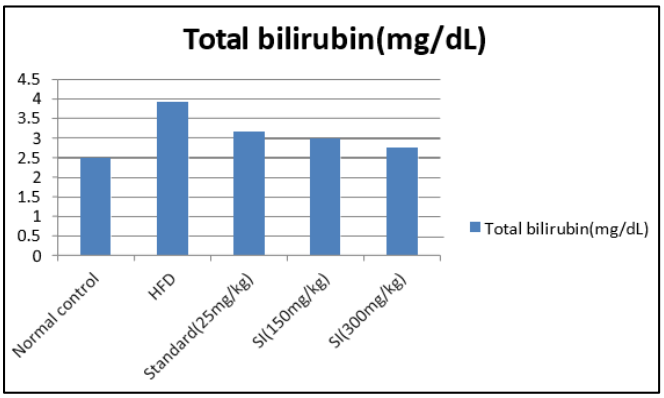


Fig 8: Effect of Treatment On total bilirubin

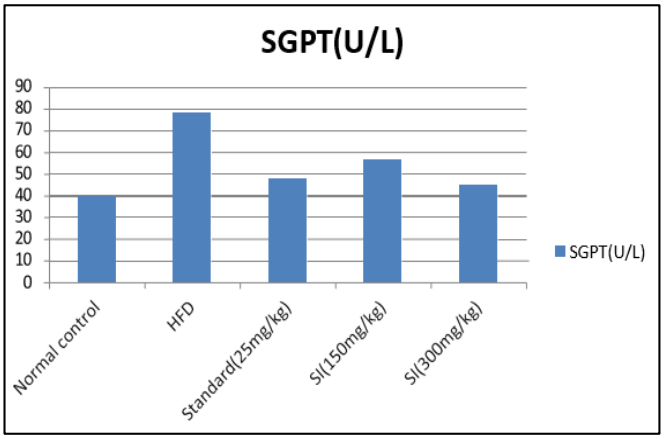


Fig 7: Effect of Treatment On SGPT

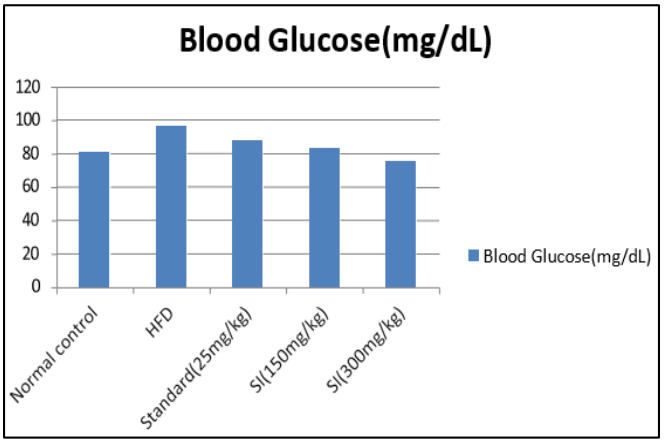


Fig 9: Effect of Treatment On blood glucose

Table 7: Effect of SI supplementation on atherogenic index and percentage protection.

Groups	Atherogenic Index	% Protection
Nc	0.08±0.53	-
HFD	$2.3\pm0.8^{a***}$	-
STD(25mg/Kg)	$0.9\pm0.12^{b**}$	60.8
SI(150mg/Kg)	$1.7\pm0.6^{b*}$	26.0
SI(300mg/Kg)	$0.87\pm0.76^{b**}$	62.1

All values are expressed as Mean ± SEM. a versus normal Control; b versus HFD-induced obesity. $*P<0.05$, $**P<0.01$, $***P<0.001$, (one-way ANOVA, Tukey's post hoc test, n = 10 per group).

Table 8: Effect of SI on Body temperature

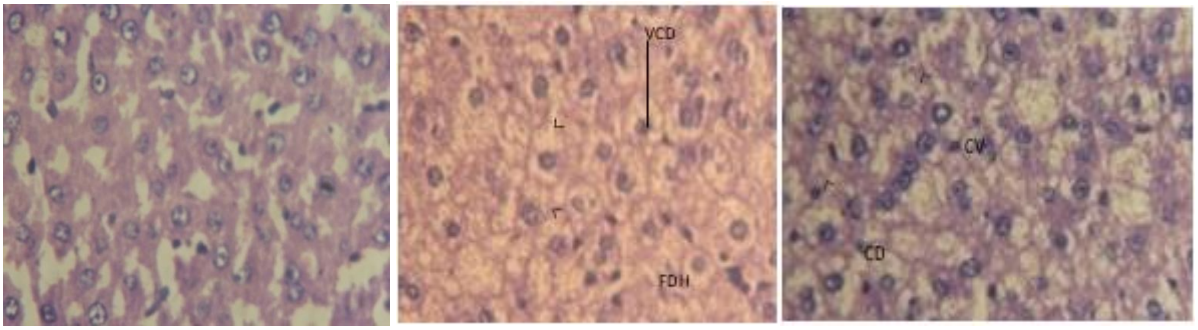
S.NO	Groups	0 min	30 min	60 min	90 min	120 min
1	Control	39.3±1.117	37.2±1.21	39.7±0.653	38.3±2.240	38.5±1.364
2	High-fat diet	32.9 ± 2.295^{ns}	$27.3\pm2.508^{a*}$	$25.0\pm2.87^{a**}$	$25.1\pm2.84^{a**}$	$23.3\pm1.83^{a***}$
3	Standard (25mg/k g)	36.1 ± 1.411^{ns}	$39.9\pm1.161^{b**}$	$35.4\pm1.161^{b*}$	$35.6\pm1.340^{b*}$	$34.6\pm2.228^{b*}$
4	SI (150mg/ kg)	39.5 ± 0.81^{ns}	$38.4\pm0.934^{b**}$	$35.4\pm1.391^{b***}$	$38.9\pm0.817^{b**cns}$	$36.1\pm1.554^{b*cns}$
5	SI (300mg/ kg)	36.2 ± 1.53^{ns}	$34.0\pm1.455^{b*}$	$39.1\pm2.026^{b**}$	$41.3\pm0.479^{b**c*}$	$40.6\pm0.702^{b***c*}$

All values are expressed as Mean ± SEM (n = 10). Statistical significance testing for the comparisons was made by ANOVA, followed by Tukey's post hoc test. $*P<0.05$, $**P<0.01$, $***P<0.001$, ns$P>0.001$. a versus Normal Control; b versus HFD-induced obesity; c versus standard control (one-way ANOVA, Tukey's post hoc test, n = 10 per group).

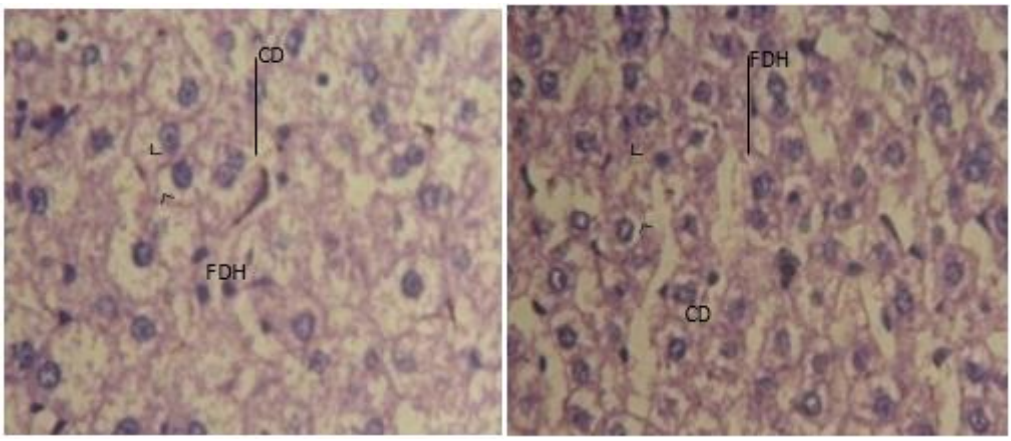
Table 9: Effect of SI supplementation on organ weight

Organ weight	Normal control	HFD	Standard (25mg /kg)	SI(150mg/kg)	SI(300mg/kg)
Liver	5.737±0.088	$8.845\pm0.982^{a**}*$	$6.158\pm0.892^{b***}$	$7.573\pm0.779^{b*}$	$6.947\pm1.754^{b**}$
Right kidney	0.765±0.012	$1.76\pm0.095^{a***}$	0.801 ± 0.053^{bns}	0.874 ± 0.073^{bns}	0.842 ± 0.017^{bns}
Left kidney	0.748±0.017	$0.958\pm0.075^{a**}$	$0.758\pm0.019^{b**}$	0.813 ± 0.012^{bns}	$0.804\pm0.009^{b*}$

All values are expressed as Mean ± SEM (n = 10) $***P<0.001$ when compared with the normal control group, $*P<0.05$; $***P<0.001$; $**P<0.01$; ns$P>0.05$. a versus high fat diet-induced obesity; b versus standard control, one-way ANOVA followed by Tukey's post hoc test.



(a) Normal (b) High-fat diet (HFD) (c) HFD + orlistat (25mg/kg)



(d) HFD + SI(150mg/kg) (e) HFD + SI(300mg/kg)

Fig 10: The following are the results of histo-pathological studies

5. Conclusion

A number of studies on *Setaria italica*, major active principles, have shown an anti-obesity, anti-oxidant, anti-microbial and hypo-glycaemic activities. The present study of whole grain extract of *Setaria italica* has shown promising results in experimental anti-obesity. These studies are valuable for identifying lead compounds for anti-obesity drugs, keeping in mind the side effects of presently used anti-obesity drugs. The standardization of the extract, identification and isolation of active principles along with pharmacological studies of these principles may be considered for further detailed studies. Still further human studies are needed to prove the safety and efficacy of long-term administration of whole grain extract of *Setaria italica*. In the light of observations made it may be envisaged that *Setaria italica* can be used as potential adjuvant in the treatment of anti-obesity disorders. The qualitative analysis of whole grain extract of *Setaria italica* revealed the prescence of alkaloids, flavanoids, phenolic compounds and terpenoids etc. The extract of *Setaria italica* showed the results for increased that the standard Orlistat drug, it indicates the test extract posses anti-obesity activity. The investigations of whole grain extract of *Setaria italica* (150 mg/kg and 300 mg/kg) in both FST and TST models in rats were showed *in vivo* anti-obesity activity. In this study the results were obtained increased such as orlistat. So it is concluded that whole grain extract of *Setaria italica* should possessed the anti-obesity activity.

6. References

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