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Evaluation of Antiobesity and Hypolipidaemic effect of Sandroos (*Trachylobium hornemannianum* Hayne.) in Diet Induced Obesity in Rats

[1] Heena Kausar S, [*2] Najeeb Jahan, [3] Kamal Ahmad

[1, 3] PG Scholars, Dept. of Ilmul Advia (Pharmacology), National Institute of Unani Medicine, Kottigepalya, Magadi main road, Bangalore, Karnataka, India

[2] Lecturer, Dept. of Ilmul Advia (Pharmacology), National Institute of Unani Medicine, Kottigepalya, Magadi main road, Bangalore, Karnataka, India

Abstract

Back ground & objective: *Sandroos* (*Trachylobium hornemannianum* Hayne.) has been mentioned in Unani literature as an important drug for the treatment of obesity (*Simne mufrit*) and its associated disorders. Therefore, the present study was carried out to evaluate its effect in Diet induced obesity in rats.

Materials and methods: The study was carried out on 48 Sprague Dawley rats of either sex, divided into six groups of 8 animals in each. Group I received vehicle and normal diet throughout the study; Group II was given *Sandroos* (350mg/kg) orally, along with normal pellet diet; Group III was given only Cafeteria diet (CD); Group IV was given *Sandroos* (350mg/kg) along with CD; Group V was given *Sandroos* (700mg/kg) along with CD and Group VI was given Orlistat (14mg/kg) along with CD throughout the study. During the study, food intake was recorded daily and on every 15th day body weight, locomotor activity, body temperature, and RBS were recorded. On 46th day, animals were sacrificed and Serum lipid profile, organ weight, fat pad weight, lipid content, histopathological examination of adipose tissue and body composition of animals was analyzed.

Results: A significant (P<0.01) decrease in food intake, body weight, RBS, lipid content, adipose cell size, fat pad weight, triglyceride(TG), total cholesterol, LDL and VLDL concentration was found in test drug treated groups and highly significant (P<0.001) effect was observed in single dose treated group. The findings of double dose treated group were found near to plain and standard control groups. Significantly (P<0.01) increase in body temperature, locomotor activity and HDL was observed in group II.

Conclusion: *Sandroos* has shown to possess potent hypolipidaemic and antiobesity effect in its therapeutic dose without any observable side effects. Thus, the study validated the claims of Unani physicians.

Keywords: antiobesity, cafeteria diet, hypolipidaemia, *sandroos*, *simne mufrit*, unani medicine

1. Introduction

Obesity is a chronic metabolic disorder caused by an imbalance between energy intake and its expenditure. It has become the sixth common cause for disease burden worldwide [1]. It is defined as an abnormal or excessive accumulation of fat that may put a person at health risk [2, 3] to such an extent that may reduce life expectancy [4]. Chronic obesity is a problem of epidemic proportions, which has an important impact on life style-related diseases such as coronary heart disease, dyslipidemia, glucose intolerance, diabetes, hypertension and some types of cancers. Several factors, including lack of exercise, sedentary lifestyles and consumption of energy rich diets are contributory to the etiology of obesity [2]. Obesity is more prevalent in developed countries than developing countries [5]. WHO has described obesity as one of today's most neglected public health problems, affecting every region of the globe [6].

Simne mufrit (Obesity) is a well-known disease since Greeco Arab period. Ancient Greeks (460-136 B.C.) were the first to know about the dangers of obesity and its associated diseases. *Buqrat* (Hippocrates), the father of Medicine was first to describe the complications of obesity like infertility and early death [7]. *Ibn Sina* in *Al Qanoon fil Tib (the Canon of Medicine)* mentioned that obese people are more prone to develop cardiac and cerebral complications like stroke, syncope, coma, palpitation, breathlessness, concealed haemorrhage and sudden death [8]. According to Unani system of medicine, *Simne mufrit* is more prone in people of *Barid Ratab Mizaj* (cold & moist temperament). Due to increased *buroodat* (coldness) and *rutoobat* (moistness) there will be an imbalance in the humours of the body which leads to accumulation of *Akhlate fasida* (morbid matter) particularly *maddae balghamiya* (phleghmatic matter) [8, 9].

Though a number of modern drugs are being used for the management of obesity in different parts of the world but these drugs have been reported to produced side effects like dry mouth, constipation, insomnia, increase heart rate and blood pressure, anxiety, sweating, heart attacks, cardiac arrest and stroke etc. [10, 11, 12]. Hence people are moving towards the traditional system of medicine for a safe and effective treatment in the management of obesity to avoid side effects produced by modern drugs. Several plants and resins in Unani System of Medicine have been used to treat obesity and *Sandroos (Trachylobium hornemannianum*) a resin obtained from Sal tree [13] traditionally is used in Unani System of Medicine as a drug of choice for the treatment of obesity and its associated disorders and almost all renowned physicians have described its therapeutic properties like *Muhazzil*

(emaciating), *Mujafif* (dessicant), *Qate balgham* (mucolytic), *Mudir e boal* (Diuretic), *Munaqi e Akhlat e Barida* (Elimination of *Barid* humours) [8, 14]. But no scientific study has been carried out on *Sandroos* to evaluate its anti-obesity activity. Therefore, present study was envisaged to evaluate its anti-obesity and hypolipidaemic effects in Diet induced obesity in rat's model.

2. Material and Methods

2.1 Plant material

The oleoresin, *Sandroos* (*Trachylobium hornemannianum),* was procured from city market Bangalore. The resin was identified by Botanist N. Prasad, Head of Processing and Product Development Division, Indian Institute of Natural Resins and Gums (IINRG), Ranchi, with File No. PPD/4.4/2013/4807. A voucher specimen of the *Sandroos* has been submitted in the department of Ilmul Advia (Pharmacology), National Institute of Unani Medicine (NIUM), Bangalore for record and future reference.

2.2 Preparation and calculation of Dose

A fine powder of *Sandroos* was prepared in an electric grinder at Pharmacy of NIUM and passed under 80 no. sieve. The human therapeutic dose of *Sandroos* as mentioned in Unani classical literature is 3g [8, 14]. The dose for SD rats was calculated by dividing it by adult human weight of 60 kg and multiplying with the conversion factor of 7 to accommodate the surface area of animal [15] and found to be 350 mg/kg. Another higher dose was also calculated that is just double of the first dose (700 mg/kg) to evaluate the efficacy of test drug in dose dependent manner. Standard drug Orlistate 14mg/kg bw was given orally [12], and 1ml of 0.5% CMC w/v in distilled water was used as vehicle for dosing in all the experimental groups which was prepared freshly daily before administration.

2.3 Animals

The study was carried out on Sprague Dawley rats of either sex, weighing about 150-200gms $\pm$ 20, obtained from the Animal House Facility of NIUM. Animals were grouped and housed in polypropylene cages (4 animals per cage) and maintained under standard laboratory conditions (temperature 25$\pm$2ºC, relative humidity 60-70% and 12h light/dark cycle). They had free access to food and water and were acclimatized for 2 weeks before experiment started. The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) for ethical clearance, NIUM, Bangalore, Karnataka; vide its registration number, IAEC/IX/06/IA.

2.4 Diet induced obesity

The obesity in rats was induced by feeding them cafeteria diet for a period of 45 days. Three different cafeteria diets were given as follows:

1. Condensed milk 40gm+ bread 40gm
2. Chocolate 15gm + biscuit 30gm + dried coconut 30gm
3. Cheese 40gm + boiled potato 50gm

The diets were prepared and calculated according to per kg b w and given to 4 groups of rats (except Group I and Group II) on day 1, 2 and 3 respectively and then repeated in the same succession [16].

2.4.1 Preparation of Cafeteria diet (CD)

The CD pellets were prepared fresh daily in combination of 70% Cafeteria diet with 30% of normal rat pellet.

2.5 Cafeteria diet and Chemicals

Cafeteria diet was purchased from Super market of Bangalore. All the chemicals were analytical grade and were purchased as follows:

TG and TC kit from Spinreact, S.A. Euro diagnostics; HDL kit from Beijing Leadman Biochemistry Co., Ltd, Chloroform from Central drug House (P) Ltd, Methanol from HIMEDIA laboratories (P) Ltd. Glucochek and Blood glucose test strips from Aspen diagnostics (P) LTD.

2.6 Experimental design.

- **Group I** (Plain control): 1ml of 0.5% of CMC (vehicle)
- **Group II** (Test drug control)**:** *Sandroos* (350mg/kg bw) + vehicle + ND (Normal pallet Diet)
- **Group III** (Negative control)**:** Cafeteria Diet (CD)
- **Group IV** (Single dose treated): *Sandroos* (350mg/kg bw) + vehicle + CD
- **Group V** (Double dose treated): *Sandroos* (700mg/kg bw) + vehicle + CD
- **Group VI** (Standard drug treated)**:** Orlistat (14mg/kg bw) + vehicle + CD

All the above groups received their respective treatment for 45 days.

2.7 Experimental Protocol

During the study, daily food intake was recorded; once in 15 days the body weight, Random Blood Sugar level (RBS), locomotor activity [17] and body temperature was recorded till 45 days; and on 46th day all the animals were fasted for 12 h and then animals were anaesthetized under thiopentone sodium (50mg/kg IP), and blood was collected by cardiac puncture for the analysis of serum lipid profile [18]. After blood collection, abdomen was opened and adipose tissues from retroperitoneal area; uterine fat pads in female rats and epididymal fat from male rats were separated and weighed; lipid content was estimated [20] and histopathological examination was carried out from uterine fat pads and epididymal fat. The vital organs like heart, liver, spleen, left and right kidney were dissected to record organ weight [20] body composition was recorded by drying carcass in an oven at 95˚C until constant weight is reached [19].

2.8 Statistical Analysis

Results were expressed as mean ± SEM (Standard error of the mean). Results among different groups were analyzed by One way Analysis of Variance (ANOVA) followed by Tukey-Kramer Multiple Comparison Test. The P value ≤ 0.05 was taken as significant.

3. Results

3.1 Food Intake

A significant (P<0.05) increase in food intake in Group III animals was observed when compared with other groups. Food intake in group II, IV and V was found to be significantly decreased on 30th and 45th day, when compared with all the groups on same day. (Table 1)

3.2 Body weight

The percentage gain of body weight in all the groups was found to be 42.52%, 39.39%, 50.31%, 36.87 %, 41.70% and 42.08%;

respectively. When these values were compared, a significant weight gain was found in Group III in comparison with Group I and significant decrease in weight was found in Group II, IV, V and VI when compared with group III. (Fig 1)

3.3 Effect of *Sandroos* on body temperature

On 30th day the body temperature of group III was found to be significantly (P<0.001) decreased when compared with other groups on the same day. A significant (P<0.05) increase in body temperature of group II was observed from 0th day to 45th day when compared with other groups. (Table 2)

3.4 Effect of *Sandroos* on Random Blood Sugar level

No significant difference was observed in the mean values of RBS of Group II, III, IV, V and VI when compared with Group I, but significant and gradual increase in the values of RBS of group III was observed from 0th day to 45th day when compared to other groups. There was slight decrease in the values of RBS observed in group V when compared with the values of group III. (Fig 2)

3.5 Effect of test drug on locomotor activity

Locomotor activity was recorded once in 15 days using Tru Scan 2 photo actometer apparatus, version no. 5.1.2600.2180 from Coulbourn Instruments. Rats were placed in the centre of the apparatus and recorded the movements for 5 min. The movements of rat were recorded on two measures such as Floor Plane Sensor Measure (FP) and Vertical Plane Sensor Measures (VP).

3.5.1 FP-Floor Plane Sensor Measure

3.5.1.1 FP- Total Movements

The results showed significant decrease in FP- total movements on 30th day when compared with the 0th day of all the groups. A significant decrease was observed in group III on 30th day when compared with other groups on the same day. All test drug treated groups showed a slight decrease in the activity on 30th day. And the FP- movements in group III on 45th day was found to be significantly decreased when compared with other groups on same day. The mean FP movements of Group IV, V and VI were almost same as that of Group I animals. (Fig 3)

3.5.1.2 FP- Mean Velocity (All Movements)

All treated groups showed a slight increase in the activity on 30th day but it was found to be decreased on 45th day. In group VI gradual increase in FP-mean velocity was observed when compared with other groups. (Fig 4)

3.5.1.3 FP- Rest Time

There was significant decrease in FP-Rest time in all the groups on 30th day when compared with 0th day and 45th day and gradual decrease in FP rest time was observed in Group II and Group VI when compared with other groups. (Fig no 5)

3.5.2 VP-Vertical Plane Sensor Measures

3.5.2.1 VP- Entries

A significant increase in VP- Entries on 30th day was observed when compared with all the groups on 0th day and again a gradual decrease on 45th day was found which was similar to Group I, except in Group VI where gradual increase in VP-Entries was observed on 45th day. (Fig no. 6)

3.5.2.2 VP- Time

A significant increased in VP-Time on 30th day was observed when compared with other days in all the groups. But there was significant (P<0.05) increase in group III on 30th day and also on 45th day when compared with other groups on same days. (Fig no. 7)

3.5.2.3 VP- Total Movements

VP -Total movements significantly increased on 30th day when compared with 0th day of all the groups, and but there was gradual increase in VP total movements in group VI from 0th day to 45th day. (Fig no.8)

3.6 Effect of *Sandroos* on Serum lipid Profile

A significant increase in serum TC, TG, LDL and VLDL was found in group III, when compared with Group I and other treated groups. A significant decrease was found in all the treated groups when compared with plain treated. Highly significant increase in serum HDL in Group II, IV and V when compared with group III, and significant decrease in serum HDL was observed in Group III when compared with group I and II. (Table 3)

3.7 Effect of *Sandroos* on lipid content in gonadal fat pad

The lipid content in gonadal fat pad was estimated by the method of Folch J *et al.* A significant increase in lipid content was found in Group III when compared with I and II respectively. A significant decrease in lipid content was observed in Group II and V when compared with III. (Table 4)

3.8 Effect of *Sandroos* on Organ weight

When the mean values of Heart, Liver, Kidneys and Spleen were compared among the groups, there was no significant difference found in all the groups except in group III. (Table 5)

3.9 Effect of *Sandroos* on Total fat pad

A significant increase in fat pad weight was observed in group III when compared with I and II. The weight was decreased significantly in Group IV, V and VI when compared with Group III. The total fat pad value was found to be decreased significantly in group II when compared with other groups. (Table 5)

3.10 Effect of *Sandroos* on Body composition

The body composition of carcass was recorded by the method of Gupta SK *et al.*

When the mean weight loss difference was compared among the groups, a significant increase was observed in group III. And significant decrease was found in Group IV and V, but highly significant decrease in weight loss was seen in group V when compared with other groups. (Table no 6)

3.11 Histopathological examination of uterine and epidydimal fat tissue

Section studies of epididymal fat pad and uterine fat pad of male & female rats showed a slight increase in adipocyte cell size in group IV when compared with Group I but there was significant decrease in adipocyte cell size when compared with Group III. Group V animals showed adipocyte size of epididymal fat pad 0.10mm, and uterine fat pad was 0.12mm.There was significant decrease in size of adipocyte cells of both epididymal and uterine fat pad in group V when

compared with group III. The section of group VI animals showed adipocyte size 0.12mm in epididymal fat pad and 0.15mm in the uterine fat pad. A significant decrease was observed in size of adipocytes of this group when compared with Group I. (Fig 9 and Fig 10)

Tables and Figures

Table 1: Effect of *Sandroos* on Food Intake in cafeteria diet induced Obesity

Food Intake in grams				
Groups	**0 day**	**15th day**	**30th day**	**45th day**
Group I	60.5± 0.8662	67.42 ± 2.37	66.42 ± 1.414	69.03 ± 3.174
Group II	58.50 ± 0.7541	66.00 ± 0.5521	61.4 ± 1.419	60.86 ± 2.702
Group III	71 ± 1.3305^{b*}	67.90 ± 2.315	68.86 ± 2.032	69.9 ± 3.167
Group IV	64.00 ± 1.1109	59.7 ± 2.6085	61.46 ± 2.718	60.1 ± 3.738
Group V	61± 1.161	63.2 ± 4.298	54.83± 2.003^{a***c**}	58.83 ± 2.093
Group VI	67 ± 0.8662	65.76 ± 2.373	66.00±3.064	64.4 ± 3.154

Values are expressed as mean ± SEM (n=8). Test used ANOVA one way with post test Tukey-Kramer multiple comparison test. *P<0.05, ** P<0.01, *** P<0.001.
a= compared with group I, b= compared with group II, c= compared with group III.

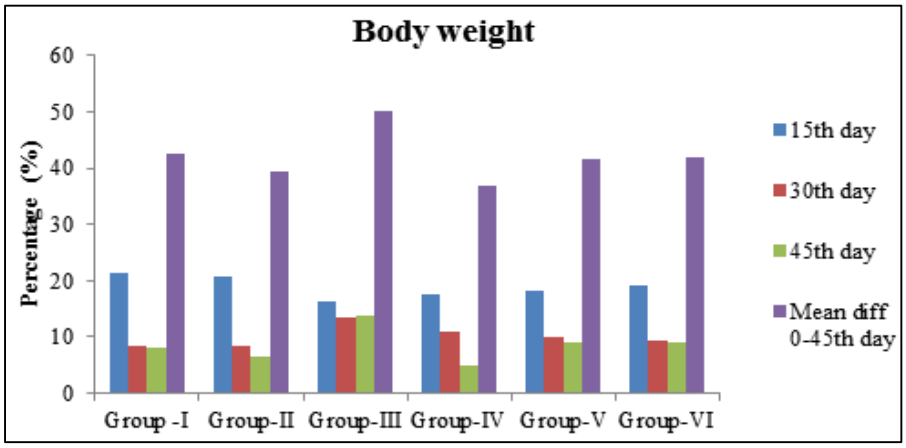

Fig 1: Effect of *Sandroos* on body weight in cafeteria diet induced Obesit

Table 2: Effect of *Sandroos* on body temperature in cafeteria diet induced Obesity

Groups	**0 Day (^{0}F)**	**15th Day (^{0}F)**	**30th Day (^{0}F)**	**45th Day (^{0}F)**
Group I	97.83 ± 0.8785	98.26 ± 0.4754	97.63 ± 0.5966	96.94 ± 0.3401
Group II	99.60 ± 0.9161	99.74 ± 0.3059 ^{b*}	98.50 ± 0.4713	99.15 ± 0.5846
Group III	98.24 ± 0.5619	96.78 ± 0.5140^{a*}	95.84 ± 0.3417 ^{a***}	96.80 ± 0.6358 ^{a*}
Group IV	98.75 ± 0.7149^{b*}	98.86 ± 0.7978^{b*}	99.54 ± 0.3822 ^{b**}	98.96 ± 0.6208 ^{b*}
Group V	98.28 ± 0.3261	98.04 ± 0.5545	98.58 ± 0.4386	98.70 ± 0.3960
Group VI	97.08 ± 0.4617	98.82 ± 0.4996	98.34 ± 0.3863	97.75 ± 0.3105

Values are expressed as mean ± SEM (n=8). Test used ANOVA one way with post test Tukey-Kramer multiple comparison test. *P<0.05, ** P<0.01, *** P<0.001.
a= compared with Group II, b= compared with group III.

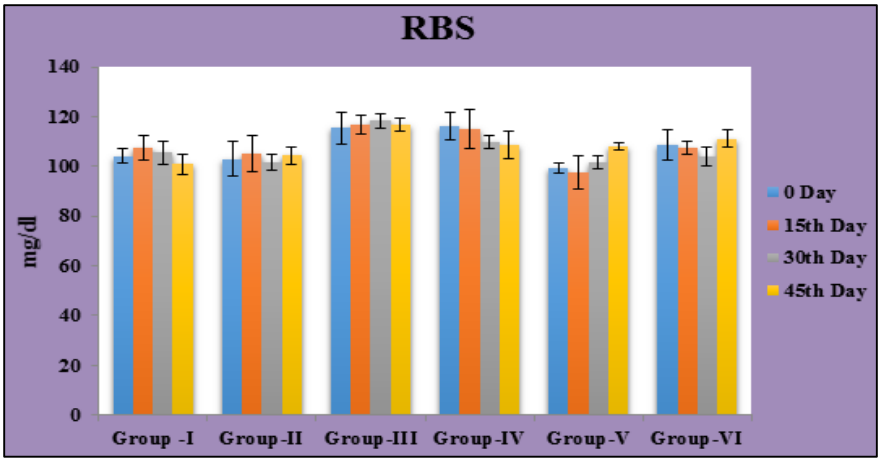

Fig. 2: Effect of *Sandroos* on Random Blood Sugar level in cafeteria diet induced Obesity

Effect of test drug on locomotor activity in cafeteria diet induced Obesity (FP-Floor Plane Sensor Measure

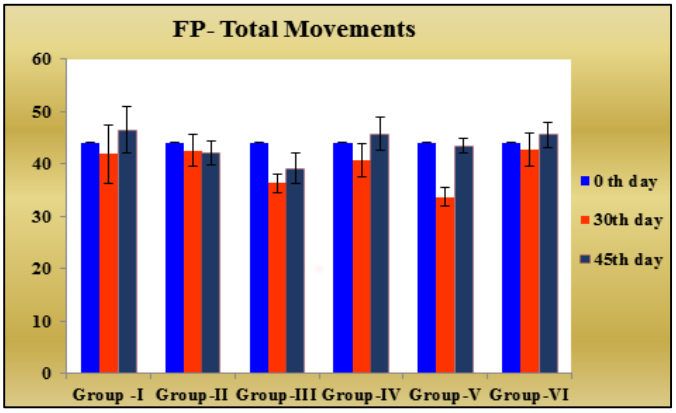

Fig 3: Effect of test drug on FP- Total Movements in cafeteria diet induced Obesity

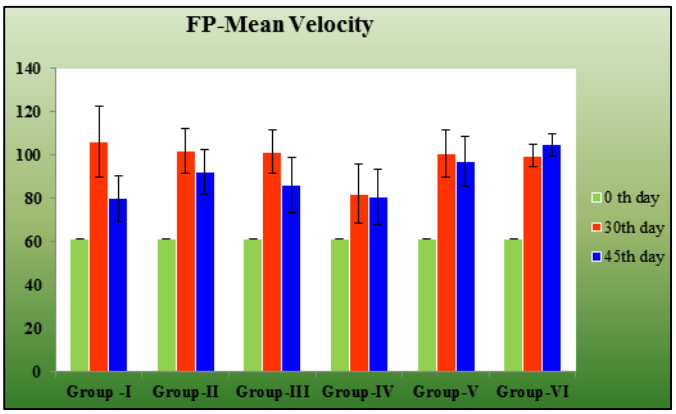

Fig 4: Effect of test drug on FP- Mean Velocity in cafeteria diet induced Obesity

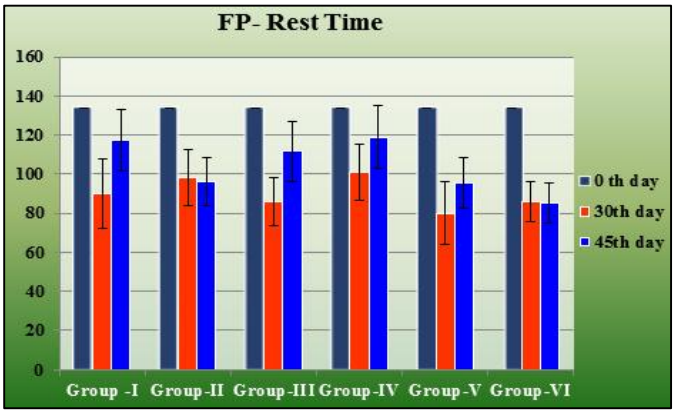

Fig 5: Effect of test drug on FP- Rest Time in cafeteria diet induced Obesity

Effect of test drug on locomotor activity in cafeteria diet induced Obesity (VP-Vertical Plane Sensor Measures)

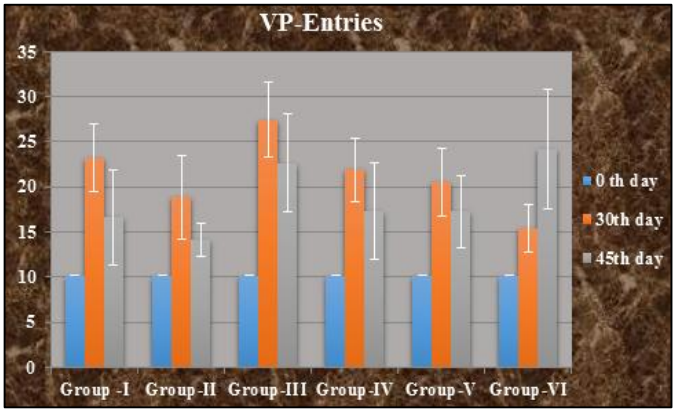

Fig 6: Effect of test drug in VP Entries cafeteria diet induced Obesity

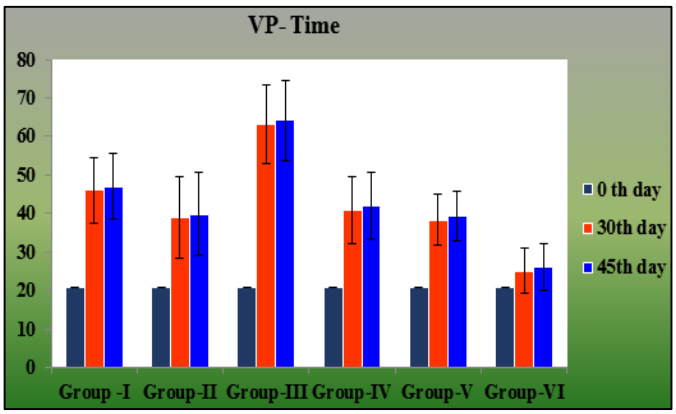

Fig 7: Effect of test drug on VP- Time in cafeteria diet induced Obesity

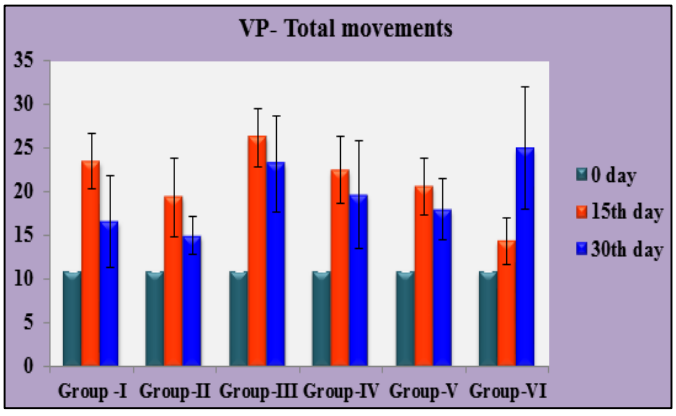

Fig 8: Effect of test drug on VP- Total movements in cafeteria diet induced Obesity

Table 3: Effect of *Sandroos* on Serum lipid Profile in cafeteria diet induced Obesity

Groups	TG	HDL	T-Cho	VLDL	LDL
Group 1	95.26 ± 15.04	46.41 ± 3.611	108.8 ± 3.447	19.05 ± 3.008	43.33 ± 7.437
Group 2	69.98 ± 6.966	66.70 ± 6.271	91.69 ± 3.277 ^{a*}	14.00 ± 1.393	38.99 ± 5.444
Group 3	176.0 ± 7.232	33.31 ± 6.319	140.80 ± 2.782	35.19 ± 1.446	72.29 ± 7.518
Group 4	106.3 ± 20.83	52.47 ± 10.16	103.4 ± 4.623	21.24 ± 4.159	29.69 ± 5.401
Group 5	110.0 ± 14.86	50.54 ± 6.490	107.4 ± 3.058	22.00 ± 2.971	34.50 ± 10.07
Group 6	95.82 ± 9.341	48.91 ± 5.895	92.92 ± 2.992 $^{a* b*c*}$	19.16 ± 1.868	24.84 ± 6.758

Values are expressed as mean ± SEM (n=8). Test used ANOVA one way with post test Tukey-Kramer multiple comparison test.* $P<0.05$ is considered as significant.

a= compared with Group I, b= compared with group III. C= compared with group III

Table 4: Effect of *Sandroos* on lipid content of gonadal fat pad in cafeteria diet induced Obesity

Groups	Lipid Content (%)
Group I	5.295 ± 0.1618
Group II	5.053 ± 0.1419
Group III	6.143 ± 0.2407 a* b**
Group IV	5.363 ± 0.09646
Group V	5.240 ± 0.2695 c*
Group VI	5.663 ± 0.1223

Values are expressed as mean ± SEM (n=8). Test used ANOVA one way with post test Tukey-Kramer multiple comparison test. **P*<0.05, ***P*<0.01.
a= compared with Group I, b= compared with group II. C= compared with group III.

Table 5: Effect of test drug on organ weight in cafeteria diet induced Obesity

Organ Weight						
Groups	**Heart**	**Liver**	**Lt kidney**	**Rt Kidney**	**Spleen**	**Total Fat**
Group I	0.7429 ± 0.05560	7.152 ± 0.5208	0.7418 ± 0.07150	0.7925 ± 0.06742	1.081 ± 0.1283	3.540 ± 0.2355
Group II	0.7441 ± 0.04256	6.863 ± 0.7275	0.7149 ± 0.05615	0.7748 ± 0.06665	0.9843 ± 0.09796	2.902 ± 0.2989
Group III	0.7111 ± 0.03093	7.248 ± 0.5751	0.7001 ± 0.04853	0.7226 ± 0.04929	1.162 ± 0.08805	6.065 ± 0.5612 a*b*
Group IV	0.6940 ± 0.04124	6.320 ± 0.4560	0.6324 ± 0.04358	0.6628 ± 0.03311	0.9131 ± 0.05273	4.001 ± 0.4140 c*
Group V	0.6983 ± 0.04179	6.909 ± 0.3508	0.6719 ± 0.05817	0.6673 ± 0.05313	0.9216 ± 0.08113	3.641 ± 0.4678 c*
Group VI	0.7621 ± 0.04412	6.868 ± 0.3046	0.7089 ± 0.06642	0.7465 ± 0.06030	1.079 ± 0.07306	4.265 ± 0.3914 c*

Values are expressed as mean ± SEM (n=8). Test used ANOVA one way with post test Tukey-Kramer multiple comparison test. **P*<0.05.
a= compared with Group I, b= compared with group II. C= compared with group III.

Table 6: Effect of *Sandroos* on Body composition in cafeteria diet induced Obesity

Groups	Before	After	Mean difference
Group 1	211.9 ± 13.99	67.88 ± 2.949	144.1 ± 12.82
Group 2	206.4 ± 13.55	69.50 ± 3.179	137.0 ± 15.25
Group 3	199.8 ± 9.454	50.63 ± 1.917	149.1 ± 8.180^{a*}
Group 4	183.5 ± 11.96	61.88 ± 3.243	121.6 ± 9.126
Group 5	184.1 ± 11.64	66.63 ± 3.162	117.5 ± 10.45^{a**}
Group 6	194.9 ± 9.238	65.13 ± 1.060	129.8 ± 8.864

Values are expressed as mean ± SEM (n=8). Test used ANOVA one way with post test Tukey-Kramer multiple comparison test. **P*<0.05, ***P*<0.01 is considered as significant.
a= compared with group IV and III

4. Discussion

CD induced obesity model is an appropriate model for human obesity as it represents the behavioral and environmental factors. CD is palatable, hyper caloric and hyperlipidimic diet, it has been reported to increase energy intake and cause obesity in humans [21] as well as in animals [22] by inducing voluntary hyperphagia and fast weight gain [23] .The model described by these experiments shares many important features with human obesity. Moreover the phenomenon is reliable and consistent from one experiment to the next. The paradigm also appears to be equally effective, at least on a relative level, in males and females. This is important because both men and women, when they eat diets high in fat, have a tendency to become obese [24]. The test drug showed loss of appetite in dose dependent manner as the double dose of the test drug shows more significant decrease in food intake when compared with single dose treated group. Further the results showed similar findings in group II and V. Loss of body weight and decrease food intake by test drug in dose dependent manner suggest that the test drug *Sandroos* may act centrally and reduce food intake by decreasing appetite or increasing satiety and it reduces body weight and thereby it can be called as appetite suppressants [12]. Significant decrease in body temperature in Group III proves that the CD increases *buroodat e mizaj* (cold temperament) in the body, which leads to decrease in *Hararate gharizia* (innate heat), hence deposition of *sheham* (fat) occurs. As it has already mentioned in classical Unani literature in *Kamilus Sanaa* that *sheham* reduces *Hararate gharizia* (innate heat) and constricts the blood vessels because of *buroodate mizaj* (domination of cold temperament) [8, 25, 26]. Hence it leads to obesity in CD induced group. A significant increase in locomotor activity was observed in test drug control groups when compared to other groups. And significant decrease in rest time was observed in test drug control groups when compared with CD group III. The high frequencies of these behaviors were observed in test drug control group indicates increased locomotion and exploration of physical activity by *Sandroos* [27]. These findings can be substantiated from the results obtained in the study on body temperature and body weight.

Significant (*P*<0.05) increase in blood sugar level in group III may be due to diminished hepatic and muscular uptake of glucose which produces hyperlipidaemia due to increased fat mobilization from adipose tissue and resistance to the antilipolytic actions of insulin, as it has been reported that an oversupply of lipids is associated with impaired insulin action. This increased availability led to either elevated lipid stored in insulin target tissues (e.g. muscle, liver, adipose) or increased plasma FFA or triglyceride [28]. A significant decrease in RBS blood sugar level in group V suggests that as the test drug '*Sandroos'* is a resin, binds with bile acid in the gut, decreases bile acid reabsorption into the circulation and increases their fecal excretion and it may also inhibit gastric lipases. There by reduces plasma FFA and enhances insulin action and decreased RBS level which produces hypolipidaemia [29, 30, 31].

In the study, organ weight was measured to access general toxicity produced by the test drug, because any change in organ weight is a sensitive indicator of toxicity. Liver is the target organ because most toxicants enter the body via the gastrointestinal tract, and after absorption the toxicants are carried by hepatic portal vein to the liver [21]. In the present study, no significant difference was observed in organ weight of test drug treated groups when compared with plain control group. This finding demonstrates that the test drug *Sandroos* produces antiobesity effect without any observable side effects.

The development of obesity in adults is accompanied by both, increases in numbers as well as increased size of adipocytes as fat is stored mainly in adipocytes of subcutaneous tissue, intraperitoneal cavity, liver and other tissues of the body [30, 32]. It is characterized by increased white fat deposits due to hyperplasia and hypertrophy of the adipocytes in these deposits [33]. In this study, treatment with *Sandroos* found to be inhibited the white adipose tissue accumulation and also inhibited increase in adipocyte size and thus decreased the weight gain of Cafeteria diet induced obese rats in test drug treated groups when compared with Negative control group.

In this study the weight of total fat pad was significantly decreased in group II, IV and V when compared with Group I, III and group VI. This decrease was more significant in group II which indicates the test drug possess antiobesity activity. These results suggest that the decreased lipid accumulation in adipose tissue and decreased total fat pad weight in test drug control group might be attributed to its resinous substance which binds bile acid and decreased its reabsorption or by binding and inhibitory action on gastric and pancreatic lipase and may regulate lipid storage and mobilization in adipocytes [34].

The lipid content which was estimated from white adipose tissue of epididymal and uterine fat pad from male and female rats demonstrates that the test drug *Sandroos* reduced the fat accumulation in adipocytes. The decreased lipid accumulation might be attributed to its inhibitory action on gastric and pancreatic lipases that prevents absorption of dietary fat like a hypoglycemic agent and regulate lipid storage in adipocytes [34].

In this study *Sandroos* showed significant decrease in serum lipid levels except HDL-C. The significant increase in values of TG, TC, LDL and VLDL and significant decrease in HDL-C was found in Negative control group when compared with all the groups, this may be due to intake of cafeteria diet which increased quantity of *sameen* (fat) thus produces *ghaleez* and *lazij khilt* (viscous and sticky humour) . This *ghaleez khilt* itself corresponds to increase in bad lipids, while T-Cho, TG, LDL and VLDL was found to be significantly decreased (P<0.05) in group II, IV and VI when compared with group I and III. This decrease was highly significant in group II and VI. The HDL-C was significantly increased in test group treated rats and was highly significant in test drug control group II, which indicates more preventive effect of test drug, since these values of test drug treated groups were found to be similar that of plain control group and more significant than the standard control group. As elevation on plasma HDL-C is beneficial to the body, since it protects the body from complications of obesity [31]. This result proved the *Muhazzil* (emaciating), *Mujafif* (dessicant), *Qate balgham* (mucolytic), *Mudir e boal* (Diuretic), *Munaqi e Akhlat e Barida* (Elimination of *Barid* humours) activities of *Sandroos* helps in elimination of excessive fat from the body by increasing liquidity of altered *barid Akhlat* and reducing its stickiness, thereby improved the overall metabolism of fat. The test drug *Sandroos* being a resin prevents bile acid reabsorption into the circulating blood. This action of resin is reported to causes conversion of more of the liver cholesterol into new bile acids rather than forming new LDLs and atherogenic plaques [30].Thus, it results in decreased absorption of exogenous cholesterol and increased metabolism of endogenous cholesterol into bile acids in the liver. *Sandroos* may also bind bile acids in the gut and increase their fecal excretion [30].Findings of this study also reveals that the test drug may act as a hypolipidaemic agent by inhibiting pancreatic lipase, hence prevents fat digestion and absorption. Thus, the improvement in dyslipidemia by test drug, *Sandroos*, demonstrated to possess anti-obesity effect [35].Body composition was estimated to investigate whether the potential anti-obesity drugs reduce body weight by producing a beneficial selective loss of fat or by producing non-specific decrease in water (dehydration) or protein content (muscle wasting or cachexia). In the present study significant decrease in body weight was observed in carcass before and after oven drying for 3 days at 95C^{o} till constant weight was found [19]. In group III highly significant decrease in body composition was found when compared with Group I and other treated groups. It might be because of more fat accumulation due to cafeteria diet [36]. The weight loss of carcass after oven drying was significantly decreased in plain control, test drug control and standard control groups and this decrease was significant in group V. But highly significant increase in weight loss was found in group III. This finding demonstrates that the *Sandroos* reduced carcass body weight by producing a beneficial selective loss of fat when compared to cafeteria diet induced rats and plain control rats and shows more preventive effect in double dose of test drug.

The different parameters assessed in this study are generally taken to evaluate efficacy of *Sandroos* in the treatment of obesity, as there is no curative treatment available for obesity in any system of medicine. Most of the results of the parameters showed pronounced effect in therapeutic dose i.e. single dose of the test drug. Further, the results of this study also demonstrated that the effect of the double dose was almost similar to orlistat and was close to plain control.

5. Conclusion

In the light of the above discussion, it can be concluded that the test drug *Sandroos* produce significant antiobesity effect without demonstrating any signs of toxicity or side effects. Therefore, the test drug can be used for the treatment of *Simne mufrit* (obesity). Since the diverse mechanism is involved in the development of obesity which is a complex disorder in nature. Therefore, some elaborate studies should also be carried out on *Sandroos* to ascertain its pharmacological action and to explore the untapped potential to provide complete safe and effective treatment for obesity.

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