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METHANOL EXTRACT OF CUUMIS SATIVUS PEEL EXHIBITS ANTI-DIABESITY AND ANTI-CANCER ACTIVITIES IN MICE: AN IN VIVO STUDY

Fakhar Abbas[1], Ayoub Rashid Ch[2], Khalid Hamid[*3], Faheem Khan[4] Muhammad Waseem Iqbal[5], Maryam Batul[6]

[1,2,4] *Department of Chemistry, Government College University, Lahore 54000, Pakistan.*
[3*,5] *Department of Computer Science & IT, Superior University Lahore, Lahore 54000, Pakistan*
[6] *Department of Chemistry, University of Okara; Okara, Pakistan*

[1]afakhar047@gmail.com, [2]ayoubrahseed@gcu.edu.pk,[*3]khalid6140@gmail.com, [4]khan48pk@gmail.com
[5]waseem.iqbal@superior.edu.pk, [6]maryambatul46@gmail.com

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Corresponding Author: *
Khalid Hamid

Abstract

The presented work aims to evaluate the efficacy of Cucumis sativus (Cucumber) peel methanol extract on diabetic-obese (Diaobese) albino mice in ameliorating hyperglycaemia, obesity, and dyslipidemia. The animals in the experimental groups were as follows: two doses of hydromethanolic extract of C. sativus at the doses of 250 mg/kg and 450 mg/kg, a glucophage-treated group, and another group fed on an HFD and a control group. In the present study, HFD caused substantial weight gain and the HFD group gained an average of 76.23 % of their initial body weight compared to 35.12% of the ND group. The higher dose of C. sativus extract at 450 mg/kg produced a greater reaction than 250 mg/kg on weight change, blood glucose level, and lipid profiles. More significantly, where a higher dose of 450 mg/kg dose, it reduced average blood glucose from 259.34 mg/dL to 175.34 after six weeks while other essential biochemical parameters such as total cholesterol, LDL, and triglycerides were also reduced to near normal levels while body HDL level is raised. Concerning fat absorption, the fecal fat analysis suggested a lowering of fat absorption since both doses of C. sativus extract increased fecal fat content, although not as steeply as glucophage. The methanol peel extract showed significant response to the HL-60 xenograft cancer cells modeland significantly decreased tumor weight by 1.45 ± 0.56 g and the inhibition rate of tumor growth of 46% while the the standard drug vinblastine had the tumor weight of 1.94 ± 0.21 g and the inhibition rate of 62 % thereby indicating that the peel extract has therapeutic properties.

This study therefore indicates that C. sativus peel extract may be of potential beneficial value in terms of its use as a natural supplement to manage metabolic disorders such as diabetes and obesity at higher concentrations of the extract.

INTRODUCTION

The international prevalence of obesity as well as type 2 diabetes mellitus (T2DM) has emerged as an essential problem in public health due to the rising prevalence rates of the condition and related comorbidities. Data obtained from the WHO reveals that the assessments of obesity have thrice the number they were in 1975 with a population of around 650 million obese adults . This worrisome situation is closely associated with an emerging increase in T2DM, which presently impacts more than 463 million people globally, according to forecasts, the number of T2DM patients may soon exceed 700 million by 2045 (Zang, et al. 2015) [1]. Being overweight is generally viewed as the main root cause of insulin resistance, which is identified as the root cause for the development of T2DM and other metabolic disorders including cardio-vascular disease, hypertension, and dyslipidemia (Michaelidou, et al. 2023) [2].Many studies reveal that the methanol extract of cucumber peel possesses the ability to suppress tumor growth and decrease the tumor weight in various experimental animals. Probable mechanisms for these effects include apoptotic activity, inhibition of oxidative stress, and inhibition of cancer cell growth signals. While its effective rate is lower than traditional chemotherapeutic agents such as vinblastine, cucumber peel extract has the advantage of a potential natural therapy or adjuvant for cancer therapy; Its focus is on its value for therapeutic research and development [3].Most of the pharmacologic therapies used to fight obesity and diabetes comprise insulin sensitizers and anti-obesity drugs, which are accompanied by numerous unwanted effects that may hamper patient compliance and deteriorate the patient's state (Michaelidou, et al. 2023). These problems have necessitated the search for safer natural products that can treat those chronic conditions with little side effects [4].Melon scientifically called cucumis melo is a popular fruit in the market for its qualities such as being a natural coolant and the presence of antioxidants. Besides being a popular fruit with good taste and a source of nutrients, melon possesses various bioactive system that comprises polyphenols, flavonoids, carotenoids, and dietary fiber (Tuama and Mohammed 2019) [5]. These phytochemicals have been described in the recent past to have some benefits to health such as anti-inflammatory, antioxidant, and anti-diabetic. For example, polyphenol contents enhance glucose metabolism and insulitis while flavonoid contents modulate lipid metabolism and decrease fatty tissues (Li, et al. 2020) [6].Due to the past findings showing that dietary intervention plays a proactive role in obesity and diabetes management, the present study intends to assess the effects of *Cucumis sativus* extract in controlling obesity and diabetes using a high-fat diet-induced in vivo model. This possible that this natural extract will be proven to have behavioral characteristics that make it an effective acar therapeutic 'option to enhance the management of some of these prevalent metabolic disorders. The specific aims of this present study are: To evaluate the effect of *Cucumis sativus* peel extarcts on body weight, fasting blood sugar levels, lipid profile, and fecal fat contents with reference to a high-fat diet [7].

Materials and methodology:

This section contains the information about chemicals, reagents, plant materials, mice model and techniques used in the current study. The whole methodology adopted for current study is depicted in the following figure**.**

Plant collection

C. *sativus* plants were gathered from different locations in the Lahore region. Leaves and seeds were discarded from the plants. Identification of all the above-mentioned plant materials was done and validated by the Department of Botany Govt. College University Lahore. Original voucher specimens of the tested plant were deposited in the Department of Botany for further use and reference with reference numbers Gc.Herb.Bot 2535. These fruits and peels were washed and dried under ambient conditions for seven days, and the resulting peels were ground to a fine powder. These powdered samples were then lyophilized for further characterization [8].

Extract preparation

The extract was obtained according to a standard procedure, with certain changes (Phuyal, et al. 2020) [9]. Extraction was made by adding 10g of peel powder to 100 mL of solvents (70% methanol). The mixture was allowed to ferment in a half-shaded area for about the period of seventy-two hours. After this, each extract was sonicated for 30 minutes at the

Soniprep150. The solvent was then removed using a rotary evaporator for the sample to dry. The obtained extracts were stored at -20 °C to be used in further investigations.

Experimental Design

This experimental protocol was approved by the Ethical Committee of the Department of Biochemistry and Biotechnology, Government College University Lahore under registration number GCU-IIB-451. In this study, a mice model was employed to determine the efficiency of the *C. sativus* peel methanol extract on diabesity with the *C. sativus* peel extract being characterized to be the most potent in our previous studies (ABBAS, et al. 2022). Sixty albino mice, 6-7 weeks old, weighing 30.08 ± 3.18 gm, were randomly purchased from the nearby market and acclimatized for one week in the animal facility of GCUL [10].

Before the experimental phase was started, all mice were given a standard diet, and tap water to standardize their metabolic rates. They were kept in cages under standard vivarium conditions with the light/dark cycle of 12/12; temperature 25-30°C, humidity 55±5.

Glucose tolerance test

The glucose tolerance test was performed to evaluate mice's ability to regulate blood glucose levels and to understand the effect of experimental treatments on glucose metabolism (Bartoli, et al. 2011). The mice ate and drank only water for about 20 hours before the experiment started. The pre-intervention blood glucose level was determined using a glucometer (Accu-Chek, Roche Diagnostics). At the end of the 30 min, each mouse was given an oral ingestion of 0.5ml/100g body weight of 20% (W/V) glucose. Glycemic control was measured by blood sugar level after glucose challenge at 30, 60, and 120 minutes and the mean glucose level of each group at each time was described [11].

HFD therapy

The mice were divided into two groups, the HFD group containing 45 mice, and the ND group containing 15 mice. HFD-grouped mice were then fed a high-fat diet (HFD) comprising 28 % protein, 45 % corn starch, 8 % sucrose, 4 % corn oil, 3 % cholesterol, 4.2 % vanaspati ghee, 1.5 % coconut oil, 4.3% butter, 1 % minerals, and 1 % vitamins. On the other hand, the normal diet (ND) was composed of 28% protein, 55% starch, 11% sugar, and 4% maize oil, 1% mineral mixtures, 1% vitamin mixtures given to the ND group. The consumption of the HFD remained constant for 10 weeks while body weight changes were recorded per week (Silva, et al. 2020) [12].

At the end of ten weeks in the HFD group, the mice's BMI was recorded. Obese mice were identified as those with a body mass index of more than 29.9 kg/m^2. Diabetes was then brought about by injecting aloxan (160mg/kg body weight) dissolved in 5ml normal saline intraperitoneally. At 62 hours, blood samples were obtained from the lateral tail veins for determination of blood glucose using a glucometer (ACCU-CHEK Roche USA Inc.). Diabetes in mice was defined by blood glucose level greater than 200 mg/dL and only those animals were used for the study. The HFD-treated mice were now considered as dia-obese and then divided into five groups, each consisting of six mice: 1 normal diet group, 2- untreated dia-obese group, 3-Glucophage treated dia-obese group, 4-dia-obese group treated with 250 mg of peel extract and 5-dia-obese group treated with 450 mg of peel extracts [13].

Acute toxicity test

The acute toxicity test was performed with previous reported method with some modifications (Kifayatullah, et al. 2015) on adult female Albino mice with an initial body weight of between 25-30 grams. First, one mouse was given an extract dose of 2,000 mg/kg bw and received an examination at 30-minute intervals for the initial 4 hours of observation time. Observation went on for some time every 24 hours when it supplemented the monitoring. Further five mice of comparable body weight were also treated with the same 2,000 mg/kg bw extract dose and behavior was monitored in the same manner. Special focus was kept on episodes of mortality, diarrhea, or vomiting for 14 consecutive days [14].

Hypoglycemic and hypolipidemic effects evaluation

The hydromethanolic extracts of *Cucumis sativus* peels at doses of 250 mg/kg and 450 mg/kg were administered orally in HFD-treated and alloxan-induced dia-obese mice (obese- diabetic) (test groups) using reported method with modifications (Aissaoui, et al. 2011). The positive control was

treated with Glucophage while the negative control was treated with distilled water. All the treatments selected were in the form of administrations with observed daily doses over six weeks. Blood glucose levels (BGL) were determined from the tail of each mouse through blood sampling. Further, total cholesterol, triglycerides, and high-density lipoprotein cholesterol levels were determined with the use of a portable lipid profile meter [15].

Body weight changes

Food intake expressed in grams of food consumed per day per cage and body weights of each group were recorded weekly (Yang, et al. 2014). The body weight of each mouse was taken and recorded once a week. The lower dose was used to compare it with the higher dose (450 mg/kg) to establish if the lower dose could elicit similar /enhanced effects than the higher dose. The design of the experiment allowed for the measurement of the percentage of change in body weight at the end of the six-week trial based on weight recorded at baseline in week 0 [16]. The percentage weight gain was determined using the following formula:

Weight change percentage formula = [new weight – initial weight]/initial weight × 100 or simply Final weight /initial weight.

Fecal fats

The mice's fecal fat was determined using the following slight modification of a previously documented method (Lee, et al. 2013). Briefly, the sample was prepared by weighing fecal matter 1.0 g adding it to 10 ml of distilled water, and homogenizing the contents. The blend was put in the refrigerator for 24 hours at 4°C and then vortexed for one minute. Lipid extraction was performed by adding 10 ml of acetone: To 1 ml of the fecal sample, the following stages were applied: first, the mixture of ethanol (1:2 v/v) to the fecal sample for 30 min and then the addition of 3 ml of chloroform and distilled water, stirring for 40 min. The lipophilic layer was collected after centrifuging the mixture at 6000 rpm for 15min and vacuum-drying [17].

Cell culture

Responsible promyelocytic leukemia cell line derived from human (HL-60) were from the ATCC (American type culture collection). RPMI-1640 medium was used as growth medium for the cells in this study; this medium was supplemented with 10% FBS (fetal bovine serum) which contains essential growth factors; 3 mM L-glutamine was added for protein synthesis; and antibiotics (150 Units/mL penicillin and 150 µg/mL streptomycin) to minimize contamination. The culture system was kept under conditions that favored physiological health at 37°C under conditions of supplemented humidity of CO2 and air as it helped the cells to grow vigorously. This standard operating procedure made it possible to have HL-60 cells ready for the other experimental assays in the following way [18].

Invivo Anticancer assay

For the purpose of tumorigenesis, 1×10^7 of HL-60 cells in 100 µL culture media were injected subcutaneously into the flank region of each mouse. To allow tumor development, animals were not treated until study day 12, and solid tumor development was confirmed. When the tumor sizes were about 200 mm^3 the animals were randomly assigned into three groups with six mice each. Treatments were administered intraperitoneally (i.p.) every four days with 30 µL of either:

1% DMSO as the control group could be used for the present study, methanol extract (450 mg/kg), group and

Vinblastine (100 µg/kg):- This is commonly used standard chemotherapeutic agent.

Tumor development was assessed thereafter daily for size measurements from day 12 until week 6 post-implantation. Tumor dimensions (length and width) were measured with calipers every four days, and tumor volumes were calculcated using the formula: Tumor volume (mm^3) = $\frac{1}{2} \times L \times W^2$ where L is the greatest dimension of the tumor and W is its shortest. Furthermore, the body weights of the mice were measured intermittently to evaluate general physiological impacts of the treatments.

All mice were then sacrificed at the end of the study, the tumours were removed, weighed and the volumes recalculated using the above formulae. This general structure of the experiment gave understanding about the impacts of the two explored treatments (methanol extract and vinblastine) upon tumor volume and advancement in HL-60 xenograft model [19].

Statistical analysis

Data analysis was done using the statistical tool, Minitab software version 16.01 and the analysis type used was analysis of variance (ANOVA). Anything with a p-value of less than 0.05 was taken as statistically significant. For several sets of numerical values, standard deviation was computed to determine the extent of variation within the data [20].

Results:

HFD treatment

The results of HFD treatment for the period of 10 weeks are depicted in the following figure 1.

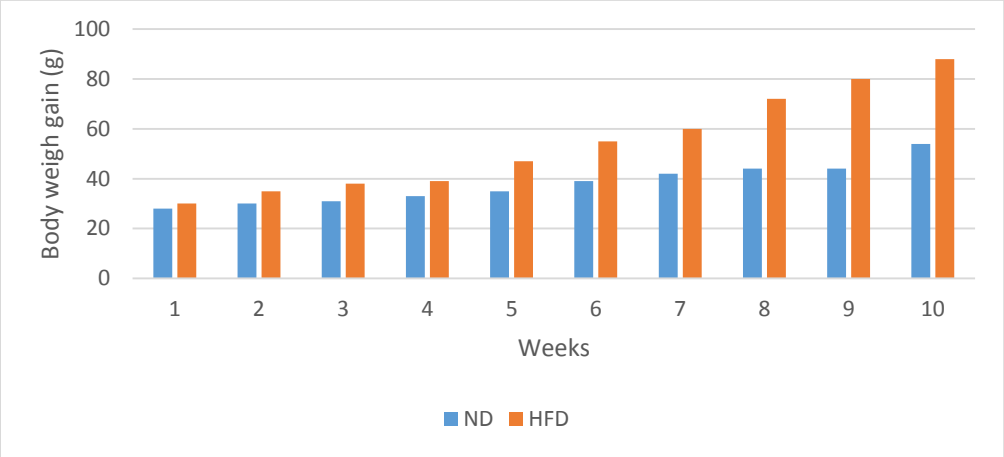

Figure 1. Body weight changes comparison between ND and HFD groups during HFD treatment for 10 weeks, the HFD treated mice group exhibited significant ($p<0.05$) weight changes as compared with ND treated group.

Glucose tolerance

These findings lucidly pointed to the glucose tolerance test; glucose levels increased from 90 ± 5.8 to 154 ± 3.8 within half an hour and then declined after sixty minutes. All groups that received glucose had restored glucose levels at 120 minutes to those of the normal group [21].

Acute toxicity test

In the acute toxicity test, none of the mice showed any sign of mortality or abnormal behaviour hence the LD50 for mice is more than 2000 mg/kg bw. This means that the tested extract dose of 450 mg/kg bw is within a safe range in the further evaluation of the hypoglycemic and hypo-lipidemic potential of the extract.

Hypoglycemic effect of methanol peel extract

The results of the effect of methanolic extract of C. sativus peel extracts on the blood glucose level of albino mice are shown in Table 1. The normal control group showed minor variation in blood glucose levels throughout the period of treatment [22].

Table 1: Effect of methanol peel extract on blood glucose mg/dl level in mice model

Treatment group	0 week	1 week	2 Week	3 week	4 Week	Week 5	Week6
Normal control	95.5 ± 1.66	6.23±1.04	00.02 ±0.98	9.23 ± 1.45	97.34 ± 2.03	8.34 ± 1.04	97.78± 2.11
Diaobese-untreated	320 ±1.23	336 ±1.54	335 ±0.76	338 ±1.45	340 ±2.23	344 ±1.12	346 ±1.13
Diaobese-Glucophage	260 ±0.23	222 ±.166	198 ±0.65	178 ±1.11	168 ±2.23	62.23 ±1.34	58.43±1.05
Diaobese-250 mg extract	62.23 ±0.97	252 ±0.77	38.12±1.34	26.23±1.23	220 ±2.21	20.32±1..23	16.23±1.24
Diaobese-450 mg extract	59.34 ±1.23	43.67±1.2	20.56±1.34	98.56±2.09	88.78±1.087	80.34 ±0.32	75.34±0.33

Body weight gain

Figure 2 represents the results of percentage body weight gain over 6 periods of the week for different treatment groups i.e. Normal group, dia-obese untreated, diaobese glucophage, diaobes low dose (250 mg) and high dose (450 mg) extract treated groups.

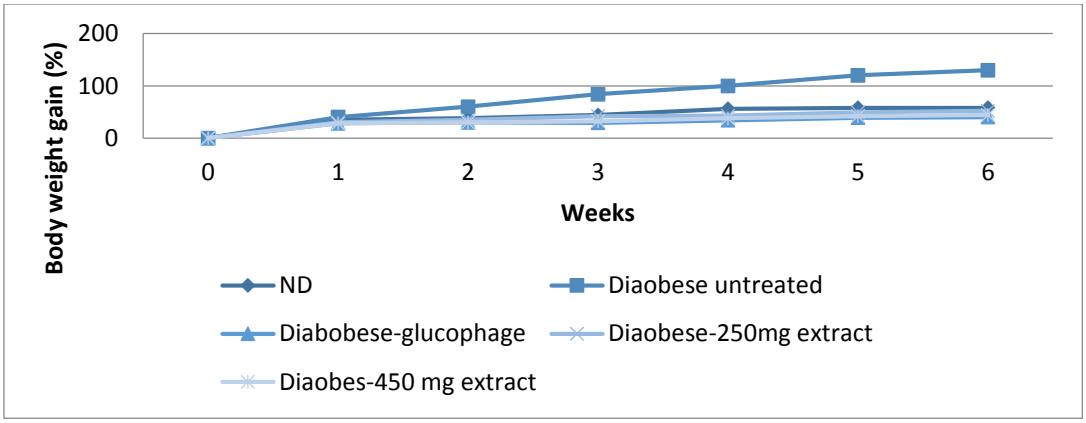

Figure 2. Effect of methanol peel extracts on weight gain percentage in various treatment groups in mice model, the methanol peel extract at dose 450 mg/kg exhibited significant ($p<0.05$) and comparable weight reducing effect with glucosephage.

Fecal fat contents

The outcome of the effect of methanol extract on the fecal fat contents in mice model is shown in the following Figure 3.

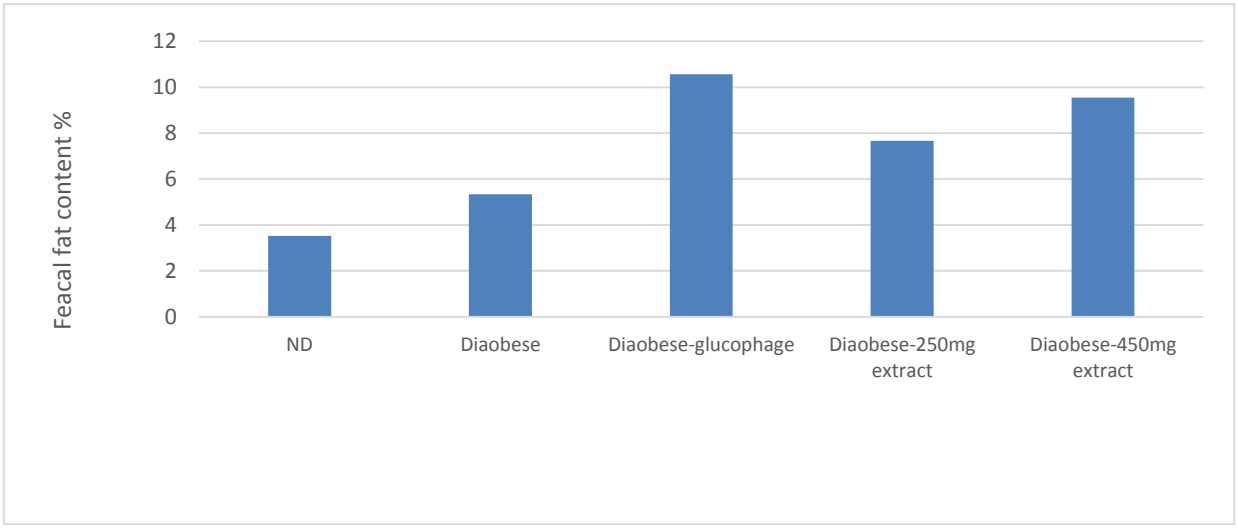

Figure 3. Effect of methanol peel extracts fecal fats contents % in HFD induced diabetic mice, the methanol extract at 450 mg/kg dose significantly increased fecal fats in mice model.

Lipid profile

The results of the effect of methanol peel extracts on various treatment groups of mice models are shown in Table 2.

Table 2. Effect of C. sativus peel extract on lipid profile in mice model

ıthological ırameters	D	iaobese-ıtreated	iaobese-lucophage	iaobese-:tract 250mg	iaobese-:tract 450mg
ɔtal cholesterol ıg/dl)	².34±0.20	[1.10±0.02	[.67±0.56	ł.23±1.23	ɜ.23±0.87
DL (mg/dl)	².22±1.11	ɜ.23±1.32	).45±1.09	).0±0.09	².45±0.82
DL (mg/dl)	ɔ.12±1.82	⁷.23±1.23	).34±0.02	⁷±0.34	).12±0.56
ɾiglycerides (mg/dl)	).34±1.23	ɜ0.34±1.23	).34±2.34	).1±0.34	[.67±1.005

Influence of peel extract on Tumor Weight and Volume in Vinblastine Induced Xenograft Model

The animal were administered either 1% DMSO (as a control), methanol extract (250 mg/kg) or Vinblastine sulphate (100 µ g/kg) for specific time intervals to assess tumor weight and tumor volume are given in the table 3 and figure 4.

Table 3: Effect of Peel extract on tumor size

ɾeatment	ɯmor weight	hibition rate
% DMSO	12 ± 0.34	
ɪnblastine	94 ± 0.21	²%
ethanol peel extract	45 ± 0.56	ɔ%

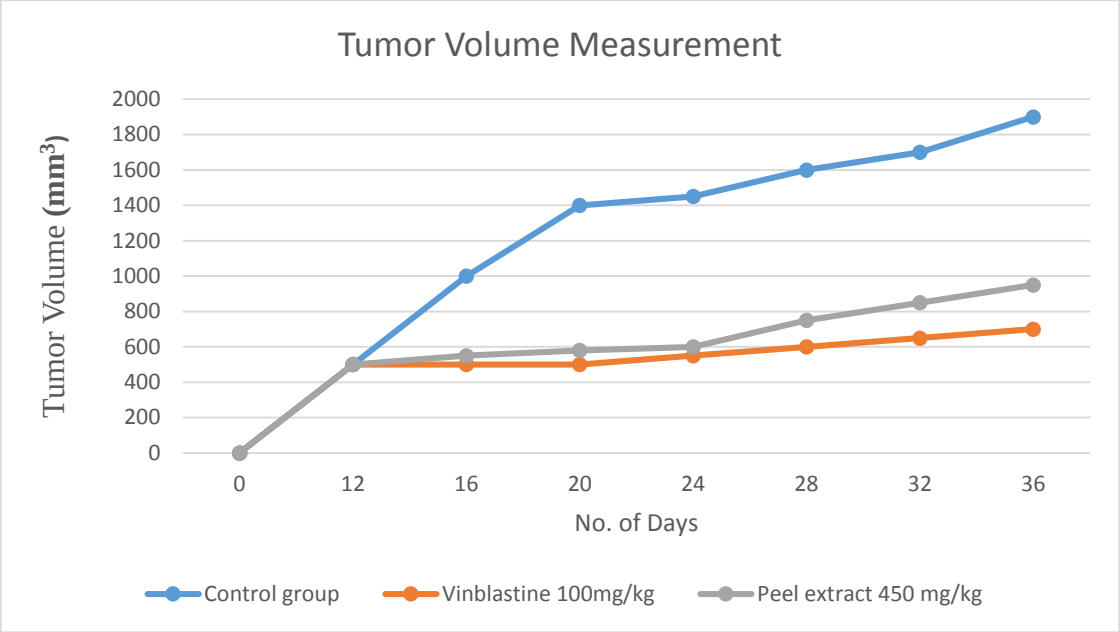

Figure 4. The ability of peel extract to inhibit growth was investigated in an in vivo xenograft model. The antitumor effects of peel extract and vinblastine on HL-60 human leukemia tumor xenografts in albino mice were evaluated. Both agents helped to cut down tumor growth in the tested animals. Quantitative tumor growth data was used which was presented as mean tumor volume (mm^3) ± S.D, calculated using caliper measurements. 1/2×length ×$width^2$. Tumor volumes were taken at day 12, 16,20, 24, 28.32 and 36 after tumor implantation contrasting the result from the 1% DMSO control group with the vinblastine and peel extract treatment groups.

Discussion

HFD treatment

The results of HFD treatment are given in the figure 1. This bar graph shows the comparison of the amount of body weight, gained in grams across two mice groups weighing over a period of 10 weeks, fed on a normal diet and high-fat diet groups respectively. In the beginning, the increase in weight in both groups seems to be almost the same but starting from week 4 there is a clear distinction as evidenced by the graph in figure 1. In the present study, the HFD group has a higher rise in body weight compared with the ND group, which reflects a drastic influence of the high-fat diet on weight gain. As the experiment ended in the 10th week, the HFD-fed mice gained 76.23% of the body weight, which was much higher than a 35.12% increase in mice fed on the normal diet. This weight gain indicated in the HFD group marked the development of obesity reached a substantial level. Also, the BMI was increased in the HFD-treated mice to about 80% of that in the normal diet group. Earlier studies have pointed towards the HF diet's ability to cause a quick gain in body weight due to increased energy intake and its effect on lipids. For example (Hariri and Thibault 2010) found out that rats fed with HFDs exhibit higher body fat content, adiposity, and metabolic dysfunction which paralleled the slow weight gain observed in the current HFD group. These effects are attributed to the body's adjusting and adapting mechanisms in response to excessive intake of fat which include energy-storing mechanisms, decreased, metabolic, and dynamic efficiency, and changes in insulin experience hence benefiting long-term weight gain.

Hypoglycemic effect

The data presented in Table 1 reveals the impact of methanol peel extract at two dosages (250mg & 450 mg) on the average blood glucose of the di-obese mouse model for six weeks. In the Diaobese-untreated group, the blood glucose level raised progressively from baseline 320 mg/dL to week 6 346 mg/dL and showed that hyperglycemia has worsened over time without any treatment. On the other hand, the Diaobese-Glucophage group that

received a standard antidiabetic drug had a significant reduction of blood glucose from 260 mg/dL at baseline to 158.43 mg/ dL at week 6. Likewise, both the low and high doses of methanol peel extract had the potential to lower glucose levels compared to the normal extract at 450 mg was more potent. The 450 mg dose showed a greater decrease in blood glucose from 259.34 mg/dL initially to 175.34 mg/dL by 6 weeks and the 250 mg dose, reduced blood glucose level to 216.23 mg/dL only by week 6. Such outcomes imply that methanol peel extract possesses antihyperglycemic properties especially in the more concentrated extract hence providing proof that the extract could be a better supplement to glucophage. From this, it can be inferred that the extract has the potential to work as an auxiliary treatment for diabetes.

The changes observed here can be compared with the results obtained in other experimental studies with effective plant-based anti-diabetic agents, in which increased dosing results in improved hypoglycemic activity (Singh, et al. 2013). As in similar cases with other botanical extracts, the Diaobese one may interfere with glucose-utilizing mechanisms by increasing insulin sensitivity or glucose utilization in the tissues.

Body weight gain

Figure 2 depicts the changes in body weight gain across six weeks for five different groups: Normal Diet (ND), Diaobese-untreated SO, Diaobese-Glucophage, Diaobese-250 mg extract, Diaobese-450 mg extract. The data presented below shows the effect of varying treatments on the body weight of their diaobese model, the untreated, the Glucophage treated as well as the experimental Diaobese extract group.

The dia-obese glucophage-treated group showed a significant decrease in body gain percentage from the first week, from week 2 there was relatively a steady weight gain percentage and remained consistently below that of the untreated group. The dia-obese 250 mg extract-treated group exhibited steady and moderate weight-reducing efficacy throughout the treatment. The 450 mg treatment group showed significant weight-reducing efficacy with weight gain percent staying below 30% after 6 weeks of treatment, closer to the Glucophage treated group, and the higher dose of peel extract was more potent in weight control.

Thus, the 450 mg of dia-obese extract had the lowest values for body weight gain among the dia-obese groups compared with the other group. The observed dose-dependent therapeutic effect signifies that probably higher concentrations of the peel extract might afford a deeper influence on the regulation of body weight, possibly by increasing the strength of the bioactive principles present in the extract and possibly eliciting a mechanism of action similar to that of the glucophage where it decreases the circulating glucose levels and increases insulin sensitivity (Han, et al. 2011). Previous studies conducted on plant sources of anti-obesity interventions like ginseng and bitter melon also give credence to this effect whereby high doses of the extract can bring about an impressive decrease in body weight through numerous integrated metabolic mechanisms, including inhibition of lipogenesis and promotion of energy expenditure (Seo, et al. 2019)

Bioactive extracts containing polyphenols and alkaloids show better insulin sensitivity, the reduction in lipid deposition, and hence decrease the differentiation of adipocytes-all the factors that may collectively lead to weight gain or potentially weight loss in obesity and diabetic animal models (Wang et al., 2017; Qiu et al., 2019). Furthermore, the results from the present study have shown that the anti-hyperglycemic potency of peel extract, especially at the higher tested doses, is in line with the effects that have been associated with other active herbal compounds including kaempferol and rutin as confirmed by HPLC analysis in our previous studies (ABBAS, et al. 2022), (Raza, et al. 2019) are capable of mimicking the effects of pharmacological agents active in metabolic regulation.

Fecal fats

Figure 3 presented the results of the fecal fat content percentage of each treatment group of the diabetic-obese (Diaobese) mouse model with the normal control (ND) group. The fecal fat content in the Diaobese group is significantly higher (10.56±0.55 %) than that in the ND group, which could be due to the change in fat metabolism or absorption in diabetes-induced obesity without treatment. Glucophage raises fecal fats making it possible that this agent may inhibit fat absorption or increase fat excretion in connection to action of weight and lipid regulation. Peculiarly, both 250 and 450 mg of

the methanol peel extract also increased fecal fat relative to (7.67 ± 0.09 and 9.55 ± 0.74 respectively) that of the ND group, although this effect was less profound than in Glucophage treated animals. Because all the extract treatments had stabilized equal fecal fat averages, it is hypothesized that the extract, similar to Glucophage, had slightly matched abilities in decreasing fat absorption, which may explain previously seen weight tempering tendencies.

Interacting with PL and increasing lipolysis can also be quoted as productive approaches to weight control. This present work also suggested that *C. sativus* peel extract reduced weight gain in mice fed a high-fat diet through the limitation of fat absorptions in the gut. Earlier research has also backed up these findings (Kübeck, et al. 2016). Thus, this investigation establishes the consciousness by *C. sativus* extracts of an increase in fecal fat excretion and plays a noteworthy role in the decrease in body weight gain among the treated mice hypothalamus, which in turn reduces appetite.

Lipid profile

Table 2 shows the result on lipid profiles of the diaobese mouse supplemented with *Cucumis sativus* (cucumber) peel extract. These lipid indices involve total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides, and give information on the possibility of using *C. sativus* extract at 250 and 450 mg daily doses as a diabetic therapeutic agent compared to the untreated and Glucophage treated diabetic groups.

Treatment with methanol extract of *Cucumis sativus* at 250 mg and 450 mg/kg on the lipid profile of diabetic mice was significant. The higher dose of 450mg/kg brought levels down to 53.23 ± 0.87 total cholesterol, paralleling the normal control 52.34 ± 0.20 and almost at par with the standard drug Glucophage 51.67 ± 0.56. Serum LDL concentrations too reduced significantly to 22.45 ± 0.82 mg/dL at this dose than the untreated diabetic group of 68.23 ± 1.32 mg/dL. Similarly, triglyceride concentration reduced to 31.67 ± 1.00 mg/dL which is as close as possible to normal ranges of 30.34 ± 1.23 mg/dL. Both doses of the extract also moderately increased high-density lipoprotein (HDL) with 450 mg/kg raising HDL to 29.12 ± 0.56 mg/dL similar to that of Glucophage 29.34 ± 0.02 mg/dL. Taken together, these outcomes imply that *C. sativus* extract exhibits substantial therapeutic potential on lipid profiles in diabetic conditions, especially at 450mg/kg, and responds similarly to conventional pharmacotherapy.

This is in line with increasing evidence for the role of plants in the treatment of metabolic disorders because they are less likely to have major side effects and their mechanisms of action are diverse .

These observations are also in consonant with other published literature on the mechanism of action to reduce hyperlipidemia in animals or men using plant extracts possessing antioxidant and anti-inflammatory properties. For instance, bitter melon which is found to have similar properties as flaxseed has reduced LDL and triglyceride levels in diabetic and obese animal models while increasing HDL (Massa, et al. 2016). These combined findings in the reduction of total cholesterol, LDL, and triglycerides evident in the present study and previous literature indicate that *C. sativus* plant extracts might provide an effective natural supplement or an addition to synthetic hypolipidemic drugs for the management of dyslipidemia among metabolic syndrome patients.

Influence of peel extract on Tumor Weight and Volume in Vinblastine Induced Xenograft Model

The table 3 reflects the differences of 1% DMSO, vinblastine and methanol peel extract treatment to tumor weight and inhibition rate in mice model. The 1% DMSO group acted as the control possessing the largest tumor weight of 3.12 ± 0.34 g and no inhibitory effect. Vinblastine on inhibiting tumor weight to 1.94 ± 0.21 g and has a better an inhibition rate of 62 %. Notably the methanol peel extract had similar tumoricidal effect by making the tumor weight to be 1.45 ± 0.56g accompanied by a lower inhibition rate of 46%. As indicated above, the results also indicate that there is a probability that methanol peel extract has therapeutic end product though slightly lower than that of vinblastine.

The graph (figure 4) illustrates the tumor volume progression over 36 days for three groups: There were another group which received only DMSO, one group which received vinblastine at a dose of 100 mg/kg and another group treated with peel extract at a dose of 450 mg/kg. As compared to the control group, the test groups show significantly reduced tumor volume the differences in size extending up to almost 2000mm³ in the control group by day 36. In turn, the tumor growth in

vinblastine group is considerably lowered, and the tumor volume is below 1000 mm^3 during the entire period. The peel extract group also exhibits tumor growth depressing effect though not as efficiently as vinblastine it reaches volumes of nearly about 1200mm^3 at the end of the study. These results indicate that the studied tumor was capable of being partially treated by the peel extract and that vinblastine was a stronger treatment than the peel extract.

Taken together, the present results suggest that both methanol peel extract and vinblastine possess potent antitumor activities in this HL-60 xenograft model.

Conclusion:

In conclusion, the methanol extract of *Cucumis sativus* peel particularly at a dose of 450 mg/kg significantly attenuated diabetes-induced hyperglycemia, weight gain, and improved lipid profiles in diabetic obese mice. Preclinical research found that the higher dose was significantly more effective than the 250 mg/kg dose and had significantly reduced glucose levels comparable to Glucophage, which is a standard drug, and nearly normal total cholesterol, LDL, and triglyceride levels and an increase in HDL. Altered fecal fat content may suggest inhibition of fat absorption, a factor potentially helpful in weight loss in high-fat-diet-induced obesity. Such results support the findings of the earlier works on hypoglycemic and hypolipidemic plant extracts, pointing to the possible application of *C. sativus* peel extract as a complementary therapy for metabolic derangement. Thus, this work stresses how plant bioactive components could innately help bring down diabetes and obesity with reduced side effects and can be a potential adjunct or substitute to conventional pharmacological prodigies for managing metabolic syndrome. Subsequent research is suggested for the identification of detailed molecular pathways and the replication of these results in clinical trials.

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Scientific Contributions

All authors contributed to the study's conceptualization and experimental design. Fakhar Abbas, Ayoub Rashid Ch, Muhammad Imran Ul Haq, and Muhammad Waseem Mumtaz conducted material preparation, data collection, and analysis. **Fakhar Abbas** drafted the initial manuscript and handled editing and formatting. **Muhammad Imran Ul Haq**, and **Syed Ali Raza** revised the manuscript for technical and structural improvements. **Ayoub Rashid Ch** and **Muhammad Waseem Mumtaz** provided critical feedback and final editorial corrections. All authors reviewed, approved, and agreed to the final version of the manuscript before submission.

Credit taxonomy:

Fakhar Abbas:
Conceptualization, Project administration, Supervision, Writing - review & editing
Ayoub Rashid Ch:
Data curation, Formal analysis, Investigation
Syed Ali Raza:
Methodology, Validation, Visualization
Muhammad Waseem Mumtaz:
Resources, Software, Formal analysis
Muhammad Imran Ul Haq:
Writing - original draft, Writing - review & editing

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REFERENCES

Abas F, Chaudhary AR, Haq MIU, Mumammad B, Hamid K, Iqbal MW, Bhatti SU (2022). Rrsponse surface methodology for the extraction of polyphenol contents and HPLC profiling of Cucumis sativus peels. Jilin Daxue Xuebao (Gongxueban)/Journal of Jilin University (Engineering and Technology Edition) 41:41-52. https://doi.org/:10.17605/OSF.IO/4YFET

Aissaoui A, Zizi S, Israili ZH, Lyoussi B (2011). Hypoglycemic and hypolipidemic effects of Coriandrum sativum L. in Meriones shawi rats. Journal of Ethnopharmacology 137:652-661. https://doi.org/10.1016/j.jep.2011.06.019

Bartoli E, Fra GP, Schianca GPC (2011). The oral glucose tolerance test (OGTT) revisited. European Journal of Internal Medicine 22:8-12. https://doi.org/10.1016/j.ejim.2010.07.008

Han TS, Tajar A, Lean MEJ (2011). Obesity and weight management in the elderly. British Medical Bulletin 97:169-196. https://doi.org/10.1016/j.jep.2011.06.01910.1093

Hariri N, Thibault L (2010). High-fat diet-induced obesity in animal models. Nutrition Research Reviews 23:270-299. https://doi.org/10.1017/S0954422410000168

Kübeck R, Bonet-Ripoll C, Hoffmann C, Walker A, Müller VM, Schüppel VL, Lagkouvardos I, Scholz B, Engel K-H, Daniel H, Schmitt-Kopplin P, Haller D, Clavel T, Klingenspor M (2016). Dietary fat and gut microbiota interactions determine diet-induced obesity in mice. Molecular Metabolism 5:1162-1174. https://doi.org/10.1016/j.molmet.2016.10.001

Lee MR, Kim BC, Kim R, Oh HI, Kim HK, Choi KJ, Sung CK (2013). Anti-obesity effects of black ginseng extract in high fat diet-fed mice. Journal of Ginseng Research. 37:308-349. https://doi.org/10.5142/jgr.

Li LS, Chiroma SM, Hashim T, Adam SK, Moklas MAM, Yusuf Z, Rahman SA (2020). Antioxidant and anti-inflammatory properties of Erythroxylum cuneatum alkaloid leaf extract. Heliyon 6.

Massa NML, Silva AS, de Oliveira CVC, Costa MJC, Persuhn DC, Barbosa CVS, Gonçalves MdCR (2016). Supplementation with Watermelon Extract Reduces Total Cholesterol and LDL Cholesterol in Adults with Dyslipidemia under the Influence of the MTHFR C677T Polymorphism. Journal of the American College of Nutrition 35:514-520. https://doi.org/10.1080/07315724.2015.1065522

Michaelidou M, Pappachan JM, Jeeyavudeen MS (2023). Management of diabesity: Current concepts. World J Diabetes 14:396-411 https://doi.org/1 10.4239/wjd.v14.i4.396

Phuyal N, Jha PK, Raturi PP, Rajbhandary S (2020). Total Phenolic, Flavonoid Contents, and Antioxidant Activities of Fruit, Seed, and Bark Extracts of Zanthoxylum armatum DC. The Scientific World Journal 2020:8780704. https://doi.org/10.1155/2020/8780704

Raza S, Rashid A, Mumtaz MW, Bashir S (2019). Antioxidant, iron chelating, lipase inhibition activities and metabolite's prediction of hyrdoethanolic leaf extract of Conocarpus erectus. Food Research 4:482-487. https://doi.org/110.26656/fr.2017.4(2).300

Seo MH, Lee WY, Kim SS, Kang JH, Kang JH, Kim KK, Kim BY, Kim YH, Kim WJ, Kim EM, Kim HS, Shin YA, Shin HJ, Lee KR, Lee KY, Lee SY, Lee SK, Lee JH, Lee CB, Chung S, Cho YH, Choi KM, Han JS, Yoo SJ (2019). 2018 Korean Society for the Study of Obesity Guideline for the Management of Obesity in Korea. Journal of Obesity and Metabolic Syndrome 28:40-45. https://doi.org/10.7570/jomes.2019.28.1.40

Silva G, Ferraresi C, de Almeida RT, Motta ML, Paixão T, Ottone VO, Fonseca IA, Oliveira MX, Rocha-Vieira E, Dias-Peixoto MF, Esteves EA, Coimbra CC, Amorim FT, Magalhães FdC (2020). Insulin resistance is improved in high-fat fed mice by photobiomodulation therapy at 630 nm. Journal of Biophotonics 13:2019 60140. https://doi.org/10.1002/jbio.201960140

Singh R, Kaur N, Kishore L, Kumar Gupta G (2013). Management of diabetic complications: A chemical constituents based approach. Journal of Ethnopharmacology 150:51-70. https://doi.org/10.1016/j.jep.2013.08.051

Tuama AA, Mohammed AA (2019). Phytochemical screening and in vitro antibacterial and anticancer activities of the aqueous extract of Cucumis sativus. Saudi Journal of Biological Sciences 26:600-604. https://doi.org/10.1016/j.sjbs.2018.07.012

Yang Y, Smith Jr. DL, Keating KD, Allison DB, Nagy TR (2014). Variations in body weight, food intake and body composition after long-term high-fat diet feeding in C57BL/6J mice. Obesity 22:2147-2155. https://doi.org/10.1002/oby.20811

Zang Y, Zhang L, Igarashi K, Yu C (2015). The anti-obesity and anti-diabetic effects of kaempferol glycosides from unripe soybean leaves in high-fat-diet mice. Food & Function 6:834-841. https://doi.org/10.1039/c4fo00844h

K. Hamid *et al.*, "Detection of Brain Tumor from Brain MRI Images with the Help of Machine Learning & Deep Learning," May 2022, doi: 10.22937/IJCSNS.2022.22.5.98.

K. Hamid *et al.*, "EMPOWERMENT OF CHEMICAL STRUCTURE USED IN ANTI-CANCER AND CORONA MEDICINES," *Tianjin Daxue Xuebao*, vol. 55, no. 08.

K. Hamid, Z. Aslam, A. Delshadi, M. Ibrar, Y. Mahmood, and M. waseem Iqbal, "Empowerments of Anti-Cancer Medicinal Structures by Modern Topological Invariants," vol. 7, pp. 668–683, Jan. 2024, doi: 10.26655/JMCHEMSCI.2024.5.1.

K. Hamid, H. Muhammad, M. waseem Iqbal, Z. Nazir, D. Irfan, and R. Rashed, "EMPOWERMENTS OF CHEMICAL STRUCTURES USED FOR CURING LUNGS INFECTIONS BY MODERN INVARIANTS," *Jilin Daxue Xuebao Gongxueban)/Journal of Jilin University (Engineering and Technology Edition)*, vol. 41, pp. 439–458, Dec. 2022, doi: 10.17605/OSF.IO/SY6KH