

Comparison Study between Drugs (Orlistat and Chitocal) and Food Supplements (Green Tea and Apple Cider Vinegar) for Weight Loss and Hepatoprotection in Rats

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ABSTRACT

Background: Obesity is a major problem in Saudi Arabia. Pharmaceutical solutions were sought for treatment. Chemical formula might lead to major health side effects. Meanwhile, the use of herbal formula is alleged to be safe. Green tea and apple vinegar are some of these products.

Objective: The study aimed to measure the effect of green tea and apple vinegar on obesity and liver status compared to medical drugs.

Materials and methods: Thirty-six adult male albino rats were divided into normal control, and other five groups fed on high caloric and hyperlipidemic diets. They were control positive and the rest 4 groups were treated with different formula (green tea, apple cider vinegar, orlistat and chitocal).

Results: All treated groups showed significant decrease in body weight when compared to control positive. Rats administered with orlistat and chitocal showed the highest significant decrease in body weight gain (BWG) when compared to control positive. Moreover, all tested groups enhanced liver functions especially chitocal and apple cider vinegar groups which showed the highest effect in ALT. Orlistat and green tea groups came in second level.

Conclusion: Although, no poor effect of chemical drugs found, natural products can provide the positive effect with no risk. Apple cider vinegar was the best natural weight control formula.

Key words: Apple cider vinegar, Chitocal, Green tea, Obesity, Orlistat, Rats.

INTRODUCTION

Obesity is now recognized as a disease condition that has a direct impact on morbidity and mortality. A third of the adult American population is now obese (age-adjusted prevalence of obesity 33.8% in 2007-2008), and another third is overweight, for a combined prevalence of 68% ⁽¹⁾. The obesity epidemic is spreading around the world, making obesity a global public health problem. Although the etiology of this global epidemic is multifactorial, most individuals suffer from the condition. Thus, you will be pleased to find a relatively easy way to lose weight ⁽²⁾. Alternative medicines have been used worldwide for many years to treat illness or promote health ⁽³⁾. Recent data on the use of nutritional supplements for weight loss indicates that more than 30% of those who have attempted to lose weight seriously have used the supplement without a prescription ⁽⁴⁾.

Weight loss and reduced visceral fat are known to cause lower blood pressure and lipid levels and the occurrence of cardiovascular disease (CVD) ⁽⁵⁾. Various agents for lowering lipid (Chitosan drug) and body weight (Orlistat drug) are available on the market. However, most of these causes potentially some side effects such as nausea and vomiting. More serious side effect is the interaction with warfarin, which might affect users with heart problems. If used

for long time it could reduce the absorption of fat-soluble vitamins and some minerals. For this reason, much attention has been paid to herbs and plant extracts that offer similar benefits without the side effects ⁽⁶⁾.

Green tea reduces adipose tissue weight in obese animal models ⁽⁷⁾, and has a pronounced effect on lipid metabolism in hyperlipidemia models ⁽⁸⁾. The visceral weight loss and lipid profile that improve the effect of green tea in rats may have been due to an enhancing thermogenesis and fat oxidation ⁽⁹⁾, inhibiting gastric and pancreatic lipases, or suppressing appetite and reduction in food intake ⁽¹⁰⁾. The health-promoting effects of green tea have been mainly attributed to the catechins content.

About the acetic acid there is limited scientific support for the claim that apple cider vinegar can promote weight loss. In this respect **Kondo et al.** ⁽¹¹⁾ found that obese people who consumed acetic acid daily for 12 weeks experienced significant decreases in body weight, abdominal fat, waist circumference, and triglycerides.

Bouderbala et al. ⁽¹²⁾ demonstrated that acetic acid may help prevent the accumulation of body fat and some fats in the liver, indicating that the metabolic disturbances caused by a high-fat diet would be regulated due to the effect of satiety by consuming



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apple cider vinegar. It also reduces fats and glucose in the blood. Moreover, it appears to prevent the risks of arteriosclerosis.

Accordingly, our research aimed to compare the effectiveness of drugs (Orlistat and chitocal) and food supplements (Green tea and apple cider vinegar) on weight loss and hepatoprotective effect in obese rats.

MATERIALS AND METHODS

Drugs: The drugs used in this investigation were orlistat and chitocal.

Food Supplements: The food supplements used in this investigation were green tea and apple cider vinegar.

Rats: Thirty-six (36) adult male albino rats Sprague Dawley were used in the research.

Basal Diet: Basal diet consisted of casein, sucrose, corn oil, choline chloride, vitamins mixture, mineral mixture, cellulose, and corn starch.

Extracts and drugs preparation:

1. Green tea; 10 g green tea was added to 100 ml of boiling water and was steeped for 15 min. The infusion was cooled to room temperature and then filtered. Tea leaves were extracted a second time with 100 ml of boiling water and filtered, and two filtrates were combined to obtain a 5% tea aqueous extract (5% tea leaf/100 ml water). Green tea extract (GTE) was orally administered to rats at a dose of 1 ml/100 g body weight.

2. Apple cedar vinegar, used as 6% v/v and the dose was 0.8 ml/kg body weight of rats.

3. Drugs: Orlistat and chitocal were completely dissolved in 1% (v/v) acetic acid solution. The mixture was forcefully shaken for a full day at room temperature.

Design of the experiment:

Thirty-six (36) adult male albino rats, which kept individually in well-aerated cages and fed on basal diet for one week for adaptation, in animal house of Faculty of Medicine, Umm Al Qura University, KSA.

Ethical approval: for animal handling acts for the University of Um Al Qura was obtained and followed across the experiment.

Rats were divided into equally six groups (n= 6 rats) one group was kept as normal rats and the remaining five groups were fed on high caloric and hyperlipidemic diets to become obese as follows:

Group (1): Normal rats control (- ve) fed on basal diet all over the experiment period.

Group (2): Obese control group control (+ ve) fed on hyperlipidemic diet.

Group (3): Obese rats with oral administration of 1 ml/100g body weight green tea extract for 28 consecutive days.

Group (4): Obese rats with oral administration of 0.8 ml/kg body weight of apple cider vinegar for 28 consecutive days.

Group (5): Obese rats with oral administration of 60 mg per kg body weight orlistat for 28 consecutive days.

Group (6): Obese rats with oral administration of 7.5 mg per kg body weight chitocal for 28 consecutive days.

Biological evaluation:

During the experimental period, the diet consumed was recorded every day; body weight for all rats was recorded every week and the food consumed were calculated. Many biological evaluations of the different diets were conducted using body weight gain (BWG), food efficiency ratio (FER). The next formulas were applied⁽¹³⁾.

$BWG (g) = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$

$FER = \frac{\text{Gain in body weight (g)}}{\text{Food Intake (g)}}$

At the end of the experimental period, rats were fasted overnight then were sacrificed. The serum was separated by collecting blood samples, allowing to clot for 15 minutes at 24-25°C then centrifuged at 3000 rpm. Serum was kept frozen till analysis. Liver, heart, kidneys, lungs, spleen, stomach, duodenum and colon were removed, cleaned and weighed then preserved in formalin.

Biochemical analysis: Lipids profiles and liver enzymes functions were determined in the serum.

Statistical analysis:

Statistical analysis were performed using SPSS program V. 22 for mean, SE and ANOVA test was applied as required. Data were presented in tables. P less than 0.05 was considered significant.

RESULTS

1. Biological evaluation

It could be observed from table (1) that there was an increase in BWG in control positive group. Concerning food intake (FI), obese rats administered with orlistat group showed significant decrease when compared to control positive group. BWG% was significantly different from control positive group for all treatments, yet, rats administered with orlistat showed the highest significant decrease when compared to control positive group.

Table (1): Biological effect of orlistat, chitocal, green tea and apple cider vinegar on body weight gain (BWG%), food intake (g) food efficiency ratio (FER) and adiposity index (Ad.I) of obese rats

Parameters	Groups	C -ve (N=6)	C +ve (N=6)	Orlistat (N=6)	Chitocal (N=6)	Green tea (N=6)	Apple cider vinegar (N=6)
		Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE
Initial weight		223.60±11.61*	261.80±8.46	293.70±11.90*	295.80±11.98	294.20±13.68	322.80±6.62
Final weight		241.40±13.62**	307.60±10.10	250.80±12.32**	281.20±12.02	286.80±14.98	312.60±7.51
Food Intake		24.14±1.36**	30.76±1.01	25.08±1.23**	28.12±1.20	28.68±1.50	31.26±0.75
BWG%		7.69±0.71*	17.85±3.16	-14.58±2.7***	-4.98±0.86***	-2.75±0.82***	-3.18±1.11***
FER		0.31±0.02*	0.57±0.10	-0.63±0.14***	-0.18±0.04***	-0.11±0.04***	-0.11±0.04***
Ad.I %		2.22±0.14***	3.52±0.04	1.92±0.10**	1.88±0.05***	2.31±0.12***	2.54±0.08***

*Differences are significant at 5% (P<0.05).

**Differences are significant at 1% (P<0.01).

*** Differences are significant at 0.1% (P<0.001) .

Data presented in table (2) shows the effect of extracts on organs weights (Liver, Lung, Heart, Spleen and Kidneys) in obese rats. Lungs were getting bigger when orlistat and green tea were consumed compared to positive control. Only orlistat increased liver size significantly. Apple vinegar reduces the colon and stomach size.

Table (2): Biological effect of orlistat, chitocal, green tea and apple cider vinegar on internal organs weight to body weight ratio of rats fed on high-fat diet

Internal organs	Groups	C -ve	C +ve	Orlistat	Chitocal	Green tea	Apple cider vinegar
		Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE
Renosomatic index		0.003±0.000	0.003±0.000	0.004±0.000	0.004±0.000	0.004±0.000**	0.003±0.000
Lung somatic index		0.007±0.001*	0.005±0.000	0.007±0.000**	0.009±0.001**	0.011±0.002*	0.006±0.001
Splenosomatic index		0.003±0.000	0.003±0.000	0.003±0.000	0.003±0.000	0.002±0.000	0.003±0.000
Hepatosomatic index		0.025±0.001	0.026±0.001	0.029±0.001*	0.026±0.001	0.027±0.001	0.025±0.001
Cardiosomatic index		0.003±0.000	0.003±0.000	0.003±0.000	0.003±0.000	0.003±0.000	0.003±0.000
Stomach somatic index		0.008±0.001	0.007±0.000	0.007±0.000	0.008±0.000	0.008±0.001*	0.006±0.000
Duodenum somatic index		0.001±0.000	0.001±0.000	0.001±0.000*	0.001±0.000	0.001±0.000	0.001±0.000
Colon somatic index		0.016±0.001**	0.013±0.001	0.014±0.000	0.013±0.001	0.011±0.000*	0.011±0.000*

*Differences are significant at 5% (P<0.05).

**Differences are significant at 1% (P<0.01).

2. Biochemical analysis

Data presented in table 3 shows that there was significant increase in serum of total cholesterol, LDL, HDL, VLDL and triglycerides levels in obese rats (C +ve) when compared to normal groups (C-ve). All treated groups with extracts showed improvement in lipid profile compared to controls. Rats administered with chitocal and apple cider vinegar showed the highest significant decrease in the level of total cholesterol, followed by green tea extract then orlistat when compared to control negative groups.

Table (3): Effect of orlistat, chitocal, green tea and apple cider vinegar on lipids profile for obese rats

Lipids profile	Groups	C -ve	C +ve	Orlistat	Chitocal	Green tea	Apple cider vinegar
		Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE
Total Lipids mg/dl		180.75±5.42	198.00±5.13	81.05±1.34*	195.90±12.58	196.2±2.9*	195.30±6.38
Cholesterol mg/dl		62.50±0.95***	89.20±2.59	58.20±1.25**	64.10±3.80***	67.40±1.25**	64.60±2.18***
Triglycerides mg/dl		59.00±1.55**	73.10±3.33	53.30±2.40*	61.50±5.27*	64.6±1.9	65.60±2.54
HDL mg/dl		33.40±0.69***	27.40±0.37	29.80±0.33*	31.00±1.69*	30.50±1.51*	30.60±2.47
VLDLmg/dl		11.80±0.31**	14.62±0.67	10.66±0.48*	12.30±1.05	13.4±0.40	13.12±0.51*
LDL mg/dl		17.30±0.45***	47.18±2.22	17.74±1.41	20.80±2.04***	21.60±0.47**	20.88±0.71***

*Differences are significant at 5% (P<0.05).

**Differences are significant at 1% (P<0.01).

*** Differences are significant at 0.1% (P<0.001) .

Data shown in table (4) indicates that there was significant increase in control positive group for AST, ALT and ALP compared to normal rats. Furthermore, table shows significant decrease in AST, ALT and ALP in all experimental groups when compared with (C+ ve) group. Moreover, chitocal and apple cider vinegar group showed the highest significant decrease in serum ALT then orlistat and green tea group when compared to control positive group.

Table (4): Effect of Orlistat, chitocal, green tea and apple cider vinegar on liver functions; (AST, ALT and ALP) in obese rats

Parameters	Groups	C -ve	C +ve	Orlistat	Chitocal	Green tea	Apple cider vinegar
		Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE
AST U/L		130.7±9.02*	145.1±6.2	115.70±3.43	109.40±5.59	119.5±9.6	111.80±2.69
ALT U/L		60.00±3.06**	101.8±4.7	81.90±10.00**	47.20±2.43***	61.60±3.12**	48.60±0.62***
ALP U/L		203.90±32.46	307.60±50.03	127.70±1.11**	240.00±24.15	270.10±34.01	263.60±10.42

*Differences are significant at 5% (P<0.05).

**Differences are significant at 1% (P<0.01).

DISCUSSION

Obesity has increased dramatically in past decades and is recognized as a risk factor for developing lifestyle-related diseases (14, 15). It is reported previously that the subcutaneous fat obesity is less connected to lifestyle-initiated diseases such as CVD and diabetes II than visceral fat obesity (16). Chronic overfeeding leads to uncontrolled inflammatory responses, leading to low-grade systemic inflammation and metabolic disorders, such as insulin resistance (17). Although anti-obesity medications (AOMs) are by far overused to lose weight quickly and easily, yet, all international medical and nutritional organizations ask to seek this solution (i.e. using AOMs) if patients failed to lose 5% of weight just following nutritional and life modifications strategies (18,19).

Our results denote that there were significant increase in BWG (body weight gain) of obese rats as compared to normal rats. Obese rats administered with orlistat, chitocal, green tea and apple cider vinegar groups showed significant decrease when compared to

control positive group. Rats administered with orlistat and chitocal showed highest significant decrease when compared to control positive group. Concerning food intake (FI), body weight gain and feed efficiency ratio there were significant increase of obese rats as compared to normal rats. Obese rats administered with orlistat, chitoca, green tea and apple cider vinegar groups showed significant decrease in all previous parameters when compared to control positive group. Rats administered with chitocal group showed the highest significant decrease in body weight gain when compared to control positive group. The results revealed that all experimental groups showed significant decrease in weight of organs (liver, lung, heart, spleen and kidneys) when compared to positive group. Rats administered with green tea extract showed significant decrease in kidneys weight, meanwhile, orlistat and chitocal groups showed significant decrease in lungs weight compared to other groups. These results agreed with **Safavi et al.** (20) who revealed that using anti-obesity medication (AOM) have significantly greater mean percentage reduction

in baseline weight than non-users. Moreover, **El-Sayed and Eslam** ⁽²¹⁾ found that the consumption of green tea extract produced a significant reduction in body weight in obese rats

There were a significant decrease of all lipid profile in rats administered by orlistat and chitocal when compared to control positive group. The orlistat was the best, followed by the apple cider vinegar and then the green tea. These results are supported by **Porsgaard et al.** ⁽²²⁾ who revealed that administration of 25 mg orlistat together with the dietary oils resulted in very small changes for fat that transported from the GIT to the lymphatic system compared to baseline, indicating almost complete inhibition of fat absorption. Orlistat could be acting by inhibiting fat hydrolysis. When compared to positive controls, obese rats that consumed green tea extract had shown a significant decrease in all lipid profiles. Rats administered with green tea extract showed the highest significant decrease in the LDL, VLDL and triglycerides levels while rats administered with apple cider vinegar and chitocal showed the highest significant decrease in the level of total cholesterol, when compared to control positive.

We found significant decrease in level of AST and ALP in rats fed with apple cider vinegar followed by green tea extract. These finding agree with **de Dios Lozano** ⁽²³⁾ who stated that the total and average daily weight gain for obese rats was reduced by vinegar. The patterns of changes in lipid and glucoses was time-bond, where within a week up to a month plasma glucose was reduced in obese rats that consumed vinegar. From the 2nd week up to a month of intake of vinegar in obese rats, triglycerides and cholesterol were getting lower. Nonetheless, vinegar did not affect plasma HDL and LDL. Thus, **de Dios Lozano** ⁽²³⁾ has concluded that vinegar might act as protective functional food that inhibit body weight gain by lowering all these parameters if consumed on daily basis. Also, **Kondo et al.** ⁽²⁴⁾ agreed with our finding as proved that body weight, BMI, visceral fat area, waist circumference, and serum triglyceride levels were significantly lower with vinegar intake. Daily intake of vinegar might be useful in the prevention of metabolic syndrome by reducing obesity, without causing adverse effects in studied obese subjects.

Our results cleared that there was highly significant decrease of enzyme level in rats administered by chitocal followed by the orlistat especially ALT and AST enzymes, while orlistat was the best in lowering the ALP enzyme when compared to control positive group. There was a significant decrease of all lipid profile in rats administered by orlistat and chitocal when compared to control positive group where the orlistat was the best. These results are supported by the finding of **Xu et al.** ⁽²⁵⁾ that chitosan could decrease levels of total cholesterol (TC), low

density lipoprotein cholesterol (LDL-C) in plasma ($p<0.05$), and TC, total triglyceride (TG) in liver ($p<0.05$), and increase fecal bile acids excretion ($p<0.05$), but the levels of TG and HDL-C in plasma was unchanged ($p>0.05$), while chitosan could increase hepatic LDL receptor mRNA levels. The plausible explanation for improving lipid metabolism could be explained on the light of that TC and LDL-C regulation at the mRNA expression level on the hepatic cells receptors were upregulated, leading to increase of bile in the stool.

As soon as, **Heck et al.** ⁽²⁶⁾ investigated orlistat effect as it may decrease the absorption of fat-soluble vitamins, a standard multiple-vitamin supplement is recommended daily during therapy to prevent abnormalities in vitamin serum concentrations. It can lead to severe gastrointestinal discomfort and the modest degree of weight loss may limit the agent's clinical utility. Its long-term safety and effectiveness for weight maintenance, cost-effectiveness of treatment, and overall reduction in obesity-related morbidity and mortality remain to be determined. FDA has added a warning regarding possible severe liver injury to the product information for orlistat (US FDA). The effect of orlistat is conducted on the stomach and small intestine lumen, where it has a reversible inhibiting control over the gastrointestinal lipases

The inhibition of triglyceride digestion reduces lipid absorption, with a subsequent positive effect on the weight control. Orlistat is indicated for the treatment of obesity in combination with a hypocaloric diet. These findings indicate that using of natural supplements used to reduce obesity is safer and with low side effect on human health. These findings are supported by **Tziomalos et al.** ⁽²⁷⁾ and **Hursel and Westerterp-Plantenga** ⁽²⁸⁾.

Manipulating a boy's weight with these treatments can be effective and varied by increasing energy expenditure and suppressing appetite. It also decreased the absorption of fats in the intestine by inhibiting pancreatic lipase. Weight loss medication may seem like a solution to obesity. However, potential side effects or adverse drug reactions are always a major public health concern and a major obstacle to developing new drug products. For example, in 1997, due to possible side effects on the heart (heart valves) two drugs (Fenfluramine and dexfenfluramine) were withdrawn. In 2010, sibutramine (Meridia) was also withdrawn due to an increased risk of heart attacks and strokes. That same year, in response to occasional reports of severe liver injury using the weight-loss drug xenical, the Food and Drug Administration (FDA) approved a revised drug label in which safety information about its potential side effects was noted ⁽²⁹⁾.

CONCLUSION

Orlistat, chitocal, green tea and apple cider vinegar could be used for weight reduction and the side effect for drugs use can be avoided by using the same food supplements as green tea and apple cider vinegar as alternatives natural supplements.

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