



The physiological effects of orlistat and efficiency extract of cinnamon on body weight and lipid profile in obese male rats

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Received: Aug. 17, 2024	Abstract The purpose of the current study was to examine the adverse effects of orlistat used alone and in combination with cinnamon with regard to weight gain, body weight percentage, and alterations in the lipid profile in male rats that were obese. Have been selected There were two groups of adult male rats. First experience (induction obesity) for six weeks to induce obesity into (Control group : 10 rats received only rats normal diet without fat as a daily dose) and (High fat diet group : 30 rats received only fed with high-fat diet contain Plate with soy fat and introduce as daily dose) , After this period (six weeks) weight gain and second main groups to ensure the induction , Second experience for six weeks , The treatment period lasted from week 6 to week 12 after confirming the induction of obesity daily oral dosing with the fallowing groups (Control group : 10 rats received only rats normal diet without fat as a daily dose , High fat diet group : 30 rats after induction of obesity divided into the following-: A) Group high fat diet with orlistat 10 rats (10 mg/kg/day). B) Group high fat diet with cinnamon 10 rats (100 mg/kg BW). C) Group high fat diet with orlistat (10 mg/kg/day) and cinnamon (100 mg/kg BW) 10 rats. The findings show that Weight gain were increase in a significant value ($P<0.05$) in fat group comparatively to control group and orlistat group , cinnamon group , combination mix group While cholesterol , Triglycerides , LDL-c and VLDL-c were increase in a significant value ($P<0.05$) while showed a significant ($P<0.05$) decrease in HDL-c in fat group comparatively to control group and orlistat group , cinnamon group , combination mix group , Conclusions In addition to its ability to inhibit pancreatic lipase, orlistat can also be used to control weight because it indirectly reduces appetite by raising glucagon, IDE, and dopamine levels and by inhibiting the glutamate neurotransmitter. Meanwhile, cinnamon improves blood sugar levels and glycaemic targets.
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Key words: cinnamon , orlistat , obesity , weight gain , lipid profile , Male Rats.

Introduction

Based on an analysis of body mass index data, the World Health Organization (WHO) declared obesity to be a global epidemic hazard in 1997 (BMI) , Since then, the prevalence of obesity has alarmingly increased and is now a significant public health concern , In fact, obesity not only contributes to the development of chronic diseases such as stroke, osteoarthritis, sleep apnea, cancers, and inflammation-based pathologies, but also to metabolic disorders such as diabetes, hypertension, and cardiovascular diseases [1,2]. The main action of the pancreatic gastric lipase inhibitor orlistat (ORL, tetrahydrolipstatin) is to reduce fat absorption, which in turn reduces calorie intake [3]. Foods containing orlistat selectively bind to gastrointestinal lipase by preventing the hydrolysis of ingested fat into glycerol and absorbable free fatty acids , Furthermore, Orlistat is a tetrahydrolipstatin that prevents the intestines from absorbing dietary fats by inhibiting the activity of the pancreatic and gastric lipase enzymes [4]. As a result, it is typically used as an anti-obesity drug to regulate and manage body weight in patients who are obese , In order to achieve this, Orlistat has shown promise in reducing obesity-related variables like BMI, lipid profile, white adipocyte size, and fecal fat excretion in animal replicas [5]. It has also been shown to be effective in reducing the consequences of obesity, such as metabolic syndrome and endothelial dysfunction in humans [6]. As a herbaceous plant, Cinnamon is a member of the Lauraceae family Due to its physiological effects, cinnamon is one of the most widely used spices in the world, both as a spice and condiment to flavor food and in medicinal mixtures , For centuries, various cultures across the world have utilized cinnamon as a culinary flavoring agent due to its organoleptic properties [7]. It has been extensively researched due to its possible health-promoting qualities and has been used historically as a treatment for digestive and respiratory issues , These include qualities that are antilipemic, anticancer, antidiabetic, anti-inflammatory, and antimicrobial , Cinnamon has been shown to have anti-inflammatory qualities by inhibiting the expression of nuclear factors, which in turn reduces the production of proinflammatory cytokines like interleukin (IL) 6, C-reactive protein (CRP), and tumor necrosis factor (TNF) [8].

Materials and Methods

Preparation of Orlistat

Drug: orlistat (Xenical ®, Jordan). A commercially available formulation of 120 mg/cap were purchased from a local private pharmacy. It was dissolved in normal saline and administered at 10mg/kg body weight.

Preparation of Cinnamon extract

Cinnamon Preparation by add 100 gm to 2000 ml of water , After two minutes of boiling together , the infusion was allowed to cool to room temperature before being filtered [9,10]. The Dosage calculation of Orlistat and Cinnamon extract for experimental animals is calculated as the following equation [11].

$$\text{Dosage in mg} = \frac{\text{Body weight of animal(g)} \times \text{dose (mg)}}{1000\text{g}}$$

The Experimental Design

Forty adult male rats divided into two groups:-

First experience (induction obesity) for six weeks to induce obesity into , as indicated below :

1) Control group : 10 rats received only rats normal diet without fat as a daily dose for six weeks.

2) High fat diet group : 30 rats received only fed with high-fat diet contain (Plate with soy fat) and introduce as daily for six weeks [12].

After this period (six weeks) weight gain , body weight , serum cholesterol , triglycerides and lipids were determined in the first and second main groups to ensure the induction.

Second experience for six weeks , The treatment period lasted from week 6 to week 12 after confirming the induction of obesity daily oral dosing with the fallowing groups

1) Control group : 10 rats received only rats normal diet without fat as a daily dose for six weeks.

2) High fat diet group : 30 rats after induction of obesity divided into the following:-

A) Group high fat diet with orlistat 10 rats (10 mg/kg/day) [13].

B) Group high fat diet with cinnamon 10 rats (100 mg/kg BW) [14].

C) Group high fat diet with orlistat (10 mg/kg/day) and cinnamon (100 mg/kg BW) 10 rats.

Results and Discussion

The mean value of Weight gain and Body weight were increase in a significant value ($P < 0.05$) in fat group comparatively to control group ,while there were a significant ($P > 0.05$) decrement for weight gain and Body weight in orlistat group and cinnamon group comparison with fat group, Also a significant ($P < 0.05$) decrement for weight gain and Body weight in group mix (orlistat and cinnamon) when comparative with orlistat group and cinnamon group , In this study, the HFD group's feed intake increased significantly during the experiment compared to the control group's , body weight significantly increased during the HFD free diet as opposed to the control diet , It was discovered that an HFD significantly increased body weight in comparison to rats fed a normal diet, the rats fed an HFD had higher body weights and WG [15,16,17]. The groups treated with water cinnamon extract experienced a reduction in body weight due to increased thermogenesis and the observed decrease in weight at the end of the experiment which was attributed to the thermogenic effect , Additionally, cinnamon was used to prepare the thermogenesis which was significantly lower in rat

adipose groups compared to fat groups because it worked synergistically with catechins to enhance thermogenesis [18]. In comparison to the control rats, HFD feeding resulted in a decrease in feed intake, which raised final body weight and weight gain, The HFD-fed rats treated with cinnamon extract had a lower final body weight and visceral fat percentage than the control rats, despite the fact that the treatment reduced body weight, fat, and weight gain in the HFD-fed rats, This is accompanied by modifications in the metabolism of fat and glucose in the diet, Cinnamon is helpful because of its antioxidant properties and responsiveness. Cinnamon extracts are known to function both in vitro and in vivo, The detrimental effects of variations in the HFD/HFD signal were mitigated by the use of cinnamon, The supplementation of cinnamon extract had improved body weight, visceral fat, and carbohydrate metabolism, including glucose and lipid profiles, antioxidant enzymes, and lipid peroxidation, in HFD-fed rats [19]. The administration of orlistat increased the metabolic rate in the treated groups, increased the release of catecholamines and increased fat oxidation in vivo through lipolysis in fat cells, The highest group showed an anti-obesity action in rats at fat groups with the administration of orlistat recording a decrease in body weight gain, On the other hand the combination of orlistat and cinnamon can reduce non-significant differences in body weight gain percentage in obese rats [20].

Table (1): Effect of High fat diet, Orlistat and Cinnamon extract on Weight gain and Body weight %

Groups	Body weight(G)		Body weight (G)
	Initial weight (G)	Final weight (g)	
Control	200.82 ±7.88a	340.58 ±13.23a	139.76 ±0.59a
Fat	253.50 ±11.23b	411.95 ±13.86b	158.45 ±1.01b
Orlistat	240.18 ±10.98c	371.56 ±12.76c	131.38 ±0.95c
Cinnamon	228.30 ±11.54d	329.89 ±14.12d	101.59 ±1.12d
Mix orlistat & cinnamon	216.39 ±12.06e	301.12 ±14.02e	84.73 ±1.43e
LSD	10.32	12.11	10.51

Data represented as mean ± SD different letters significant differences at P-value (P<0.05).

The mean value of cholesterol, Triglycerides, LDL-c and VLDL-c were increase in a significant value (P<0.05) while showed a significant (P<0.05) decrease in HDL-c in fat group comparatively to control group, Also there were a significant (P<0.05) decrease in cholesterol, Triglycerides, LDL-c and VLDL-c while showed a significant (P<0.05) increase in HDL-c in orlistat group and cinnamon group as compared to fat group, while in group mix (orlistat and cinnamon) showed a significant (P<0.05) decrease in cholesterol, Triglycerides, LDL-c and VLDL-c with a significant (P<0.05)

increase in HDL-c when comparative with orlistat group and cinnamon group , In the current study, feeding HFD resulted in a substantial alteration in the lipid profile and the induction of hyperlipidemia , When compared to the control group showed the Table (2). A high-fat diet (HFD) raises blood levels of cholesterol, triglycerides, low-density lipoprotein (LDL), and very low density lipoprotein-cholesterol (VLDL-c), with the exception of lower levels of high-density lipoprotein (HDL-c) in group fats [21,22]. Globally, obesity is now a serious health concern , Furthermore, endocrine, metabolic, and cardiovascular disorders are significantly increased by obesity , Therefore, using synthetic medications or functional foods that have safe properties would be very beneficial in the management of obesity [23]. Numerous traditional herbal plants were widely used to control or lower blood lipid levels through lipid management , however, when using Natural plants like cinnamon have therapeutic benefits and almost certainly no negative side effects [24]. Its numerous benefits include being high in calcium, iron, manganese, and fiber, as well as having antibacterial and antioxidant properties that Furthermore, rats given cinnamon extract (CE) exhibited decreased levels of low density lipoprotein cholesterol (LDL), triglycerides (TG), and total cholesterol (TC) when compared to the fat group, and Very Low Density Lipoprotein-Cholesterol (VLDL-c) with the exception of elevated High Density Lipoprotein-Cholesterol (HDL-c) however When compared to the fat group [25]. The lipid profile following HFD feeding was improved by the administration of cinnamon extract , The extract of cinnamon has a Strong lipolytic activity of cinnamon extract lowers free fatty acid levels in kidney subjects and prevents hypercholesterolemia and hypertriglyceridemia , Additionally the presence of cinnamon extract lowers cholesterol in rats given a high-fat diet by preventing the liver's 5-hydroxy-3-methylglutaryl-coenzyme A reductase from doing its job [26]. Both groups in the current study lose weight after receiving treatment with either orlistat or cinnamon , When comparing the orlistat and cinnamon-treated groups to the pretreatment, it was significantly lower in both [27]. the administration of a mixture of orlistat and cinnamon to hyperlipidemic rats resulted in a significant reduction in total cholesterol, triglycerides, and VLDL+LDL, with the exception of an elevated level of HDL-c, or high density lipoprotein cholesterol [28]. The outcomes of the experiment demonstrated a noteworthy impact of cinnamon treatment on rats , Rats given cinnamon extract orally experienced a marked reduction in their lipid level [29]. Feeding a high-fat diet causes hyperlipidemia and obesity, which have an impact on overall health , The risk associated with hyperlipidemia is the possibility of cellular damage brought on by changes in cellular function, which can result in a variety of pathological conditions [30]. One of the most researched methods for assessing the possible effectiveness of weight-management medications is the anti-lipase effect , The bacteria *Streptomyces toxytricini* is the source of orlistat, which is intended to control obesity by decreasing the digestion of fats by forming a covalent bond with the serine residue of the lipase enzyme , The outcomes show how orlistat therapy reduced the level of lipase concentration , Hence , suggesting that orlistat has the potential to impact the metabolism of fat [31].

Cinnamon is also the most well-known strong natural botanical inhibitor of Pancreatic lipase , The findings of the study suggest that cinnamon inhibits the lipase enzyme because it contains flavonoids and phenolic acids, both of which have an inhibitory effect on the release of Pancreatic lipase , Additionally demonstrates that taking cinnamon seriously lowers body weight [32]. However, the chylomicron formation and subsequent cholesterol synthesis in animal intestinal cells depend on the lipase enzyme , When compared to the control group, the treatment of both groups in the current study with orlistat and cinnamon resulted in significant changes in the lipid parameters, including a significant decline in triglycerides, total cholesterol, LDL cholesterol, and VLDL cholesterol , that have provided strong evidence that the antihyperlipidemic effect of orlistat may be caused by the drug's strong inhibitory action on pancreatic lipase, which slows down the breakdown of fat and prevents the body from absorbing fat [33].

Table (2): Effect of High fat diet , Orlistat and Cinnamon extract on Serum total cholesterol (TC) , triglycerides (TG), High Density Lipoprotein-cholesterol (HDL-c) , Low Density Lipoprotein-cholesterol (LDL-c), Very Low Density Lipoprotein-cholesterol (VLDL-c)

Lipid Profile test					
Groups	Cholesterol (TC) mg/dl	Triglycerides (TG) mg/dl	HDL-c mg/dl	LDL-c mg/dl	VLDL-c mg/dl
Control	60.09 ±0.92a	110.80 ±1.63a	33.91 ±1.28a	44.21 ±0.93a	51.3 ±1.28a
Fat	85.11 ±0.51b	168.20 ±0.61b	19.06 ±0.51b	74.43 ±1.01b	78.28 ±1.43b
Orlistat & Fat	66.81 ±0.86c	149.48 ±1.32c	24.02 ±0.86c	60.59 ±0.92c	67.91 ±0.92c
Cinnamon & Fat	74.83 ±1.14d	116.79 ±0.81cd	29.38 ±0.92ad	51.07 ±0.83d	59.37 ±0.66d
Mix & Fat	59.99 ±1.07e	104.12 ±0.86e	32.78 ±0.92e	40.94 ±0.61e	44.48 ±0.30e
LSD	3.36	5.85	2.79	2.60	2.87

Data represented as mean ± SD different letters significant differences at P-value (P<0.05).

References

- 1) Mohajan, D., & Mohajan, H. K. (2023). Obesity and its related diseases: A new escalating alarming in global health. *Journal of Innovations in Medical Research*, 2(3), 12-23.
- 2) Elmaleh-Sachs, A., Schwartz, J. L., Bramante, C. T., Nicklas, J. M., Gudzone, K. A., & Jay, M. (2023). Obesity management in adults: A review. *JAMA*, 330(20), 2000-2015.

- 3) Hamza, R. Z., & Alsolami, K. (2023). Ameliorative effects of Orlistat and metformin either alone or in combination on liver functions, structure, immunoreactivity, and antioxidant enzymes in experimentally induced obesity in male rats. *Heliyon*, 9(8).
- 4) Rajan, L., Radhakrishnan, A., Selleppan, G., & Mohankumar, S. K. (2021). Susceptible genetic polymorphisms and their association with adverse effects of Orlistat therapy. *Obesity Medicine*, 25, 100-360.
- 5) Othman, Z. A., Zakaria, Z., Suleiman, J. B., Ghazali, W. S. W., & Mohamed, M. (2021). Anti-atherogenic effects of Orlistat on obesity-induced vascular oxidative stress rat model. *Antioxidants*, 10(2), 251.
- 6) Abdel-Baky, E. S., & Abdel-Rahman, O. N. (2021). Assessing the effects of Orlistat as an anti-obesity drug in high-fat diet-induced obesity in male rats. *Bulletin of Pharmaceutical Sciences, Assiut*, 44(1), 131-138.
- 7) Abeysinghe, P. D., Bandaranayake, P. C., & Pathirana, R. (2020). Botany of endemic Cinnamomum species of Sri Lanka. In *Cinnamon: Botany, Agronomy, Chemistry and Industrial Applications* (pp. 85-118).
- 8) Ben Lagha, A., Azelmat, J., Vaillancourt, K., & Grenier, D. (2021). A polyphenolic cinnamon fraction exhibits anti-inflammatory properties in a monocyte/macrophage model. *PLOS One*, 16(1), e0244805.
- 9) Mohammed, I. M., Surchee, S. M., & Wala'a, T. Y. (2020). In vivo antibacterial effect of green and black tea extracts on infected liver and kidney of rats. *Tikrit Journal for Agricultural Sciences*.
- 10) Yulianto, W. A., Tistianingrum, N. W., & Swasono, F. (2021). The effect of soaking temperature and cinnamon extract concentration on the quality of par-boiled rice. *International Food Conference (IFC)*.
- 11) Erhirhie, E. O., Ekene, N. E., & Ajaghaku, D. L. (2014). Guidelines on dosage calculation and stock solution preparation in experimental animals' studies. *Journal of Natural Sciences Research*, 4(18), 100-106.
- 12) Oliveira, M. D. C. (2020). Effect of training with a vibrating platform on the morphology of the diaphragm muscle in rats with hypothalamic obesity.
- 13) Zakaria, Z., Othman, Z. A., Suleiman, J. B., Jalil, N. A. C., Ghazali, W. S. W., & Mohamed, M. (2021). Protective and therapeutic effects of Orlistat on metabolic syndrome and oxidative stress in high-fat diet-induced metabolic dysfunction-associated fatty liver disease (MAFLD) in rats: Role on Nrf2 activation. *Veterinary Sciences*, 8(11), 274.
- 14) Li, B., Li, J., & Hu, S. (2022). Cinnamon could improve hepatic steatosis caused by a high-fat diet via enhancing hepatic beta-oxidation and inhibiting hepatic

- lipogenesis, oxidative damage, and inflammation in male rats. *Journal of Food Biochemistry*, 46(6), e14077.
- 15) Shang, C., Lin, H., Fang, X., Wang, Y., Jiang, Z., Qu, Y., ... & Cui, X. (2021). Beneficial effects of cinnamon and its extracts in the management of cardiovascular diseases and diabetes. *Food & Function*, 12(24), 12194-12220.
- 16) Suleiman, J. B., Nna, V. U., Zakaria, Z., Othman, Z. A., Bakar, A. B. A., & Mohamed, M. (2020). Obesity-induced testicular oxidative stress, inflammation, and apoptosis: Protective and therapeutic effects of Orlistat. *Reproductive Toxicology*, 95, 113-122.
- 17) Iftikhar, N., Hussain, A. I., Chatha, S. A. S., Sultana, N., & Rathore, H. A. (2022). Effects of polyphenol-rich traditional herbal teas on obesity and oxidative stress in rats fed a high-fat–sugar diet. *Food Science & Nutrition*, 10(3), 698-711.
- 18) Alhodieb, F. S. (2024). Therapeutic potential of polyphenol-rich foods in the management of diabetes and dyslipidemia in diabetic male rats. *Romanian Journal of Diabetes, Nutrition and Metabolic Diseases*, 31(1), 880-892.
- 19) Yigit, A. A., Kilinc, S., Olcuoglu, R., & Arnous, E. A. (2024). The effects of Orlistat on oxidative stress, recognition memory, spatial memory, and hippocampal tissue in experimentally induced obesity in rats. *Behavioural Brain Research*, 462, 114894.
- 20) Chen, S. T., & Rao, Y. K. (2022). A comprehensive review on phytochemical, pharmacological and future prospective of dietary medicinal plant *Cinnamomum osmophloeum* Kanehira. *Current Research in Complementary & Alternative Medicine*, 6(160), 2577-2201.
- 21) Katoch, G. K., Nain, N., Kaur, S., Rasane, P., & Panesar, P. S. (2024). Hyperlipidemia/obesity crisis: Healthy food and lifestyle changes to tackle obesity. In *The Role of Nutrition in Integral Health and Quality of Life* (pp. 271-294). Apple Academic Press.
- 22) Feingold, K. R. (2024). Triglyceride lowering drugs. *Endotext [Internet]*.
- 23) Khedr, N. F., Ebeid, A. M., & Khalil, R. M. (2020). New insights into weight management by Orlistat in comparison with cinnamon as a natural lipase inhibitor. *Endocrine*, 67, 109-116.
- 24) Mohammed, H. A., & Abdel Fattah, D. M. (2018). Hypolipidemic and hypoglycemic effect of cinnamon extract in high fat diet fed rats. *Zagazig Veterinary Journal*, 46(2), 160-167.
- 25) Nagaty, B. A. (2019). Evaluation of the potential protective effect of cinnamon extract against carbon tetrachloride-induced oxidative stress and hepatotoxicity in male albino rats (Doctoral dissertation, King Abdulaziz University Jeddah).



- 26) Khaafi, M., Tayarani-Najaran, Z., & Javadi, B. (2024). Cinnamaldehyde as a promising dietary phytochemical against metabolic syndrome: A systematic review. *Mini Reviews in Medicinal Chemistry*, 24(3), 355-369.
- 27) Saglam, K., & Sekerler, T. (2024). A comprehensive review of the anti-obesity properties of medicinal plants. *Pharmedicine Journal*, 1(2), 46-67.
- 28) Vijayakumar, K., Prasanna, B., Rengarajan, R. L., Rathinam, A., Velayuthaprabhu, S., & Vijaya Anand, A. (2023). Anti-diabetic and hypolipidemic effects of Cinnamon cassia bark extracts: An in vitro, in vivo, and in silico approach. *Archives of Physiology and Biochemistry*, 129(2), 338-348.
- 29) Idoko, A. S., Bonomi, Z. M., & Eneji, M. S. (2023). Supplementation of high-fat diet with garlic and cinnamon powder ameliorated high fat-induced oxidative damage in liver and kidney of Wistar rats via redox balancing. *FUOYE Journal of Pure and Applied Sciences (FJPAS)*, 8(2), 124-138.
- 30) Costa-Beber, L. C., Goettems-Fiorin, P. B., Dos Santos, J. B., Friske, P. T., Frizzo, M. N., Heck, T. G., & Ludwig, M. S. (2023). Air pollution combined with high-fat feeding aggravates metabolic and cardiovascular diseases: A dangerous, oxidative, and immune-inflammatory association. *Life Sciences*, 317, 121468.
- 31) Ahmed, N., Asif, S., Arfan, M., Mahmood, Q., Islam, A., Gatasheh, M. K., & Zia, M. (2024). Synthesis and characterization of short α and β -mixed peptides with excellent anti-lipase activities. *Molecules*, 29(4), 765.
- 32) Albzoor, R. (2019). Medicinal plants as a source of inhibitors of the digestive enzymes: Alpha-glucosidase, alpha-amylase and pancreatic lipase (Doctoral dissertation, Raghad Albzoor).
- 33) Miah, M. A., Himel, M. H., Sujan, K. M., Mustari, A., & Haque, M. I. (2022). Protective effects of cinnamon powder against hyperlipidemia and hepatotoxicity in butter fed female albino mice. *Saudi Journal of Biological Sciences*, 29(4), 3069-3074.