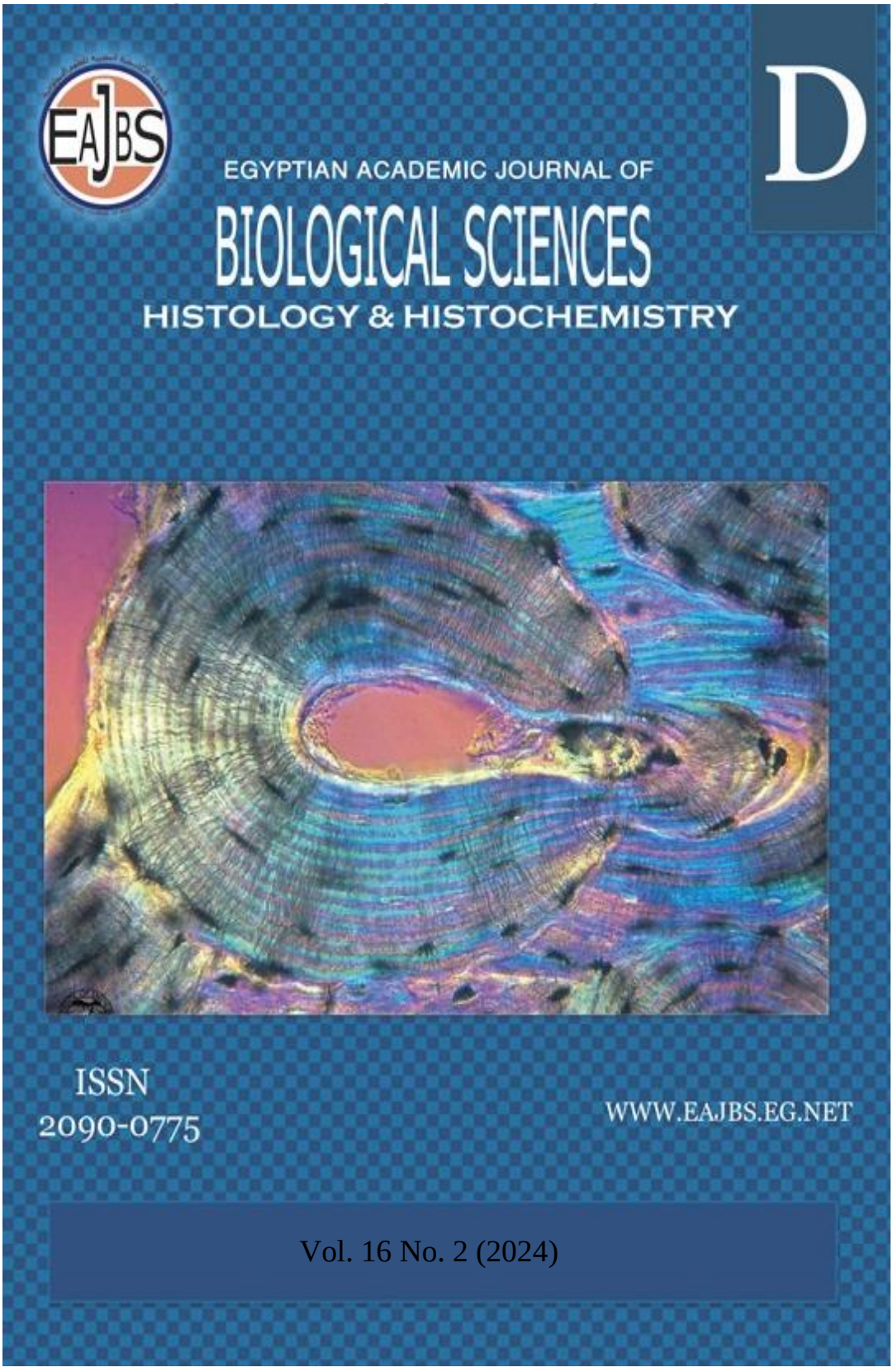

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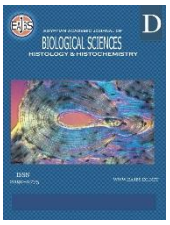

Antiobesity Effect of Chromax Drug and *Plantago ovata* Seeds on Female Rats

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HFD, Obesity, chromax, *Plantago ovata* seed, Female rat.

ABSTRACT

Objective: To study the anti-obesity effect of oral administration of Chromax and/or *Plantago ovata* seed powder on female rats fed a high-fat diet. **Materials and methods:** The control or lean group included six females and was fed a normal fat diet for 18 weeks. While the other twenty-four were fed a high-fat diet containing 45% animal fat for 3 months to induce obesity and then randomly divided into four homogeneous groups (6 for each group) as follows: Group II or obese control group which was fed a high-fat diet throughout the experimental period. Group III or Chr which was fed a high-fat diet with 200 µg/kg/day for 12 weeks. Group IV or Pla which was fed a high-fat diet mixed with 30% Ispaghula seed powder for 12 weeks. The fifth group or Mix was fed a high fat diet with 200 µg/kg/day and 30% of ispaghula seed powder for 12 weeks. Anthropometric parameters such as (body weight change, body weight gain percentage, body mass index, and Lee index) and serum glucose were assessed along with histological examinations of fat. Results: The results showed an increase in body weight, body mass, lee indexes, abdominal fat, blood glucose, and several histopathological lesions in obese females of the second group while body weight, body mass index, and Lee index decreased and blood glucose improved in the chromax group more than the plantago seed powde. **Conclusion:** the mixture of chromax with plantago seed showed anti-obesity results compared to other groups.

INTRODUCTION

Obesity is a global health difficulty and chronic illness that characterized by massive accumulation of fat in white adipose tissue leading to increases body weight with severe health problems (Safaei *et al*., 2021) and poses a serious threat to worldwide public health (Lin & Li, 2021). WHO (2018) defined Body Mass Index (BMI) as a handy index of weight and height and commonly used for the classification of adults as obese or overweight. Currently, more than 650 million are considered obese and more than 1.9 billion adults are overweight (Haththotuwa *et al*., 2020). Many authors reported that obesity can lead to bone damage cardiovascular diseases and diabetes (Safaei *et al*., 2021; Ren *et al*., 2022; Lohmander *et al*., 2023). Also, obesity has been recognized to be associated with chronic inflammation in different tissues, such as liver, adipose tissue and islets in the last two decades (Michalakis & Ilias, 2020; Wu & Ballantyne, 2020; Taylor, 2021).

There are many treatment methods for obesity, such as improving the diet and the lifestyle of obese patients (Johnson *et al*., 2022), drugs therapy (Bays *et al*., 2022; Calcaterra *et al*., 2022).

High risk of operation, long treatment periods and dangerous side effects of these drugs are the main factors, affecting obesity treatment. Prevention of obesity or dietary treatment for obese patients has become promising method to lose weight **(**Yang *et al*., 2023). In addition, Reynolds *et al*. (2019) reported that diet is the main cause of obesity; so the replacement of dietary fiber with animal proteins and refined grains in the diet leads to an excess of nutrient intake and ultimately to obesity.

Using herbs to control obesity is expanding as there are many researchers working on the development of anti-obesity agents from natural compounds obtained via dietary or herbal plants. These natural compounds may decrease the fat accumulation through the inhibition of adipocyte differentiation or adipogenesis, as well as decreasing the level of triacylglycerol by enhancing reducing lipogenesis or lipolysis pathways (Sun *et al*., 2016; Jamous *et al*., 2018).

It has been shown that the impact of the natural antioxidant plays a central role in effects associated with the phyto-compounds (Mohamed & Fayed 2020). The bioactive substances found in typical functional foods, such as dietary fibre, polyunsaturated fatty acids, phytochemicals, and antioxidants, may help lower the risk of developing chronic diseases (Gazem & Chandrashekariah, 2016). Psyllium seeds were the first used by North Americans and Europeans for their effects on lowering cholesterol and blood sugar (Ashwini *et al*., 2015) According to (Karhunen *et al*., 2010), diets with psyllium fibre enhance blood sugar, insulin, and cholesterol levels much more than diets without dietary fibre. Furthermore, soluble fibre may postpone stomach emptying, decreasing the absorption of carbohydrates. Additional mechanism: psyllium seeds. By sequestering the carbohydrates consumed with the diet and delaying their absorption by digestive enzymes, psyllium seeds may also play a role in the postprandial effect. Also, the inhibition of liver gluconeogenesis may be the cause of the hypoglycemic effects of psyllium seeds (Pal *et al*., 2022).

Our research aimed to evaluate the harmful effects of high fat diet on female rat and the possible ameliorative effect of oral administration of the anti-obesity chromax drug and ⁄or *Plantago ovata* seed powder against these toxic effects.

MATERIALS AND METHODS

Plantago ovata seed:

Dried *Plantago ovata* seeds were purchased from the local market in Fayoum, (Egypt). The seeds were grinded (powdered) by mechanical grinder. *Plantago ovata* seed powder

Chromax:

400 μg/kg of Chromax were used according to El Azab *et al*. (2022) and prepared using capsule which contain a synergistic combination of 500 mg of Garcinia Cambogia extract and 281.569 mcg (Equivalent to chromium 35 mcg) of Chromium Picolinate. Manufactured by: EVA PHARMA for Pharmaceuticals && Medical Appliances SAE - Egypt.https://seif-online.com/en/product/chromax-60-cap/

Experimental Animal:

A total of 30 healthy female albino rats were purchased from the animal house of VACSERA, Cairo, Egypt with average weight of 122 ± 2 grams. The animals were kept under standard environmental conditions on 12 hours' light/dark cycle under temperature of (25±1) °C, and free access to water and fed standard chow diet. Animals acclimated to laboratory conditions for 14 days and housed five per sterilized plastic cages of adequate size allowing free spontaneous motility with wood shaving bedding.

Experimental Design:

Thirty female rats were divided into five equal groups randomly. Animals in the normal control (first group) supplied with tap water ad libitum and feed on normal standard pellet diet that formulated following the composition authorized by the

Association of Official Analytical Chemists (A.O.A.C.,1988) during the experimental period (12 weeks). Other female rats were first made obese by feeding on a high fat diet (HFD) and water ad libitum for 12 weeks' duration according to (Aftab & Usmanghani, 1995). HFD were consisting of Milk Powder 15%, Corn Flour 25%, Sucrose 15%, Egg Yolk 3%, Casein 5%, Cholesterol 1% Lard 35%, and Salt Mixture 1%. Then after, and after gaining obese; the 24 female rats were divided into equl four groups that treated orally with different studied materials (chromax and/or *Plantago ovata* seed powder) along with continuation of HFD for 12 weeks as shown in Table 1.

Table 1: Showing experimental design.

Groups		
GP I Control (Lean)		Feed on normal stander diet for 12 weeks
To induce obesity: Female Rats Feed on high fat diet (HFD) for 12 Weeks	GPII obese	Complete Feeding on high fat diet (HFD) (100gm/day/6 rats) for 12 weeks
	GPIII Chromax	Complete Feeding on high fat diet (HFD) (100gm/day/6 rats) for 12 weeks and administered orally 400 μg/kg /day of chromax drug
	GPV *Plantago ovata*	Complete Feeding on high fat diet (HFD) (100gm/day/6 rats) mixed with 30 gm *P.ovata* seeds powder for 12 weeks
	GPIV Chromax + *P. ovata*	Complete Feeding on high fat diet (HFD) (100gm/day/6 rats) for 12 weeks mixed with 30 gm *P. ovata* and administered orally400 μg/kg /day of Chromax drug for 12 weeks

Anthropometrical Parameter:

Body weight of all rats in each group was recorded on every alternate day by using a digital balance. The weight (change) gain of rats was monitored weekly and the food intake was monitored daily throughout the experimental period. The length between the anus and nose was measured on ventral side in cm unit using an inch tape to calculate naso-anal lengths of all female rats in each group twice weekly to calculate the body mass index and Lee index according to the following Novelli *et al*. equation (2007):

Body mass index (BMI) = body weight (g)/length^2 (cm^2)

Lee index = cube root of body weight (g)/nose to anus length (cm).

Blood Samples Collection for Glucose:

Blood was drawn from all animals in each group and centrifuged at 3000 rpm for ten minutes. Serum and plasma samples were stored at 0°C until biochemical analysis in the same day. The level of glucose in the serum was measured by Boehringer Mannheim kits (Trinder 1969).

Histological Preparation for Light Microscopy (paraffin sections):

At the end of experiment, the females were sacrificed by cervical dislocation. Dissected to obtain adipose tissues that cutting into small pieces and fixed in neutral formalin solution (10%) for 24 hours, the specimens were washed, dehydrated in ascending series of ethanol 70, 80, 90 and 96% for 20 minutes each, then in two changes of 100% ethanol for 30 minutes each. Then cleared in xylol for 20 minutes (two changes) and impregnated in paraplast (three changes) at 60 ºC for three hours and embedded in paraplast forming tissue blocks. Sections of 4 to 5 μm thick were prepared by microtome and stained with hematoxylin & eosin according Bancroft & Gamble (2002).

Statistical Analysis:

Results were expressed as mean ±S.E. One-way ANOVA was applied in statistical analysis and Tukey's post hoc test was used to evaluate the relationship between the groups. $P < 0.05$ was considered significant (Newman & Federer, 1963).

($p * < 0.05$) Significant difference between normal control and all treated groups

(p #<0.05) Significant difference between HFD group and all treated groups

RESULTS

The present study was carried out to induce obesity in female rats as an animal model by feeding on high fat diet (HFD) containing 45% animal fat for 12 weeks. Then, studying the different effects of the obesity and examine the anti-obesity effect of oral administration of anti-obesity drug chromax at a 400-mcg /k/d dose of mg/kg.b. wt once per day for additional 6 weeks on obese female albino rats feeding on HFD. Also, our study was extended to assess the anti-obesity effect of *Plantago ovata* seeds powders oral administration. Anthropometric parameters as (body weight change, body weight gain %, BMI, Lee index), serum biochemical parameters Data presented in these investigations showed that oral administration of chromax individually, *Plantago ovata* (Treatment groups) have highly significant effect (P < 0.05).

1. Short Toxicity Symptoms and Mortality Rate:

Female rats of chromax treated groups showed some clinical toxicity symptoms and signs starting from the second day and also after receiving other doses such as: loss of appetite (decrease food and water intake), general weakness, yellowish and brittleness of skin hair and nails, then hair loss. Also, female rats in obese group showed obvious decrease in their general activity. The mortality percent among treated animals were zero in all different studied groups.

Part I: Effect of High Fat Diet (from day 1 till day 90):

2. Anthropometrical Parameters:

Female obese rats in group II that feed on HFD feeding for 6 weeks showed significantly increased in their body weights, BMI and the Lee index comparing with the control non obese and obese female rats in group 2 as shown in Table 2 and figure 1.

Table 2: Showing different anthropometric parameters of female albino rats in different studied groups. (Mean ± SME).

Groups	GPI Control (Lean)	GPII obese	T-value
Initial Weight (g)	122.9 ±0.16	123.7 ±0.41	0.305
Initial Length (cm)	23.07 ±0.02	23.07 ±0.014	0.136
Initial BMI (g/cm^2)	0.232 ±0,0016	0.232 ±0.00010	0.710
Initial Lee index (g/cm)	0.216 ±0.00076	0.216 ±0.00057	0.522
Final Weight (g)	208 ±0.97	309.5 ±1.41	-59.4
Final Length (cm)	24.05 ±0.013	24.05 ±0.014	- 0.889
Final BMI (g/cm^2)	0.36 ±0.001	0.53 ±0.004	-31.03
Final Lee index (g/cm)	0.25 ±0.002	0.28 ±0.0004	-14.50
Body Weight change (g)	40.1	64.9	-
Change %	19.3 %	20.97 %	-

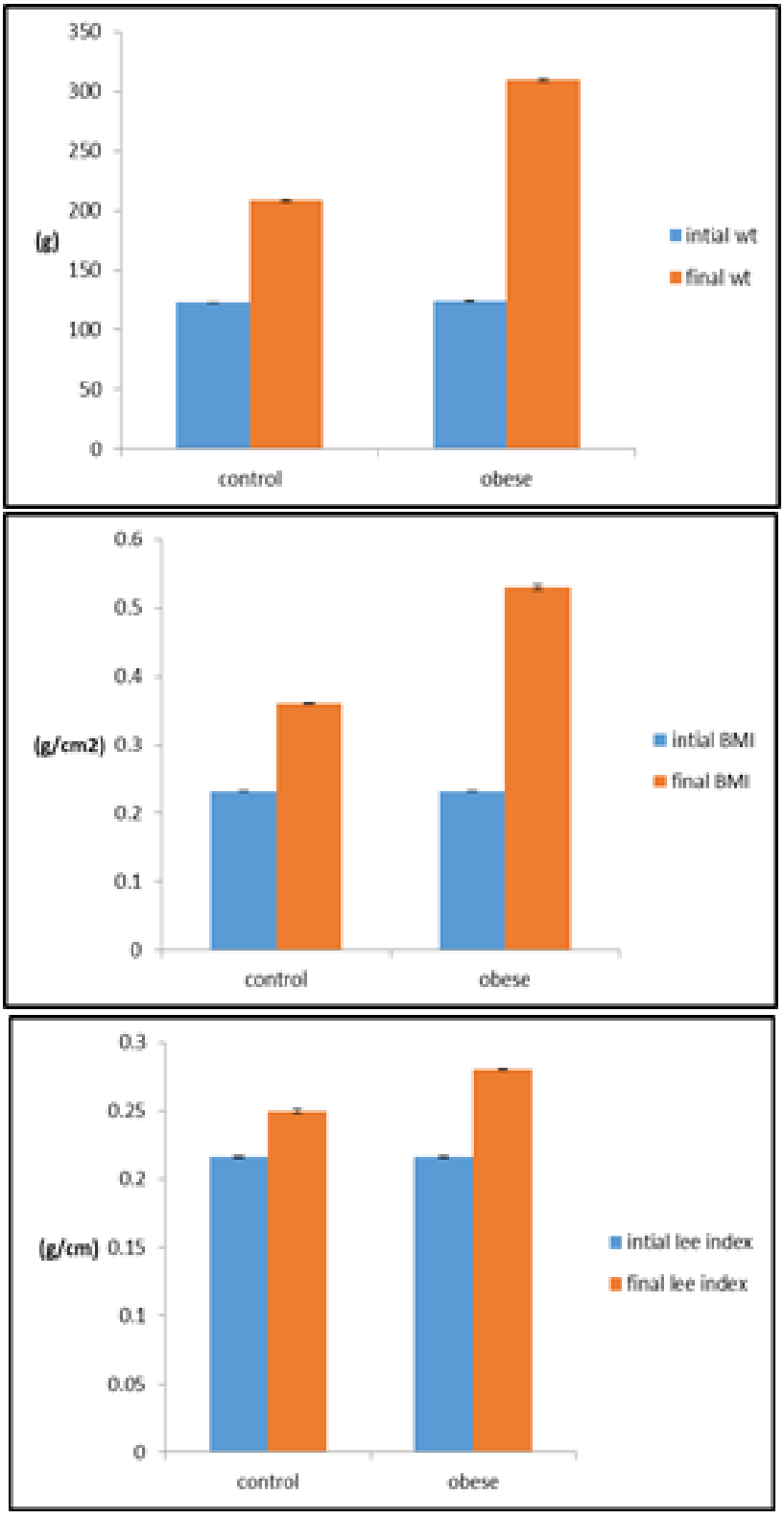

Fig. 1: Initial and final lee index (LI) of female albino rats treated with chromax and/or *Plantago ovata* seeds as antioxidant against side effects of chromax for 12 weeks.

Part II: The Effect of Chromax and Or Plantago Ovata on Obese Female Rat (day 91 till the end of experiment):

Female obese rats in group II that Ad libitum HFD feeding for additional 12 weeks showed significantly increased in their body weights, BMI and the Lee index compared with control non-obese and all other studied groups. Other groups feed on HFD containing *Plantago ovata* seeds powder

showed significant decrease the body weights, BMI and the Lee index vs. animals in control non-obese group I and obese female rats in group II. In contrast, obese female rats that treated with chromax only (GPIII) or in combination with *Plantago ovata* (GPVI) showed significant decrease in their body weight (%), BMI and Lee index comparing with obese and other groups (Table 3 and Fig.2**).** The body weight gains in control (untreated) and obese female rat showed noticeable increase as the period extended, the body weights were recorded as (the mean ± stander main error) at first day of the experiment and at the end of the experiment.

Table 3: Showing different anthropometric parameters of female albino rats in different studied groups. (Mean ± SME).

Groups	**GP_I Control (Lean)**	**GP_{II} obese**	**GP_{III} chromax**	**GP_{IV} *P. ovata***	**GP_V Chromax+ *P. ovata***	**T-value**
Initial Weight (g)	208 ± 0.97	309.5* ± 1.4	308.6* ±1.0	309.9* ± 0.6	308.2***** ± 0.6	2175.310**
Initial Length (cm)	24.05 ±0.013	24.07 ±0.014	24.07 ±0.014	24.05 ±0.013	24.07 ±0.014	0.469**
Initial BMI (g/cm^2)	0.361 ±0.002	0.533 ±0.002*	0.533± 0.002*	0.533 ±0.009*	0.538 ±0.002*****	2200.895**
Initial Lee index (g/cm)	0.247 ±0.0002	0.281 ±0.0005*	0.281 ±0.0005*	0.281 ±0.0009*	0.281 ±0.0002*****	2042.325**
Final Weight (g)	248.1 ±0.91	374.4 ±1.4*,#	260.6 ±1.27*#	277.5 ±0.79*,#	241.8 ±0.35***,#**	2699.829**
Final Length (cm)	24.053 ±0.013	24.07 ±0.014	24.07 ±0.019	24.07 ±0.014	±24.05	0.450******
Final BMI (g/cm^2)	0.429 ±0.001	0.646 ±0.003*	0.449 ±0.002*#	0.488 ±0.002*#	0.419 ±0.002***,#**	2104.248**
Final Lee index (g/cm)	0.262 ±0.0002	0.299 ±0.0004*	0.265 ±0.0007*#	0.271 ±0.0003*#	0.261 ±0.0003*#	1660.099**
Body Weight change (g)	40.1	64.9	- 48	- 32.4	-52	-
Change %	19.3 %	20.97 %	15.6 %	10.6 %	9%	-

(p * <0.05) Significant difference between normal control and other groups
(p #<0.05) Significant difference between HFD group and other groups

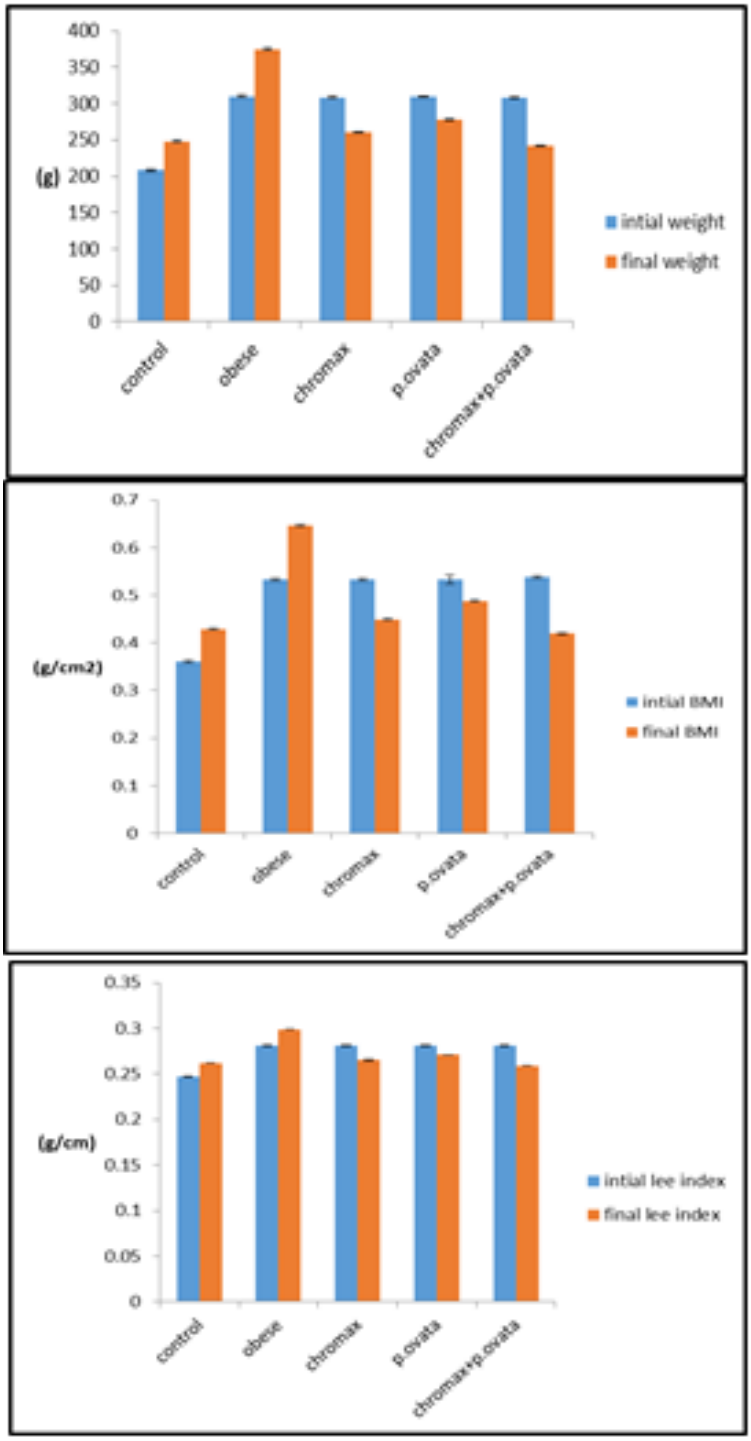

Fig. 2: Initial and final lee index (LI) of female albino rats treated with chromax and/or *Plantago ovata* seeds as antioxidant against side effects of chromax for 12 weeks.

Table 4: Showing blood glucose concentrations of female albino rats in different studied groups. (Mean ± SME).

Groups	GP_I Control (Lean)	GP_{II} obese	GP_{III} hromax	GP_{IV} *P. ovata*	GP_V Chromax+ *P. ovata*	F-Value
Glucose	**79.83 ± 0.45**	**132.17* ± 0.53**	**115.50 *,# ± 0.76**	**122.05*,# ± 0.59**	**96.48*,# ± 0.53**	**1293.750****

(p * <0.05) Significant difference between normal control and other groups
(p #<0.05) Significant difference between HFD group and other groups

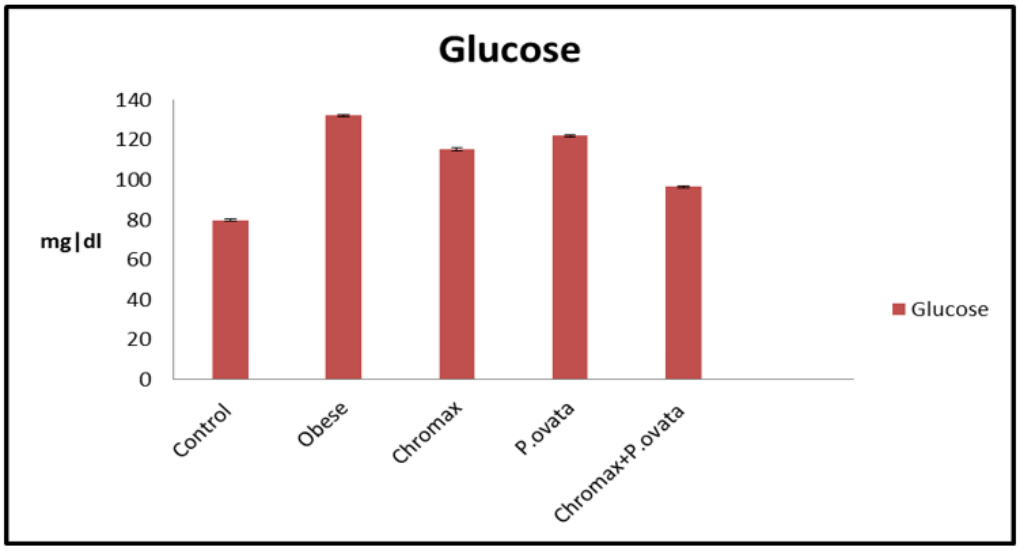

Fig. 3: Showing blood glucose in different studied groups.

Body Mass Index (BMI).

Female obese rats in group II that Ad libitum HFD feeding for 6 weeks showed significantly increased in their BMI vs. control non-obese. In contrast, obese female rats in group III that treated with chromax showed marked significant decrease in their BMI comparing with obese (GPII) and other groups. Also, other groups feed on HFD containing *Plantago ovata* seeds powder showed significant decrease in the BMI vs. animals in group II (Table 2 & Fig. 2).

Lee Index:

Table and Figure showing that female obese rats in obese group (II) that Ad libitum HFD feeding for 6 weeks showed significantly increased in their Lee index vs. control non-obese and all other studied groups. Other groups treated with chromax alone or feed on HFD containing *Plantago ovata* seeds powder or and in combination with chromax showed significant decrease in their Lee index vs. animals in group II (Table 2).

The decrease in both BMI and Lee index among treated groups with the order, GPV > GPIII > GPIV tested groups.

Blood Glucose:

Table 4 and Figure 3 showing that female obese rats in obese group (II) that Ad libitum HFD feeding for 6 weeks showed significantly increased in their serum glucose concentration vs. control non-obese and all other studied groups. Other groups treated with chromax alone or feed on HFD containing *Plantago ovata* seeds powder or and in combination with chromax showed significant decrease in their glucose level comparing with animals in group II (Table 4).

Adipose Tissue:

The studied paraffin sections of the adipose tissue in the different studied groups showed that there were no histological abnormalities of the adipocytes in the control non obese group (GP_I) with normal size (Fig. 4A), whereas hyperplasia and hypertrophy were observed in the fat cells with inflammatory response in GP_{II} (control obese group) (Fig. 4B). In contrast, treatment with *P. ovata* seeds powder individually and in combination with chromax lead to decreased in size and number of fat cells (smaller and fewer adipocytes) were noticed comparing with those in the HFD group, using the same field of view and magnification. Therefore, the studied materials can exert anti-obesity effects by suppressing the accumulation and the growth of fat cells (Fig. 4C, D&E).

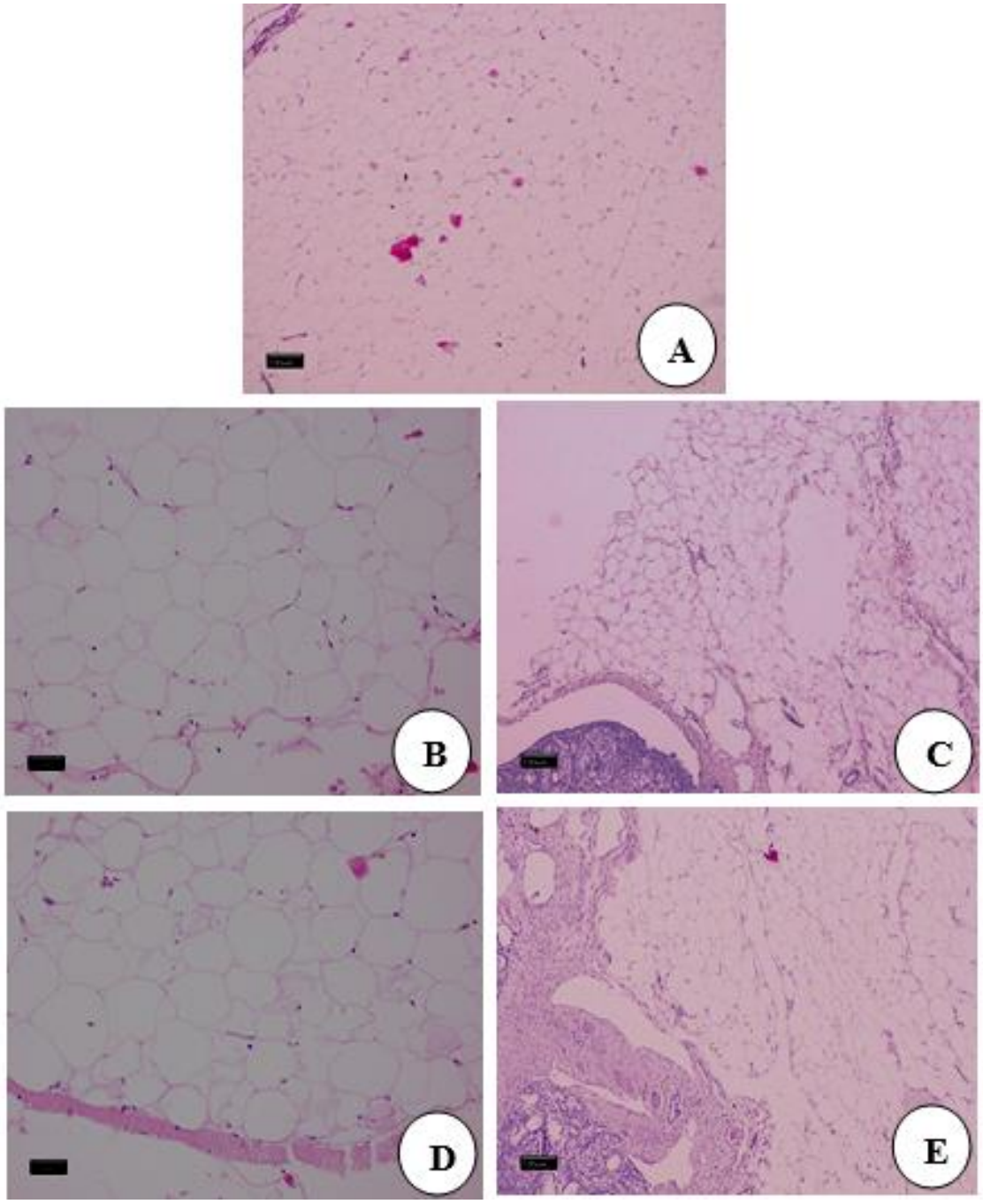

Fig.4: Photomicrographs showing the histological structures of the adipose tissue in different studied groups, **A.** Control. **B.** Obese group. Note hyperplasia and hypertrophy (increased size) of adipocytes **C.** chromax group **D** *Plantago ovata* group. **E.** Mix group. Note: Large sized adipocytes in group II (B) comparing with other groups. HE, bar 100 µm.

DISCUSSION

Significance of the Study:

Diets with high fat that consumed in excess of requirements make a major contribution to excess chronic calorific surplus leading to obesity and its complications (Vannice & Rasmussen, 2014). The results of Ma *et al*. (2017) suggesting that obesity may be correlated with many metabolic disorders, such as cardiovascular disease and cancer diabetes. So, obesity and its complications considered a global concern (Choa *et al*., 2021) and its prevalence has tripled in a lot of nations around the world (Çayli *et al*., 2023).

Obesity treatment has been challenging for the fact that the anti-obesity drugs usually have serious side effect reactions (Daneschvar *et al*., 2016). In addition, several anti-obesity drugs have been withdrawn from the

market because of their unexpected adverse side effects although they approved by the Food and Drug Administration (Onakpoya *et al*., 2016; Srivastava & Apovian, 2018). So, it is necessary to develop natural compounds as alternative sources agents for the loss weight due to their considerable anti-obesity activity, novel structure and potentially lower advers side effects (Pan *et al*., 2018). A growing number of human and animal studies showed that the constituents from food origin could be counteract obesity with little side effects (Waddell & Orfila, 2023).

Mir *et al*. (2019) reported that many plants used in the management of many metabolic dysfunction including obesity owing to the presence of natural active components or plant-derived secondary metabolites including polyphenols, anthocyanins and flavonoids. Using natural preparations have many advantages such as better usability, easy availability, economic cost-effectiveness and lack of adverse effects (Oršolić *et al*., 2019; Wen *et al*., 2019). So, the present investigation aimed to evaluate the harmful effects of high fat diet on female rat, the possible ameliorative effect of oral administration of the anti-obesity drug chromax and/or the powder of *Plantago ovata* seed against these toxic effects and comparing the anti-obesity effect of chromax and/or *Plantago ovata* seeds in obese female rats. Some anthropometric parameters and biochemical parameters together with some histological examinations of the heart and adipose tissues will be assessed to highlight the effects of *Plantago ovata* individually or in against chromax toxicity and antiobesity effect of these natural plants in HFD-induced obese female rat model.

High Fat Diet and Animal Model:

Studies on HFD-induced obesity in rats are regarded as a useful model because the conditions have been found to be similar to obesity in humans (Bhutani *et al*., 2007). Furthermore, due of their similarity to human behavior in acquiring weight after consuming a high-calorie diet, rats are frequently employed in experimental trials to examine the many effects of obesity (Novelli *et al*., 2007). Although care must be taken to extend these findings to human individuals, experimental models are generally required in the study of obesity because they allow for more controlled experimental circumstances (Besbes *et al*., 2013).

The induction of obesity in the present study were done by feeding female rats on high fat diet containing 45 % animal fat for 12 weeks reaching (320 ± 10g). Then female rats divided into five equal groups and treated with different studied materials (Chromax, *Plantago ovata*) individually and in combination for another 12 weeks. In addition to control non obese female rats that feed on normal diet during the experimental period (18 weeks). Since humans typically gain weight and become obese through high-fat diets, this is the primary approach of inducing obesity in rats. One of the most popular techniques for gaining animals to be overweight and causing statuses is feeding them a high-fat diet (HFD), where fats typically make up 45–60% of the total calories (Hariri *et al*., 2010) or feeding on a high-fat diet that contained 40% animal fats for three months (Besbes *et al*. (2013).

The hallmarks of the metabolic syndrome and obesity in humans, including hyperlipidemia, insulin resistance, and glucose intolerance, are typically developed in mice given a high-fat diet for at least 10 to 14 weeks (Winzell & Ahrén 2004; Ito *et al*., 2007). Also, consumption of HFD was associated with increased body weight, BMI and risk of overweight and obesity (Wang *et al*., 2020) and may cause complications associated with obesity, including glucose intolerance, fat accumulation in diverse tissues, and hypertrophy of fat cell (Fujisaka *et al*., 2020).

Effect of High Fat Diet on Female Rat: Clinical Signs and Food Intake:

In the current study the food and water intake were decreased significantly

in obese female rats' groups feed on HFD in combination with oral treatment with 400 μg/kg chromax (GPIII) and in HFD containing *Plantago ovata* seeds powder (GPIV, GPV). But, control obese female rat in (GPII) that feed on HFD, showed higher rate of food and water consumption and control non-obese lean rat. Dietary fiber increment glucagon-like peptide-1, a chemical in the stomach engaged with satiety control, gastric discharging and small digestive system travel **(**Costabile *et al*., 2018).

Anthropometrics Parameters:

In the present work, the studied anthropometric parameters were significantly altering in female rats that feed on high fat diet in obese groups rats and others in the different Chromax and/or plantago ovata seeds powder treated obese rats.

Body Weight & Body Mass Index:

Overweight and obesity are defined by the WHO (2018) as a BMI of 25-29.9 kg/m^2 and a BMI ≥ 30 kg/m^2, respectively. Here, the body weight and body length were measured according to the described methods by Novelli *et al*. (2007) and Aguh *et al*. (2013). The administration of HFD resulted in increased body weight in rats but in contrast, the treatment with 150 or 300 mg/kg.bw of aqueous extract of *Salvia officinalis* was significantly normalized the body weight of the rats (Alsherif *et al*., 2024). Also, Heo *et al*. (2018) showed that the overconsumption of calorie may leads to an increase in abdominal fat accumulation and body weight gain. Rats fed a high-fat diet for an appropriate amount of time acquire obesity, increased adipose tissue and a marked rise in belly weight (Woods *et al*., 2003).

All obese female rats that feed on HFD mixed with *Plantago ovata* seeds powder revealed significant decrease in their body weights comparing with other groups. An animal study by Kang *et al.* (2007) showed that psyllium is associated with a reduction in weight and body fat in mice with HFDs. Addition of chromium in the diet of obese people reduces appetite and led to reduce their body weight (Anton *et al*., 2008).

Dietary fat and lipids have deep effect on the broadening of obesity in SD rats and this is in accordance with other studies on high calorie diet that induced higher body fat accumulation and increased the body weight (Kusunoki *et al*., 2000; Woo *et al*., 2008; Seo *et al*., 2009; Barakat and Mahmoud, 2011; Besbes *et al*., 2013; Cho *et al*., 2018). The dietary fibers control body weight via the drawing out satiety and diminishing gastric discharging, balancing glucose, further developing insulin sensitivity and lipid oxidation (Kasubuchi *et al*., 2015). Also, dietary fiber useful effect on stomach microbiota could make sense of the conceivable fiber impact on body weight regulation intervened by expanding caloric extraction from food (Simpson & Campbell, 2015). By delaying the absorption of glucose, psyllium can lead to increased satiety and satiation, which can decrease food intake. It can also induce the production of short-chain fatty acids by gut microbes, which have anti-inflammatory and immunomodulatory properties. Additionally, psyllium can trap bile acids and carcinogenic substances and increase the intake of active biologically compounds like antioxidants and phytochemicals (Clark *et al*., 2020; Pal *et al*., 2022).

Body Mass Index (BMI):

The consequences of Novelli *et al*. (2007) showed that BMI might predict these unfavorable outcomes of the fat in rodents since the changes in BMI were related with dyslipidemic profile and oxidative stress in serum of rodents. The results of the current study showed that the BMI along with body weight significantly increased in female rats who were given HFD (GpII) comparing with the other studied obese groups. In the same situation, the BMI and the body weight increased significantly in male Wistar rats feeding on either *ad* libitum sucrose diet or high carbohydrate diet for 4 weeks starting at the age of two months.

The cause found for this increased BMI was lack of dietary control in users who consumed high caloric and high fat diet supposing that they are taking a drug and do not require dietary control. This misperception resulted in rather an increase in BMI (Sugiyama *et al*., 2014) Also, the body mass index was higher in animals treated with diet supplemented with sucrose (300 g/l of water) but with no difference in their Lee index (Malafaia *et al*., 2013).According to (Xiao *et al*., 2020) psyllium has no effect on weight or BMI, studies indicate it can be used to lower blood glucose, when combined with diet and medication therapy.

Lee Index:

According to Lee (1929), the Lee index is the body weight (g) cube root divided by the naso-anal length (cm) and multiplied by 1000. The final body weights and body lengths were used to calculate the Lee index = cube root of body weight (g) divided on nasoanal length (cm) (Novelli *et al*., 2007). Since then, various researchers have evaluated the degrees of obesity in rats using the Lee index (Stephens, 1980; Li *et al*., 2004).

The current study's findings demonstrated that, in comparison to the other obese groups under investigation, female rats receiving HFD (GpII) had considerably higher Lee indices, body weights, and BMIs.The highest values were recorded in high fat diet (HFD) alone. While groups HFD plus chromax, HFD plus *Plantago ovata* showed decrease in the lee index, in comparison with high fat diet (HFD) alone and the lowest values were reported in the HFD plus chromax and *P. ovata*. Certain studies have identified strong relationships between the body's fat content and the Lee index (Kanarek & Mark skaufman, 1979; Rogers & Webb, 1980).

Blood Glucose:

The potential mechanism for increased lipid peroxidation in cardiac tissue may be due increased lipid substrate within the myocardium in which canserve as a larger target for oxidation by free radicals (Vincent & Taylor, 2006). Activities of glutathione peroxidase catalase and cardiac superoxide dismutase, were higher significantly, whereas level of oxidized LDL was lower significantly in HFD+Orilstat group compared to HFD group. HFD group had significantly higher necrotic patch area in myocardium while minimal histological changes were seen in HFD+Orilstat group (Othman *et al*., 2019).

HFD showed significant increase in the level of serum glucose in control obese group comparing with control and the other obese groups. Similarly, there are studies in which the levels of blood sugar were higher in rats feeding on HFD compared to the control group (White *et al*., 2016; Qin *et al*., 2018). Also, fasting blood glucose and fasting insulin levels were significantly higher in the group feeding HFD compared to the control group (Moran-Ramos *et al*., 2017). The high levels of serum glucose in obese or chromax groups were decreased significantly and become more or less as in control non-obese group after *Plantago ovata* administration. Psyllium can also reduce the glycemic index in both diabetic and non-diabetic patients (Abutair *et al*., 2016; Gibb *et al*., 2015) or can be used to lower blood glucose (Xiao *et al*., 2020).

Studies indicated that psyllium ingestion reduced blood glucose levels after a single dosage (Gibb *et al*., 2015; Darooghegi Mofrad *et al*., 2020; Belorio & Gomez, 2021). Also, diabetic rats feed on psyllium husks at a concentration of 5% had the best levels of HDL and LDL cholesterol (Elhassaneen *et al*., 2021). Another explanation showed that psyllium seed husk fibers may decreased glycemic response due to reduced glucose absorption, linked to reduced insulin levels (Ali, 2017)

Adipose Tissues:

Treatment with chromax and/or *Plantago* seed individually and in combination inhibited the proliferation

and size of adipocytes, as fewer and smaller adipocytes were observed compared to those in the high fat group, using the same magnification and field of view. Therefore, chromax and/or *Plantago* seeds powder can effectively exert anti-obesity effects by suppressing the accumulation and growth of fat cells. Similar results were reported by (Pan *et al*., 2018).

In sum, the results of the current study reflect clearly that, HFD induced obesity and exhibited many toxic effects in female rat of GP_{II} as indicated by the elevated body weight, BMI and lee index with dyslipidemia, higher values of AI, CRI, blood glucose. There is also no doubt that chromaxdrug has clear leaning or anti-obesity effect on obese female rats more than *Plantago* seeds powders as showed in a decreased body weight, BMI, Lee Index. Also, it improved the lipid profile parameters, atherogenic index and coronary risk index and blood glucose.

On the other hand, chromax treatment caused many toxic side effects in liver, heart, kidney and ovary as showed in the disrupted biochemical parameters and decreased total antioxidant that coincides with the recorded histopathological lesions in the studied paraffin sections. In contrast, treatments with Plantago seed powder individual and in combination with chromax improve the values of the measured biochemical parameters and the histopathological observations in both control obese and chromax treated groups indicating their treated effect against HFD and chromax toxicities.

Hence it is recommended that HFD and chromax toxicities in obese female rats could be reduced or ameliorates by adding *Plantago* seeds powder. So, further studies are recommended to evaluate whether doses less or more than the studied doses of chromax and *Plantago* may prove effective and less toxic effects. Also, other species may be subject to similar investigations taking into consideration the sensitivity of the species tothe studied materials.

Summary and Conclusion:

The present investigation aimed to evaluate the harmful effects of high fat diet on female rat, the possible ameliorative effect of oral administration of the anti-obesity drug chromax and/or the powder of *Plantago ovata* seeds against these toxic effects and comparing the anti-obesity effect of chromax and/or *Plantago ovata* seeds in obese female rats. In the current study the food and water intake were decreased significantly in obese female rat's groups feed on HFD in combination with oral treatment with 400 μg/kg chromax (GPIII) and in HFD containing *Plantago ovata* seeds powder (GPIV, GPV). But, control obese female rat in (GPII) that feed on HFD, showed higher rate of food and water consumption and control non obese lean rat. In the present work, the studied anthropometric parameters were significantly altering in the high fat diet induced obese rats and other different Chromax and/or *Plantago ovata* seeds powder treated obese rats.

The current study's findings demonstrated that, in comparison to the other obese groups under investigation, female rats receiving HFD (GpII) had considerably higher Lee indices, body weights, and BMIs. The highest values were recorded in high fat diet (HFD) alone. While groups HFD plus chromax, HFD plus *Plantago ovata* showed decrease in the lee index, in comparison with high fat diet (HFD) alone and the lowest values were reported in the HFD plus chromax and *P. ovata*. HFD showed an increase in serum glucose level in female rats in control obese group in comparing with the other groups. The high levels of serum glucose in obese or chromax groups were decreased significantly and become more or less as in control non obese group after *Plantago ovata* administration. In conclusion: The findings imply that Plantago seed powder in combination with chromax drug could be used as a new pharmaceutical formula in the treatment of obesity.

Declarations:

Ethics Approval: The work has been approved by scientific and ethical committee of Fayoum University Institutional Animal Care and Use Committee NO AEC 2369.

Conflict of Interest: The authors declare that there is no conflict of interest regarding the publication of this paper.

Author contribution: Abdelkarim M. Abd el Latif contributed to the paper by researching and editing the article.

Data Availability Statement: The collection of data developed and/or assessed throughout the present work is available through the corresponding author upon reasonable request.

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