Evaluation the Efficacy of Combined Mixture of Spirulina Platensisand Cinnamon Extracts in Overweight Rats Fed on a Fatty Diet

Ghada Ibrahim Abd El-Rahman

Department of Clinical Pathology, Faculty of Veterinary medicine, Zagazig University, Egypt.
gana660@gmail.com

Abstract: Objective: This existing work was planned to appraise the interactive effect of both spirulina platensis and cinnamon in ameliorating the oxidative damage and the body weight increaseelicited by high- fat diet (HFD) ingestion in rats with investigating their hypolipidemic activity. **Methods**: we utilized in this study seventy five albino ratsof male sex with body weight ranging between 130-150 g. They were randomly grouped into 5 equal setswith 15 animals in every one. All groups were fed on HFD (20 % fat) for 4 weeksto cause obesity and hyperlipidemia except the 1st one was kept as normal control. Group 2 (positive control) was remained obese without any treatments, despite groups 3, 4 and 5 were orally given S. Platensis (500 mg /kg b.wt), cinnamon aqueous extracts (400 mg/kg b.wt) and a combined mixture of S. Platensis and cinnamon extracts at the previous doses respectively after inducing hyperlipidemia for another 4 weeks. With ending ofthis experiment, serum lipid profile, antioxidant and histopathological tests were performed with recording body weight gain. **Results:** Treating of obese rats with individual and combined doses of spirulina and cinnamon extracts showed a considerable decrease in the serumtriglyceride (TG), total cholesterol (TC), LDL, VLDL and tissue malondialdehyde (MDA) concentration with an elevation in the serum HDL level, tissue catalase (CAT) and superoxide dismutase (SOD) activities in comparison to obese group (positive control), Also improved data was recorded in the body weight and histopathological picture. Furthermore, our results declared that the combined group of both plant and algae exhibited better effects comparing to the separated one. **Conclusion:** Co-administration of S. Platensis with cinnamon exerted more potent effects against hyperlipidemia and oxidative hazards in obese rats than each one separately, that may be a future aid tool for developing a novel challenge against obesity impacts.
[Ghada Ibrahim Abd El-Rahman. **Evaluation the Efficacy of Combined Mixture of Spirulina Platensisand Cinnamon Extracts in Overweight Rats Fed on a Fatty Diet.** *Life Sci J* 2018;15(7):37-46]. ISSN: 1097-8135 (Print) / ISSN: 2372-613X (Online). http://www.lifesciencesite.com. 6. doi:10.7537/marslsj150718.06.

Keywords: Obesity, Spirulina platensis, High-fat diet, Antioxidant, Hypolipidemic activity, lipid profile

1. Introduction

Obesity is a rapidly growing global health problem that increases the danger for many diseases [1]. It facilitates the progress of many metabolic disorders which include diabetes mellitus, hypertension, dyslipidemia and heart disease [2]. Increased the quantity of nutritive substances (particularly fats) together with the excess of fat reserve in the organ tissues is one of the main causes of obesity [3]. Obesity is associated with ashortage in the antioxidant defense capacity with an increase in oxidative stress, due tooverproduction of superoxide anionby activation of NADPH oxidase that promote the production ofreactive oxygen species (ROS) [4].

Recently great attention converged on the use of natural substances for weight loss as alternative strategy for developing future effective, safe anti-obesity drugs with low side effects [5].

Spirulina is a cyanobacteria under the class of Cyanophyceae, Order of Oscillatoriaceae. It is also named Arthrospira, with photosynthetic effects. Many species of spirulina were detected, but the most used one is Spirulina platensis (S. platensis) [6]. The high nutritious value of S. platensis make it a good provenance of numerous pharmaceutical agents with multi organ protection against many toxic chemicals. S. platensiscontains high levels of multiple B vitamins and minerals (calcium, potassium, manganese, iron, magnesium, zinc) [7], in addition great amount of protein (70% dry weight), carotenoid (4000 mg/kg) [8], essential F. A, amino acids, glycolipids and potent antioxidant compounds (B carotene, vitamin C, vitamin E and selenium) [9]. So ithas multiple therapeutic actions such as antiviral, immunomodulation, immunostimulant, anti-inflammatory, hepatoprotective, anti-cancer, antioxidant and lipid-lowering effects [10-15].

Cinnamomum zeylanicum L. (Cinnamon) is a natural plant belongs to the family Lauraceae, it was used for many years in Asia as traditional folk herbs to treat inflammation. It is also applied in food manufacture as antioxidant and spicy agent [16]. The cinnamon bark is one of multiple common spices used in folk and epochal medicines around world [17]. One of the importantingredients of essential oil extracted from C. zeylanicumis cinnamaldehyde that is the essential compound liable for its activity [18]. Recently, several reports have documented that

cinnamon extract has anti diabetic, anti hyperlipidemias, anti-obesity, antioxidant and hepatoprotective actions [19-22]. Preceding studies investigated the hypolipidemic and antioxidant activities of S. platensis and cinnamon separately, however, As far as we know, this is the incipient report dealing with the joined form of algae and natural plant as an attempt to find outmedications with low side effects for controlling obesity related dyslipidemia.

2. Material and Methods

Tested compounds and chemicals.

Spirulina is a bright, blue-green dried powder with a characteristic smelling produced by power nutritional, Jin Shun, Guangzhou, Trading Co., USA. It was obtained from Delta Trade Company, Alexandria. A dried bark of cinnamon (Cinnamomum zeylanicum L) was purchased from thelocal market of Agricultural Herbs, Spices and Medicinal Plants, Zagazig, Egypt. It was pulverized using an electric mixer into a fine powder and thereafter subjected to the preparation of aqueous extract. All chemicals and reagents were purchased from Sigma and El-Gomhoria Companies.

Preparation of the Plant extracts.

Aqueous extractsof Spirulina and cinnamon powderswereobtained by maceration method. 10 g of finely-powdered substances were weighed and mixed with 100 ml of water and kept in a water bath at 60°C for two hours [23], and then the mixture was thieved through double layer of gauze and filtered by Whatman no. 1 filter paper. The rotary evaporator was applied in the concentration of the finalfiltrate under reduced pressure, which immediately lyophilized after there.

Animals

The study was done on total number of 75 clinically healthy male rats (130- 150 g) collected from the Laboratory Animal's Farm, Faculty of Veterinary Medicine, Zagazig University. The chosen animals were kept in metal cages under hygienic condition and maintained on standard balanced rationwith water ad-libitum. This experiment was performed under the guidanceof the National regulations of animal welfare and Institutional Animal Ethical Committee (IAEC).

Inductance of obesity by high- fat diet supplement (HFD)

Keeping the rats on a fat rich dietfor 3- 4 weeks may be sufficient to cause obesity and acute hyperlipidemia [24]. HFD is composed ofstandard diet with 20 % added fat [25] (18 % lard and 2% corn oil). Because the focus in this experiment was on dietary fat, the content of essential vitamins, minerals and protein in the feed was the same in both HF and standard diets (Table 1).

Experimental protocol

After one week of acclimatization, 75 albino rats (male sex) were assigned to 5 equal groups randomly (15 in each).

Group 1(normal control) was given a normal diet for 28 days, however, the remaining 4 groups were maintainedon a fat rich dietfor 4 weeks to induce obesity.

Group 2 was kept as obese control (positive control) .

Groups 3 and 4 were orally administered with water extracts of S. Platensisin dose500 mg /kg b.wt [26] and cinnamon at adosage of 400 mg/ kg b.wt [27] respectively dissolved in distilled water via gastric tube for another 28 days after inducing hyperlipidemia.

Group 5 was received combined doses of S. Platensis and cinnamon extracts by the same previously mentioned route and duration after induction of obesity.

Body weights of all rats in every group were recorded at the onsetand the end of the experiment.

Table 1: Composition of the high- fat diet (g/ 100g diet) used in the experiment

Ingredients	HFD
Yellow corn	16
Soybean meal (SBM)	12
Ground barely	20
Corn gluten	3
Egg yolk powder	10
Milk powder	10
Wheat bran	5.8
Lard	18
Corn oil	2
Dicalcium phosphate	1.5
Salt	0.5
Mineral premix	0.1
Vitamin premix	0.1
Choline	0.5
Cholesterol	0.5

Collection of blood and tissue preparation

At the terminus, we collected blood samples from the retro-orbital venous plexus of rats without anticoagulant on clean, sterile and chemical free centrifuge tubes for serum isolation for biochemical analysis (Lipid profile). The animals were then sacrificed and specimens from liver and kidney were rapidly collected from all groups and separated into 2 parts; the 1st part kept on -20º C until used for measuring the oxidative stress markers however, the

2nd part was preserved in 10% neutral formalin for histopathological examination.

Serum chemical analysis

Estimation of lipid profile included: the total cholesterol (TC) [28], triglycerides (TG) [29], high density lipoprotein cholesterol (HDL-C) [30], low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) [31] that were measured colorimetrically using commercial kits of Vitro Spectrum, Egypt on semi-automated Photometer 5010 V5+ (RIELE GmbH & Co, Berlin, Germany) related to the manufacturer's schedule.

Determinationof lipid peroxidation and antioxidant status.

Malondialdehyde (MDA) concentration, Superoxide dismutase (SOD) and Catalase (CAT) activities were determined in hepatic tissues by kits of Biodiagnostics-Egypt using the method depicted by [32-34] respectively.

Histopathological examination

Liver and kidney samples were taken from all groups, fixed at 10% buffered formalin, processedand soaked in paraffin. Sections (4–5 mm thick) were prepared, stained with hematoxylin and eosin (H–E) and examined for the pathological findings of hepatic and renal changes [35].

Statistical Analysis

The data of all experimental groups werecompleted using one-way ANOVAfollowed by Duncan's testto differentiate between meanswith the SPSS 16.0 computer program [36]. A value of $p< 0.05$ was considered as statistically significant.

3. Results

Alterations of oxidant and antioxidant parameters

Hepatic levels of SOD and CAT in the rat group received HFD (GP. 2) for4 weeks were less than those in the negative group, also tissue MDA concentration recorded a significant ($P < 0.01$) increase in obese animals compared to normal control. Conversely, it was found that daily dosing of obese animals with aqueous extracts of spirulina and cinnamon for 28 days evoked an elevation in the SOD and CAT enzymes in the liver tissue with a significant ($P < 0.01$) reduction in hepatic MDA content comparable to the positive control group (GP. 2) as showed in table (2).

Table 2. Hepatic levels of MDA, CAT and SOD in HFD received rats after 28 days of S. Platensis and Cinnamon administration

Treatments					
Parameters	**Control**	**HFD**	**Spirulina treated group**	**Cinnamon treated group**	**Combination treated group**
MDA (nmol/g tissue)	$8.44^{d} \pm 0.46$	$21.34^{a} \pm 0.53$	$16.66^{b} \pm 0.52$	$17.46^{b} \pm 0.31$	$13.66^{c} \pm 0.55$
CAT (u/g tissue)	$35.26^{a} \pm 0.90$	$18.89^{d} \pm 0.20$	$25.46^{c} \pm 0.98$	$27.50^{c} \pm 0.51$	$30.30^{b} \pm 0.72$
SOD (u/g tissue)	$75.70^{a} \pm 1.43$	$58.66^{d} \pm 1.65$	$65.53^{c} \pm 1.07$	$64.43^{c} \pm 0.74$	$71^{b} \pm 0.25$

Means within the same row having various superscripts are significantly variable (one-way ANOVA) ($P \leq 0.05$). [a]compared to normal control, [b]compared to the positive control group (HFD) **Abbreviations**: HFD: high-fat diet, MDA: Malondialdehyde, CAT: Catalase, SOD: Superoxide dismutase

Table.3 Lipid profile of different treated groups

Treatments					
Parameters	**Control**	**HFD**	**Spirulina treated group**	**Cinnamon treated group**	**Combination treated group**
TC (mg/dl)	$80.06^{d} \pm 1.47$	$121.16^{a} \pm 2.16$	$92.46^{b} \pm 0.99$	$94.23^{b} \pm 0.63$	$85.1^{c} \pm 0.95$
TG (mg/dl)	$61.76^{d} \pm 1.87$	$86.06^{a} \pm 2.20$	$74.83b^{b} \pm 0.98$	$76.30^{b} \pm 0.56$	$68.53^{c} \pm 0.43$
HDL (mg/dl)	$44.86^{a} \pm 1.33$	$25.26^{d} \pm 1.45$	$32.76^{c} \pm 0.95$	$33.76^{c} \pm 1.12$	$39.50^{b} \pm 0.51$
LDL (mg/dl)	$23.68^{d} \pm 0.60$	$78.68^{a} \pm 0.66$	$44.73^{b} \pm 0.56$	$45.30^{b} \pm 1.01$	$31.89^{c} \pm 0.41$
VLDL (mg/dl)	$12.35^{d} \pm 0.37$	$17.21^{a} \pm 0.44$	$14.96^{b} \pm 0.19$	$15.26^{b} \pm 0.11$	$13.70^{c} \pm 0.08$

Means within the same row having various superscripts are significantly variable (one-way ANOVA) ($P \leq 0.05$). [a]compared to normal control, [b]compared to the positive control group (HFD) **Abbreviations**: HFD: high-fat diet, TC: total cholesterol, TG: triglyceride, LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, VLDL-C: low density lipoprotein cholesterol

Anti-obesityand antihyperlipidemic activities

Feeding of rats on fat rich dietcauseda statistical ($P < 0.01$) increase in the total cholesterol (TC), triglyceride (TG), LDL-C and VLDL-Cserum levels relative to the normal control group. This elevation was decreased in treatment groups received oral doses of spirulina and cinnamon extractsindividually or together, which represented by lowering theserum TC, TG, LDL-C and VLDL-C concentrations relative to the HFD group (GP. 2). These results showed more potent effects in the combined spirulina and cinnamon group than the separated administration as given in table (3). The serum HDL-C significantly ($P < 0.01$) reduced in the HFD supplemented groupcomparing with the controlone (GP. 1), which recorded an observable enhancement in the treatment groups

Changes of rats body weight.

The body weight of rats in all groups increased gradually. Table (4) illustrates a significant ($P < 0.05$) elevation in the final b.wt of rats received high-fat diet (HFD) comparable to the negative control. Administration of spirulina and cinnamon extracts alone or togetherwitha HFD group (GP. 2) for 4 weeks caused a significant ($P < 0.05$) decrease in the final body weight relative to the positive control group (obese control). This effect was better in the treated

group with both extracts than the separated one. The differences in the changes of initial b.wt of rats treated with spirulina and cinnamon extracts and control were non-significant.

Table.4 Effect of aqueous extracts of S. Platensis and Cinnamon on the rat body weight

Treatments					
Parameters	**Control**	**HFD**	**Spirulina treated group**	**Cinnamon treated group**	**Combination treated group**
Initial body weight (g)	148.6 ± 4.41	153.6 ± 3.21	154.4 ± 3.61	151 ± 4.30	150 ± 3.53
Final body weight (g)	176.4 ^{d} ± 2.50	243^{a} ± 2.21	209.8 ^{b} ± 1.77	215.6 ^{b}± 1.07	197.6 ^{c} ± 2.50

Means within the same row having various superscripts are significantly variable (one-way ANOVA) (P≤0.05). ^{a}compared to normal control, ^{b}compared to the positive control group (HFD)
Abbreviations: HFD: high-fat diet

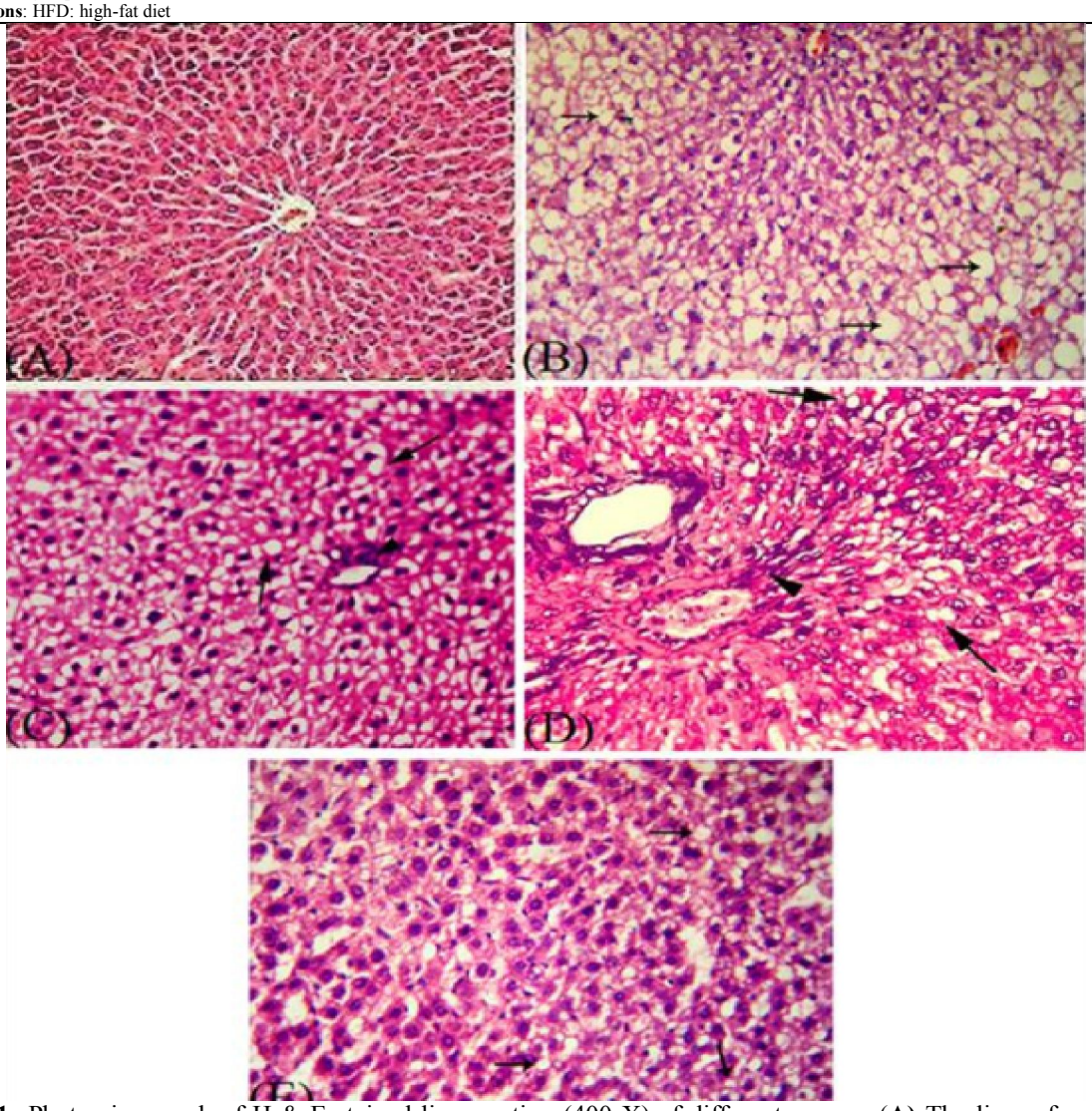

Figure 1: Photomicrograph of H & E-stained liver section (400 X) of different groups. (**A)** The liver of negative control showing normal cellular architecture with distinct hepatic cells, sinusoidal spaces and central vein. However, rats fed with HFD only showing Centro lobular fatty change (arrows) (**B**). The liver of HFD fed rats treated with spirulina and cinnamon extractsshowing moderate fatty change with fat vacuoles (arrows) in some hepatocytes and mild mixed inflammatory cell infiltration (arrow head) around the central vein **(C, D)**. The hepatic parenchyma of combination treated group showingslight hydropic degeneration and fatty change (arrows) **(E)**

Histopathological observation

Microscopical examinationof H & E-stained liver section of control group (GP. 1) revealed normal cellular hepatic tissues and central vein (Fig.1 A). Conversely, hepatic tissue analysis from rats supplemented with HFD (GP. 2) for 28 days showed Centro lobular macrovesicular steatosis (fatty change) in the picture of infiltration of cells by fat vacuoles

pushing the nucleus peripheral with signet ring appearance and typically vacuolated cytoplasm (Fig.1 B). The treatment with spirulina or cinnamon extracts after induction of hyperlipidemia (GPs. 3,4) showed moderate fatty changes with fat vacuoles in some hepatocytes and mild mixedinfilteration of inflammatory cell surrounding the central vein, while other hepatic cells appear normal (Fig. 1C, D) The histopathological changes in these groups were milder than those mentioned in gp. (2)**.** The hepatic parenchyma of combination treated group (GP. 5) showed mild hydropic degeneration and fatty change (arrows), some regenerative attempts were focally noticed (Fig. 1E).

The kidney of control group (1) showed normal renal glomerular and tubular architecture (Fig. 2 A), while the renal tissue of high-fat diet feeding rats (GP. 2) showed focal accumulation of large fat vesicles intramedullary in between renal tubules compressing them and tubules showed the moderate disturbed shape, also mild peritubular mixed inflammatory filtrate was observed (Fig. 2 B). Obese rats received spirulina or cinnamon extracts for 4 weeks (GP. 3,4) showed vacuolation and hydropic degeneration of the lining epithelium of the renal tubulesin form of loose adhesion between adjacent cells (Fig. 2 C, D). The co-treated group with both extracts showed mild vacuolation (arrow), the spare of renal parenchyma was mostly normal (Fig. 2 E).

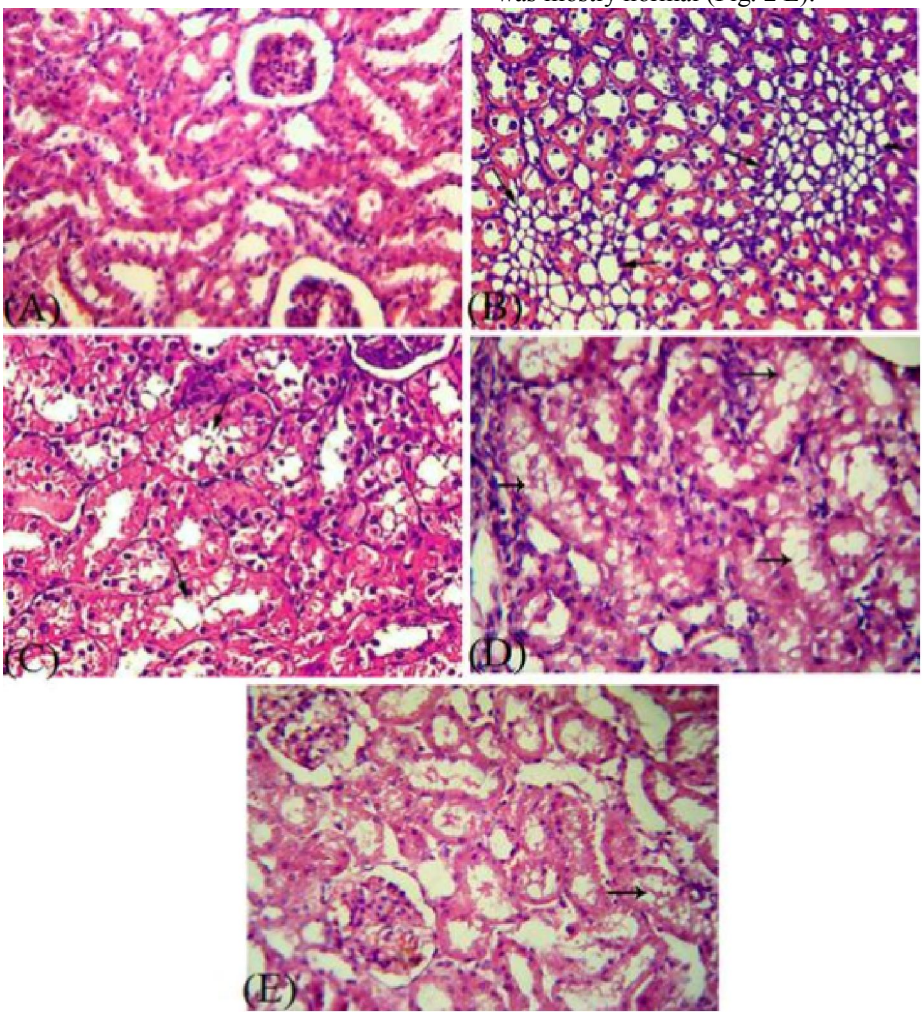

Figure 2: Photomicrograph of H & E-stained kidney section of normal control showing normal renal tubules, glomeruli and bowman's capsule (A) (300 X). The kidney of obese rats (gp.2) showing focal accumulation of large fat vesicles with signet ring appearance intramedullary in between renal tubules compressing them (arrows) (B) (400 X). Spirulina and cinnamon treated groups showing vacuolation and hydropic degeneration of the lining epithelium of the renal tubulesin form of loose adhesion between adjacent cells (arrows) (C, D) (400 X). The renaltubular epitheliumof co-treated group with spirulina and cinnamon extracts together showingmild vacuolation (arrow), the spare of renal parenchyma was mostly normal (E) (400 X).

4. Disscussion

Suppression of antioxidant defensemechanisms with excessfree radicalsoutput, possibly hasa part in an animal form of obesity [37]. This imbalance leads to oxidative stress, which is obvious from depressed hepatic SOD and CAT levels in the obese group in our study with an elevation of tissuemalondialdehyde level. Reduction of enzymes of the antioxidant system in hyperlipidemic rats may be owing to rapid consumption and exhaustion of storage of these enzymes in fighting free radicals produced during the development of obesity. Thisobservation are unison withpast studies [38,39] who demonstrated that obesity is an autonomousdangerous factor for increasing lipid peroxidation and decreased activity of cytoprotective enzymes. Some researchers declared that consuming a diet with high fat calories result in down regulation of antioxidant vitamin (β- carotene and α -tocopherol) levels and several key antioxidant enzymes: Catalase, superoxide dismutases, glutathione peroxidase, heme oxidase [40]. Obesity can cause progressive and cumulative cell injury resulting from pressure of the large body mass, cell injury produces the liberation of cytokines, especially tumor necrosis factor alpha (TNF-a) which generates reactive chemical species (ROS) from the tissues that leading to lipid peroxidation [41]. Dyslipidemic changes occur in obesity could be owing to the increased triacylglycerol concentration in the liver owing to the increased influx of excess NEFAs into the liver [42]. Increase of LDL-C in high-cholesterolemic animalsprobably caused by the reduction in the binding capacity of LDL to its receptor or reduction in its receptor numbers [43]. The observed hypertriglyceridemia might be related to the increased triglycerides formation or absorption after giving a diethigh in fat or through higher production of hepatic very low density lipoprotein (VLDL) and reduced the uptake of triglyceride in peripheral tissues [44]. Additionally, increased dietary cholesterol absorption from the small intestine could bea possible mechanism for the high level of serum cholesterol following the HFD intake [45]. For explaining the metabolic cause of decreasing the blood HDL-C in rats given HFD, [46] proposed that HFD may cause the stimulation of the hepatic lipoprotein lipase and endothelial lipase enzymes that accelerates the hydrolysis of HDL-C resulting in its low serum level. Preceding studies [47,48] are inconsistent with our findings. Feeding with enriched fat diet caused an elevation in the weight gain, this increase, perhaps due to the use of a high energy diet with saturated fats (lard) and its further accumulation in many body fat stores [49]. Alteration of lipid profile and increase of oxidative damageaccompanied with obesity leading to hepato-renal injuries that confirmed microscopically by hepatic macrovesicular lipid droplets and peritubular fatty change in renal tissue, similar observations were procured by [50,51].

In the current investigation, the dietary supplementation of overweight rats with spirulina or cinnamon extracts for 28 days decreased the oxidative damage produced by HFD via enhancement the levelsof antioxidant enzymes (CAT, SOD) or by suppression of lipid peroxidation products, the results were more obvious in the combined group of two extracts that might be owing to the synergistic effect of their antioxidant components. Spirulina contains several active ingredients, particularly phenolic acids, phycocyanin, phycocyanobilin, and β-carotene, all of which show promise antioxidant activity [52,53]. Cinnamate is a phenolic compound present in cinnamon bark that accountable for its protective action andthe activation of antioxidant enzymes. The antioxidant action of cinnamate is fundamentally due to its redox effects and maycausedifferent mechanisms, as: free-radical scavenging activity, transition-metal-chelating and singlet-oxygen-quenching capacity [54]. Our findings are concomitant with the data reported by [55,56] who demonstrated the efficacy of spirulina treatment in ameliorating the antioxidant defense of experimental animals with suppressive effect on lipid peroxides accumulation and oxidative injury caused by high cholesterol diet. Concerning cinnamon, Hypercholesterolemic rats received oral dose of cinnamon extract (20mg/day) for 6 weeks showed lower levels of hepatic MDA concentration, meanwhile, the activity of SOD and CAT enzymes in hepatic tissue were elevated significantly relative to group kept without treatment [57]. Improvement of lipid profile picture upon using plant extracts was noticed in this investigation that reflect the protective actionof both spirulina and cinnamon against obesity induced lipid metabolism abnormalities. However, the best findings were recorded in the combination group, suggesting the interaction of their active components to restore the lipid profile changes near to normal level. These results are compatible with [58,59] for spirulina and with [60,61] for cinnamon. The lipid lowering mechanism of spirulina may be owing to its potential to provoke the activity of lipoprotein lipase enzyme that hydrolyzes triglyceride to release F. As which can be utilized or stored [62]. Recently, it was reported that C-phycocyanin derived from spirulina produced hypocholesterolemic activity in rats where it binds to bile acids in the jejunum, this binding suppresses the absorption of cholesterol by influence on its micellar solubility [63]. Also,β-carotene and linolenic acids present in this algaelowersplasma triacylglycerol and inhibits the synthesis of hepatic fatty acids in hyperlipidemic rats [64,65]. Moreover, few previous

studies proposed that the amounts of carbohydrate and dietary fiber in spirulina are able to cause cholesterol lowering effect by increasing thebile acid pool size and fecal steroid excretion [66,67]. Another studysuggested the capacity of spirulina aqueous extract to activate lecithin cholesterol acyl transferase (LCAT) enzyme [26]. LCAT has a major role in the incorporation of free cholesterol into HDL and its transfer back to VLDL and LDL, which are later returned in liver cells andthus reducing the cholesterol level [68]. Correlating with such improvement in lipid profile, the hypolipidemic effect of cinnamon, possibly related to suppression of the hepatic HMG Co-A reductase activity causingthe decrement of cholesterol content in the liver [69]. It was shown that cinnamon water extract regulate lipid metabolism through the stimulation of PPAR γ and α (Peroxisome Proliferator-Activated Receptors) mRNA expression in the liver resulting in lower serum lipids and elevated plasma HDL-C [70]. Liver PPARα expression increased the cellular uptake of fatty acids liberated from fat tissues [71], it also increase the expression of the lipoprotein lipase gene and reduce the expression of the gene encoding for apo-C, which is an inhibitor of lipoprotein lipase producing antihyperlipidemic action [72]. According to [73], the polyphenols content of cinnamon may inhibit the absorption of cholesterol from the intestine, thus reducing itslevel in the serum of experimental animal models. Suppression of weight gain by spirulina or cinnamon recorded in this search are relevant to those of [74,75]. These favorable effects supporting the relief of histopathological alterations noticed in the treatment plant groups. Theobservable body weight decrease in obese rats received a cinnamon extract supposedly for its role in reducing the level of serum leptinhormone [76]. In this concern, [77] mentioned that leptin is a peptide hormone released from adipose tissue into the blood in proportion to its mass. It exert its effect on the brain to regulate food intake and energy expenditure. When body fat mass decreases, the plasma leptin levels decrease so prompting the appetite and inhibiting energy expense till fat mass is restored.

References

1. McGuire S. (2012) Accelerating progress in obesity prevention: solving the weight of the nation. Washington, DC: the national Academies press, Adv. Nutr.,3: 708-709.
2. Sowers J. R. (2003) Obesity as a cardiovascular risk factor, Am. J. Med., 115: 37-41.
3. Caballero A. E. (2003) Endothelial dysfunction in obesity and insulin resistance. A road to diabetes and heart disease. Obes. Res.,11: 1278-1289.
4. Delbosc S, Palzanis E, Magous R, Araiz C, Cristol J P, Cros G amd Azay J. (2005) Involvement of oxidative stress and NADPH oxidase activation in the development of cardiovascular complications in a model of insulin resistance, the fructose -fed rat. Atherosclerosis, 179 (1): 43-49.
5. Mayer M. A., Hocht C, Puyo A, Taira C. A. (2009) Recent advances in obesity pharmacotherapy. Curr. Clin. Pharmacol., 4:53–61.
6. Sapp J. (2005) The prokaryote-eukaryote dichotomy: meanings and mythology. Microbiol. Mol. Biol. Rev., 69:292–305.
7. Khan Z, Bhadouria P, Bisen P. S. (2005) Nutritional and therapeutic potential of Spirulina. Current Pharmacology and Biotechnology, 6: 373.
8. Hoseini S. M., Khosravi-Darani K. and Mozafari M. R. (2013) "Nutri-tional and medical applications of spirulina microalgae,"Mini-Reviews in Medicinal Chemistry, vol.13, no.8, pp. 1231–1237.
9. Soheili M. and Khosravi-Darani K. (2011) The potential health benefits of algae and micro algae in medicine: a review on Spirulina platensis. Curr. Nutr. Food Sci., 27(4):279–285.
10. Ngo-Matip M. E., Pieme C. A., Azabji-Kenfack M., Moukette Moukette B., Korosky E., Stefanini P., Yonkeu Ngogang J., Mbofung C. M. (2015) Impact of daily supplementation of Spirulina platensis on the immune system of naïve HIV-1 patients in Cameroon: a 12-months single blind, randomized, multicenter trial. Nutr. J.,14:70.
11. Deng R. and Chow T. J. (2010) Hypolipidemic, antioxidant and antiinflammatory activities of microalgae Spirulina. Cardiovasc Ther., 28(4): 33–45 .
12. Bhat V. B. and Madyastha M. (2001) Scavenging of peroxynitrite by phycocyanin and phycocyanobilin from Spirulina platensis: protection against oxidative damage to DNA. Biochem. Biophys. Res. Commun., 285:262–266.
13. Ou Y., Zheng S., Lin L., Jiang Q. and Yang X., (2010) Protective effect of C-phycocyanin against carbon tetrachloride-induced hepatocyte damage in vitro and in vivo. Chem. Biol. Interact., 185(2): 94–100.
14. Ming-Jyh S., Yao-Yuan H., Ching-Hsiu L., Chi-Chen C. and Chieh-Hsi W. (2013) Antihyperlipidemic and antioxidant effects of C-phycocyanin in Golden Syrian Hamsters fed with a hypercholesterolemic diet. J. Tradit. Complement Med., 3(1): 41–47.

15. Ismail M. F., Ali D. A., Fernando A., Abdraboh M. E. and Gaur R. L., et al. (2009) Chemoprevention of rat liver toxicity and carcinogenesis by Spirulina. Int. J. Biol. Sci., 5: 377–387.
16. Qin B., Nagasaki M., Ren M., Bajotto G., Oshida Y. and Sato Y. (2003) Cinnamon extract (traditional herb) potentiates in vivo insulin-regulated glucose utilization via enhancing insulin signal in ginrats. Diabetes Res. Clin. Pract., 62: 139-148.
17. Vangalapati M., Sree Satya N., Surya Prakash D. and Avani-gadda S. (2012) A review on pharmacological activities and clinical effects of cinnamon species. Research Journal of Pharmaceutical, Biological and Chemical Sciences, 3 (1): 653–663.
18. Chou S-T., Chang W-L., Chang C-T., Hsu S-L., Lin Y-C. and Shih Y. (2013) Cinnamomum cassia Essential Oil inhibits □-MSH-induced melanin production and oxidative stress in murine B16 melanoma cells. International Journal of Molecular Sciences, 14 (9): 19186–19201.
19. Moselhy S. S. and Ali H. K. (2009) Hepatoprotective effect of cinnamon extracts against carbon tetrachloride induced oxidative stress and liver injury in rats. Biol. Res., 42: 93-98.
20. Azab K. S. h., Mostafa A. H., Ali E. M. and Abdel-Aziz M. A. (2011) Cinnamon extract ameliorates ionizing gradiation-induced cellular injury in rats. Ecotoxicol Environ Saf., 74: 2324-2329.
21. Vafa M., Mohammadi F., Shidfar F., Sormaghi M. S., Heidari I. and Golestan B., et al. (2012) Effects of cinnamon consumption on glycemic status, lipid profile and body composition in type 2 diabetic patients. Int. J. Prev. Med., 3: 531-536.
22. Lee S. C., Xu W. X., Lin L. Y., Yang J. J. and Liu C. T. (2013) Chemical composition and hypoglycemic and pancreas-protective effect of leaf essential oil from indigenous cinnamon (Cinnamomum osmophloeum Kanehira). J. Agric. Food Chem., 61: 4905-4913.
23. Kreydiyyeh S. I., Usta J. and Copti R. (2000) Effect of cinnamon, clove and some of their consti-tuents on the Na+-K+-ATPase activity and alanine absorption in the rat jejunum. Food Chem. Toxicol., 38 (9):755-762.
24. Bhatt B. A., Dube J. J., Dedousis N., Reider J. A. and O'Doherty R. M. (2006) Diet induced obesity and acute hyperlipidemia reduce Ikappa B alpha levels in rat skeletal muscle in a fiber-type dependent manner. Am. J. Physiol. Regul. Integr. Comp. Physiol., 290: 233-240.
25. Ghasi S., Nwobodo E. and Ofili J. O. (2000) Hypocholesterolemic effects of crude extract of leaf of Moringa oleifera Lam in high-fat diet fed wistar rats. Journal of Ethnopharmacology, 69: 21 – 25.
26. Ama Moor V. J., Nya Biapa P. C., Nono Njinkio B. L. and Moukette Moukette B., et al. (2017) Hypolipidemic effect and activation of Lecithin Cholesterol Acyl Transferase (LCAT) by aqueous extract of Spirulina platensis during toxicological investigation. BMC Nutrition, 3-25.
27. Mahmood S., Talat A., Karim S, Khurshid R. and Zia A. (2011) Effect of Cinnamon extract on blood glucose level and lipid profile in alloxan induced diabetic rats. Pak. J. Physiol., 7(1): 13-16.
28. Finley P. R., Schifman R. N., Williams R. J. and Lichti D. A. (1978) Cholesterol in high-lipoprotein: use of Mg+2/ dextran sulfate in its enzymatic measurement. Clin. Chem. Jun., 24: 931-933.
29. . Wohlefeld A. W. (1974) Quantitative enzymatic calorimetric determination of triglycerides in serum or plasma. Methods of Enzymatic Analysis. Vol.5, Bergmeyer Ed., Academic Press. New York.
30. Warnick G. R., Benderson V. and Albers N. (1983) Estimation of HDL-cholesterol. Selected Methods. Clin. Chem., 10: 91-99.
31. Friedewald W. T., Levy R. I. and Fredrickson D. S. (1972) Estimation of the concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. Clin. Chem., 18(6): 499:502.
32. Ohkawa H., Ohishi I. and Yagi E**.** (1979) Assay for lipid peroxides in animal tissues by thiobarbitturic acid reaction. Anal. Biochem., 95:351-358.
33. Kakkar P., Das B. and Viswanathan P. N. (1984) A modified spectrophotometry assay of superoxide dismutase. Indian J. Biochem. Biophys.,21: 130-132.
34. Aebi (1984) Catalase in vitro. Meth. Enzymol., 105:121-130.
35. Suvarna S. K., Layton C. and Bancroft J. D. (2013) Bancroft's Theory and Practice of Histological Techniques. Elsevier, Churchill Livingstone.
36. Duncan D. B. (1995) Multiple ranges andmultiple F-test. Biometric, 11:1– 42.
37. Keaney J. F., Larson M. G., Vasan R. S., Wilson P. W. F., Lipinska I. and Corey D., et al. (2003) Obesity and systemic oxidative stress: clinical correlates of oxidative stress in the Framingham study. Arterioscler. Thromb. Vasc. Biol., 23: 434.

38. Valdecantos P., Matute P. and Martínez A. (2009) Obesity and oxidative role of antioxidants supplementation. Rev. Invest. Clin., 61:127.
39. Noeman S. A., Hamooda H. E. and Baalash A. A. (2011) Biochemical study of oxidative stress markers in the liver, kidney and heart of high fat diet induced obesity in rats. Diabetology & Metabolic Syndrome, 3:17
40. Roberts C. K., Barnard J., Sindhu R. K., Jurezak M., Ehdaie A. and Vaziri N. D. (2006) Oxidative stress and dysregulation of NADPH oxidase and antioxidant enzymes in diet-induced metabolic syndrome. Metabolism, 55: 928-934.
41. Lachieitner M., Koch T., Harold M., Dzien A. and Hoppiahler F. (2000) Tumour necrosis factor-alpha plasma level in patients with type 1 diabetes mellitus and its association with glycaemic control and cardiovascular risk factors. J. Intern. Med., 248:267.
42. Fried M., Hainer V., Basdevant A., Buchwald H. and Dietel M., etal. (2008) Inter-disciplinary European guidelines on surgery for severe obesity. Rozhl. Chir.,87:468-468.
43. Amin K. A. and Abd El-Twab T. M. (2009) Oxidative markers, nitric oxide and homocysteine alteration in hypercholesterolimic rats: role of atorvastatine and cinnamon. Int. J. Clin. Exp. Med., 2: 254-265.
44. Srinivasan K., Patole P. S., Kaul C. L. and Ramarao P. (2004) Reversal of glucose intolerance by pioglitazone in high-fat diet fed rats. Methods Find Exp. Clin. Pharmacol., 26: 327–333.
45. Colca J. R., Dailey C. F., Palazuk B. J., Hillman R. M., Dinh D. M. and Melchior G. W., et al. (1991) Pioglitazone hydrochloride inhibits cholesterol absorption and lowers plasma cholesterol concentrations in cholesterol fed rats. Diabetes, 40:1669–1674.
46. Broedi U. C., Jin W., Marchadier D., Secreto A. and Rader D. J. (2005) Tissue- specific expression pattern of human endothelial lipase in transgenic mice. Atherosclerosis, 181: 271-274.
47. Woo M. N., Bok S. H., Lee M. K., Kim H. J., Jeon S. M., Do G. M., Shin S. K., Ha T. Y. and Choi M. S. (2008) Anti-obesity hypolipidemic effects of a proprietary herb fiber combination (S & S PWH) in rats fed high-fat diets. J. Med. Food, 11:169-78.
48. Kamal A. A. and Mohamed A. N. (2009) Effect of Carnitine and herbal mixture extract on obesity induced by high fat diet in rats. Diabet & Metab. Synd., 1:1-17.
49. Srinivasan K., Patole P. S., Kaul C. L. and Ramarao P. (2004) Reversal of glucose intolerance by pioglitazone in high-fat diet fed rats. Methods Find Exp. Clin. Pharmacol., 26:327–333.
50. Meli R., Mattaco Raso G., Irace C., Simeoli R. and Di Pascale A., et al. (2013) High fat diet induces liver steatosis and early dysregulation of iron metabolism in rats. PLOS ONE (Public Library of Science), 8(6): e66570.
51. Altunkaynak M. E., Özbek E., Altunkaynak B. Z., Can I., Unal D. and Unal B. (2008) The effects of high-fat diet on the renal structure and morphometric parametric of kidneys in rats. J. Anat., 212: 845–852.
52. Karadeniz A., Yildirim A., Simsek N., Kalkan Y. and Celebi F. (2008) Spirulina platensis protects against gentamicin-induced nephrotoxicity in rats. Phytotherapy Res., 22: 1506-1510.
53. Guan X. Y., Zhang W. J., Zhang X. W. and Li Y. X. (2009) A potent antioxidant property: fluorescent recombinant alpha-phycocyanin of Spirulina. Appl. Microbiol., 106: 1093-1100.
54. Lee J. S., Jeon S. M., Park E. M., Huh T. L., Kwon O. S., Lee M. K. and Choi M. S. (2003) Cinnamate supplementation enhances hepatic lipid metabolism and anti-oxidant defense systems in high cholesterol-fed rats. J. Med. Food, 6(3): 183-191.
55. Kim M. Y., Cheong S. H. and Lee J. H., et al. (2010) Spirulina improves antioxidant status by reducing oxidative stress in rabbits fed a high-cholesterol diet. J. Med. Food, 13(2):420–426.
56. Muga M. A. and Chao J. C. (2014) Effects of fish oil and spirulina on oxidative stress and inflammation in hypercholesterolemic hamsters. BMC Complement Altern. Med., 14:470.
57. Amin K. A. and Abd El-Twab T. M. (2009) Oxidative markers, nitric oxide and homocysteine alteration in hypercholesterolimic rats: role of atorvastatine and cinnamon. Int. J. Clin. Exp. Med., 2: 254-265.
58. Colla L M, Muccillo-Baisch A L, Vieira Costa J A. Spirulina platensis effects on the levels of total cholesterol, HDL and triacylglycerols in rabbits fed with a hypercholesterolemic diet. Brazilian Arch. Biol. Technol., 2008; 51: 405-411.
59. Cheong S H, Kim M Y, Sok D E, Hwang S Y, Kim J H, Kim H R, et al. Spirulina prevents atherosclerosis by reducing hypercholesterolemia in rabbits fed a high-cholesterol diet. J. Nutr. Sci. Vitaminol.2010; 56: 34–40.
60. Neveen S I. Protective Effects of Aqueous Extracts of Cinnamon and Ginger Herbs Against Obesity and Diabetes in Obese Diabetic Rat. World Journal of Dairy & Food Sciences. 2014; 9 (2): 145-153.

61. Gehan F A, Mohamed K Y, Hala M M. Phytochemical Evaluation, Anti-obesity and Antihyperlipidemic Effects of Combined Administration of Green Coffee, Cinnamon and Ginger. Plant. 2017; 5(5): 80-84.
62. Iwata K, Inayama T, Kato T. Effects of Spirulina platensis on plasma lipoprotein lipase activity in fructose-induced hyperlipidemic rats. J Nutr Sci Vitaminol (Tokyo). 1990; 36(2):165–171.
63. Nagaoka S, Shimizu K, Kaneko H, Shibayama F, et al. Novel protein C-phycocyanin plays a crucial role in the hypocholesterolemic action of Spirulina platensis concentrates in rats. J. Nutr.2005;135: 2425-2430.
64. Seo J S, Lee K S, Jang J H, Quan Z, Yang K M, Burri B J. The effect of dietary supplementation of β-carotene on lipid metabolism in streptozotocin-induced diabetic rats. Nutr. Res. 2004; 24: 1011-1021.
65. Kim H K, Chois S, Choi H. Suppression of hepatic fatty acid synthesis by feeding –linolenic acid rich perilla oil lowers plasma triacylglycerol level in rats. J. Nutr. Biochem. 2004; 15: 485-492.
66. Dvir I, Chayoth R, Sod- Moriah U, Shany S, Nyska A, Stark A H, Madar Z, Arad S M. Soluble polysaccharide and biomass of red microalgae porphyridium sp alter intestinal morphology and reduce serum cholesterol in rats. Br J nutr. 2000; 84: 469-476.
67. Palmer G H, Dixon D G. Effect of pectin dose on serum cholesterol levels. Am J Clin Nutr. 1996; 18: 437-442.
68. Boque N J, Campion J, de la Iglesia R, de la Garza A G, Milagro F I. Screening of polyphenolic plant extracts for anti-obesity properties in Wister rats. Journal of Science and Food Agriculture, 2013; 93(5): 1226-1232.
69. Lee J S, Jeon S M, Park E M, Huh T L, Kwon O S, Lee M K, et al. Cinnamate supplementation enhances hepatic lipid metabolism and antioxidant defense systems in high cholesterol fedrat. J. Medicinal Food. 2003; 6(3): 183-191.
70. Sheng X, Zhang Y, Gong Z, Huang C, Zang Y Q. Improved Insulin Resistance and Lipid Metabolism by Cinnamon Extract through activation of Peroxisome Proliferator-Activated Receptors. PPAR Research. 2008; 581348.
71. Kersten S, Seydoux J, Peters J M, Gonzalez F J, Desvergne B, Wahli W. Peroxisome proliferator-activated receptor alpha mediates the adaptive response to fasting. J. Clin. Invest. 1999;103: 1489-1498.
72. Staels B, Dallongeville J, Auwerx J, Schoonjans K, Leitersdorf E, Fruchart J C. Mechanism of action of fibrates on lipid and lipoprotein metabolism. Circulation.1998; 98: 2088-2093.
73. Shatwan I A, Ahmed L A, Badkook M M. Effect of barley flour, crude cinnamon and their combination on glycemia, dyslipidemia and adipose tissue hormones in type 2diabetic rats. Journal of Medicinal Food. 2013; 16(7): 656-662.
74. Couturier K, Batandier C, Awada M, Canini F, Roussel A M. Cinnamon improves insulin sensitivity and alters the body composition in an animal model of the metabolic syndrome. Archive of Biochemistry and Biophysics. 2010; 501(1): 158-161.
75. Balasubramanian V, Swetha B, Md. Gayasuddin, Samreen S. Antiobesity activity of spirulina platensis in high fat diet induced rats. International Journal of Pharmacological Screening Methods. 2013; 3(1): 1-5.
76. Neveen S I. Protective effects of aqueous extracts of cinnamon and ginger herbs against obesity and diabetes in obese diabetic rat. World Journal of Dairy & Food Sciences.2014; 9 (2): 145-153.
77. Friedman J M. Leptin and the regulation of body weight. The Keio Journal of Medicine. 2011; 60: 1-9.

7/17/2018