

## **Comparative Study between the Effect of Ginger and Cinnamon Aqueous Extracts and their Mixtures on Hyperlipidemic Rats**

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### **Abstract**

This study was performed to comparing the effect of different levels of ginger and cinnamon extracts and their mixture on Hyperlipidemic rats. Sixty six adult albino rats were divided into eleven groups (6 rats each group). Group1: Negative control group fed on standard diet, group 2: Positive control group fed on high fat diet (HFD). Group: 3, 4 and 5 the rats fed on high fat diet (HFD) containing 200mg, 300mg and 400mg/100g diet ginger water extracts concentrated (Con). Group: 6, 7 and 8 the rats fed on HFD containing 200, 300 and 400mg cinnamon water extracts Con.. Group: 9, 10 and 11 the rats fed on HFD containing mixture (100mg ginger+100mg cinnamon extracts Con.), (150 mg ginger + 150mg cinnamon extracts Con.) and (200mg ginger+200mg cinnamon water extracts Con.) for 8 weeks. The aqueous extract of ginger and cinnamon are containing 1.21 mg/g and 1.15 mg /g total phenolic compounds. Meanwhile total flavonoids were 0.38 mg/g and 0.41 mg/g of ginger and cinnamon water extracts. Cinnamon extract contained high level sinapic acid ( $59.22 \pm 03 \mu\text{g/g}$ ) meanwhile ginger extract have high concentration of zingerone ( $33.28 \pm 0.01 \mu\text{g/g}$ ). The results showed that all treatment after 8 weeks caused a significantly decrease of triglycerides (TG), total cholesterol (TC), low density lipoprotein (LDL), very low density lipoprotein (VLDL) and atherogenic index (AI). The high level (400 mg) of cinnamon water extract showed a significantly decrease of TG, TC, LDL, VLDL and AI ( $67.33 \pm 7.9$ ,  $144 \pm 7.2$ ,  $99.67 \pm 5.8$ ,

13.5±1.5 mg/dl and 0.36± 0.04) respectively more than ginger water extract (78.83±10.7, 154.17±20.1, 123.5±15.5, 15,8±2.1mg/dl and 0.44±0.05) respectively. Urea and in creatinin hyperlipidemic rat was a significant increased  $P\leq 0.05$  in contract to antioxidant enzymes were revealed a significantly decrease compared to negative control group. High concentration of cinnamon extract (400 mg) showed the highest decrease in urea (30.83±6.05 mg/dl) and aspartate amino transferase AST (22.33±1.63 IU/L) and the highest increase in superoxide dismutase (SOD) activity (0.23±0.01 IU/L). **Conclusion:** Using cinnamon and ginger extracts for 8 weeks have beneficial effects to reduced serum lipid profile in hyperlipidemic rats. The high concentration of cinnamon extract had hypolipidemic effect more than ginger extract because its content high levels of cinnamic acid and cinapic acid which have antioxidant effects. The present study recommended that the admenstration of cinnamon water extract when consuming high fat diet.

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**Key words:** Serum lipid profile, Phenolic compounds, Antioxidant enzyms, Histopathology, Liver enzymes.

### Introduction

Hyperlipidemia is defined as an excess of any or all lipid profile and/or lipoproteins in the blood (**National Institute Health, 2018**). Diets contain too much cholesterol and fat, low activity, smoking and obesity are risk factors of hyperlipidemia (**Nouh et al., 2019; Mouhamed and Najjar, 2013; Mozaffrian et al., 2016**). Other factors which contribute to raise cholesterol levels and development of hyperlipidemia such as age and gender, diuretics drugs,  $\beta$ -blockers and medicines used to treat depression (**Lipman et al., 2000**).

The prevalence of hyperlipidemia in men was higher than women in southwestern China. The men suffered from hyperlipidemia represent 53.6% while the women 44.7% (**Deng et al., 2012**). There are 19.4 % of Egyptian populations suffering from hyperlipidemia According to Egyptian Ministry of Health, (2006). In Egypt, hyperlipidemia is slightly increased in chronic hepatitis C

(**Ghassanf, 2014**), 32% from patients dyslipidemia in Egypt had elevated LDL-C levels (**El Etriby et al., 2013**). The overall prevalence of dyslipidemia among apparently healthy Fayoum University students was 63.8% of hypercholesterolemia, 38.8%, of hypertriglyceridemia and 33.1% of LDL-C (**Abdel Wahed et al., 2016**).

The main stages for management of hyperlipidemia include medical, nutritional and lifestyle modifications (**Nouh et al., 2019**). Medicinal plants and their constituents have long been recognised for their potential role in illness management through biological activity modulation (**Ma et al., 2021**). Catechins and other active component in functional food have potentially reduce serum lipid profile and improve hyperlipidemia and cholesterol lower in liver (**Zhang et al., 2002**) and **Bursill et al., 2007**).

Cinnamon (*Cinnamomum zeylanicum*), is an herbaceous plant, belonging to the Lauraceae family. Cinnamon is one of the most popular spices used worldwide as spice and condiments for food flavoring and in medicinal mixtures for their physiological effects (**Dasanayaka, 2019**). Different studies have reported cinnamon is safe when consuming and have more pharmacological effects like, antimicrobial, antioxidant, anti-inflammatory, and effective in lowering lipid levels (**Ashraf et al., 2013; and Sathya et al., 2014 and Blaszczyk et al., 2021**), anticandidial, antiulcer, analgesic and memory improvement (**Quin et al., 2010 and Rawat et al., 2020**). Different Polyphenols isolated from cinnamon like cinnamaldehyde and eugenole this main compounds have antioxidant effect and various biological activities (**Weerasekera et al., 2021**).

Ginger (*Zingibe officinale*) is rich bioactive phenolics such as zingerons, gingerols and shogaols which are nonvolatile pungent chemical (**Bhattarai et al., 2018**). 6-gingerol is well-known for its anti-inflammatory and antioxidant capabilities, as well as a variety of medicinal qualities (**Suciyati, 2021**). Ginger root is used to treat a variety of ailments, including pains, colds, nausea, and emesis. Many bioactive components in ginger, such as phenolic and terpene compounds, have been found **Mao et al., (2019)**. High levels of lipid is associated with cardiovascular disease and stroke so, lipid

lowering drugs used to reduces the levels of lipid. Many of synthetic drugs used to treat hyperlipidemic are side effects potential including muscle pain, liver enzyme increases and fatigue (Muscari et al., 2002), while herbal medicines are effective in decrease the toxicities and safe. Therefore, the current work aims to conducte a comparative study between the effect of ginger and cinnamon aqueous extracts and their mixtures on hyperlipidemic rats.

## **Materials and Methods**

### **Materials**

Raw Ginger and Cinnamon were purchased from local market in El-Fayoum city (Egypt). All chemicals were obtained from El-Gomhoriya Company for Trading Drugs, Chemicals and Medical Instruments, Egypt; Bile salts were obtained from Sigma Company, USA. Soybean oil was obtained from Sila Company, Egypt; kits were purchased from Biodiagnostic Company, Dokki, Giza, Egypt.

### **Methods**

#### **Preparation of cinnamon and ginger aqueous extracts**

Cinnamon and ginger a aqueous extracts were prepared according to Rout et al., (2015) as Follows: Tow hundred grams of either cinnamon or ginger powder were soaked in one liter of distilled water and kept in room temperature for 3 hours, then heated at 60-65 °C for 30 minutes .The extracts were then left to cooling and filtered using muslin cloth, and filtered again with Whatman Filter No. 1. Rotary Evaporator (HS- 2005S Hahnshhin Scientific Korea) was used to remove the excess of water from extract under pressure with heating at 55 °C for evaporate one liter to 100g concentrated.extract The extract stored in refrigerate at 4°C until use.

#### **Chemical analysis of cinnamon and ginger powders**

Moisture content, crude fiber, oil and ash were determined according to the methods described by A.O.A.C., (2000) Protein of cinnamon and ginger powder was determined according to the methods described by A.O.A.C., (2010).Determined of total carbohydrates were calculated by the difference.

### **Chemical analysis of cinnamon and ginger aqueous extracts**

Total carbohydrate of cinnamon and ginger aqueous extracts was determined using colorimetric method by Phenol–Sulfuric Acid method according to the method described by **DuBois et al., (1956)**. Total lipid and soluble proteins in aqueous extracts were determined by **Bligh and Dyer, (1959)** and **Bradford, (1976)**. Moisture content, crude fibers were determined according to the methods described by **A.O.A.C., (2000)**.

### **Total phenols and total flavonoids of cinnamon and ginger powder and aqueous extracts**

Total phenols content of cinnamon and ginger, powders and aqueous extracts, were determined using Spectrophotometer uv\vis `Analytik jena Spectro D250 Germany according to the procedure described by **Kaur and Kapoor, (2002)**. Total flavonoids in powder and aqueous extracts were determined using aluminum chloride colorimetric method according to **Whisky and Salatino, (1998)**

### **HPLC analysis of phenolic compounds in cinnamon and ginger aqueous extracts**

Identification of phenolic compounds was analyzed by **Hung and Morita (2008)**. HPLC analysis was carried out using an Agilent 1260 series. The separation was carried out using Eclipse Plus C18 column (4.6 mm x 250 mm i.d., 5 µm). The mobile phase consisted of water (A) and 0.02% tri-floro-acetic acid in acetonitrile (B) at a flow rate 1 ml/min. The mobile phase was programmed consecutively in a linear gradient as follows: 0 min (80% A); 0–5 min (80% A); 5-8 min (40% A); 8-12 min (50% A); 12-14 min (80% A) and 14-16 min (80% A). The injection volume was 10 µl for each of the sample solutions. The column temperature was maintained at 35 °C. The peaks of all components were detected at 280nm. Peak area and retention time were used to calculation phenolic compounds concentration.

### **Experimental design**

The study was performed on total number of sixty six adult Albino rats weighting (120-140g) were obtained from Animal House, Food Technology Research Institute Agriculture Research Center-Giza. The animals housed in polypropylene cages at ventilated room temperature with natural day night cycle. The

animals were distributed into eleven different groups with six animals in each group.

Group 1: Normal control group (negative control) fed on basal diet preparation according to AIN-93M by **Reeves et al., (1993)** as Followes: 14% Casein, 10% sucrose, 1% vitamin mixture, 5% fiber, 3.5% mineral mixture, 1.8 L-Cystine, 0.25% choline bitartrate, 4% soybean oil (no additives) and the remainder was starch. vitamin and salts were preparation according to **Reeves et al., (1993)** Group 2: hyperlipidemic group (positive control group) fed on high fat diet (16% saturated fat (Sheep tail fat), 1% cholesterol and 0.25 % cholic acid according to **Harnafi et al., (2009)**. Group (3,4,5): fed on high fat diet containing 200, 300 and 400mg ginger extract concentrated /100g diet. Group (6,7,8): fed on high fat diet containing 200, 300 and 400 mg cinnamon extract concentrated/ 100g diet. Group (9,10,11): fed on high fat diet containing concentrated mixture (100 mg ginger extract+ 100 mg Cinnamon extract/ 100g diet), (150 mg ginger extract+ 150 mg Cinnamon extract/ 100g diet) and (200 mg ginger extract + 200 mg Cinnamon extract/ 100g diet).

At the end of the experimental period (8 weeks), blood samples withdrawn by heparinized capillary tube from the retro orbital plexus of each rat under anesthesia with diethyl ether, then centrifuged at 3000 rpm for 15 min to separate serum ,which stored at - 20 °C until biochemical analysis.

#### **Determination of serum lipids profile**

Total cholesterol (TC), Triglycerides (TG), high density lipoprotein (HDL-Cholesterol), low density lipoprotein (LDL-Cholesterol) of serum were determined with enzymatic colorimetric method according to **Allain, (1974); Fossati and Prenape, (1982); Lopez-Virella et al., (1977 ) and Wieland and Seidel (1983)**. Very low density lipoprotein (VLDL-Cholesterol) was calculated according the **Friedewald et al (1972)**. Athergenic index (AI) was calculated according to **Dobiasova and Frohlich, (2001)** by the following equation:

$$AI = \text{Log (TG/HDL)}$$

$$VLDL = TG/5$$

### **Liver enzymes**

Alanine amino transaminase (ALT) and aspartate amino transferase (AST) were determined by the method of **Young and Woodside (2001)**.

### **Determination of kidneys functions**

Urea, creatinine and uric acid were determined with colorimetric endpoint method according to **Barham and Trinder (1972)**.

### **Antioxidant enzymes activity**

Catalase (CAT), glutathione reductase (GSH), superoxide dismutase (SOD) and glutathione peroxidase (GPX) were determined using colorimetric method according to **Aebi, (1984); Goldberg and Spooner, (1983; Wheeler et al.,(1990) and Paglia and Valentine, (1967) respectively.**

### **Histological examination**

Liver and kidneys were fixed in 10% buffered formalin until analysis. Tissue of liver and kidney were processed for paraffin embedding and sections was prepared and stained with hematoxylin and eosin (using light microscopy). Histopathological assessment was performed of control and treatments groups according the method described by **Luna (1968)**.

### **Statistical analysis**

The statistical analysis of obtained data was conducted using one way analysis of variance technique followed by Duncans multiple range test. The significance of difference among means was evaluated by least significant differences (L.S.D) method at two levels of significant:  $P>0.01$  and  $P>0.05$  was non significant while  $P<0.05$  is a significant. The results were expressed as Mean  $\pm$ SD according to **Snedecor and Cochran (1967)**. A DELL computer with a software system SPSS version 22 was used for these calculations.

### **Results and Discussion**

#### **Chemical analysis of cinnamon and ginger powders**

Chemical composition of cinnamon and ginger powder is shown in Table (1). The highest percentage of moisture was

(10.7%) and crude fiber (26.24%) of cinnamon powder. While the highest percent of protein (9.6%), carbohydrates (69.38%) and oil (3.04) were recorded to ginger.

Previous studies by (Khan et al., 2016); Gul and Safdarm 2009) reported that the percent protein in ginger and cinnamon ranged (9% - 35%) while (60-70% and 52% carbohydrate and (3-6% and 4% oil) and (4%- 2.4% ash) respectively.

**Table (1): Chemical composition of ginger and Cinnamon powder (on dray weight basis %)**

Constituents	Ginger (g/100g dw)	Cinnamon (g/100g dw)
Moisture	9±0.19	10.7±0.27
Ash	5±0.13	2.6±0.17
Crude protein	9.6±0.16	3.6±0.29
Crude fiber	3.98±0.55	26.24±3.67
Crude oil	3.04±0.01	1.95±0.02
Total carbohydrates	69.38±0.03	54.91±0.01

### **Chemical analysis of cinnamon and ginger aqueous extracts**

Chemical composition of ginger and cinnamon aqueous extracts is present in Table (2). The moisture content almost the same in ginger and cinnamon extract ranged from 94.45% to 95.45%. The highest value of crude protein and total carbohydrate were recorded for ginger extract (1.622% and 3%). The oil content of ginger and cinnamon extracts was found to be lower content (0.092% and 0.097% respectively). These results are according to our knowledge, present study is the first one determination of chemical analysis of cinnamon and ginger water extracts.

**Table (2): Chemical composition of ginger and cinnamon water extracts**

Constituents	Ginger water extract (%)	Cinnamon water extract (%)
Moisture	94.45±0.04	95.45±0.03
Crude protein	1.62±0.03	0.873±0.15
Crude fiber	0.836±0.17	1.58±0.38
Crude oil	0.092±0.03	0.097±0.03
Total carbohydrates	3.00±0.01	2.00±0.24

**Total phenols and total flavonoids of cinnamon and ginger (powder and aqueous extracts)**

Total phenolic and total flavonoids compounds of ginger and cinnamon powder and aqueous extract are shown in Table (3). The total phenols of cinnamon powder were more than total phenols of ginger powder. Total flavonoids of ginger powder were more than total flavonoids of cinnamon powder. Meanwhile, most content of total phenols was recorded of ginger aqueous extract, while total flavonoids were recorded to cinnamon aqueous extract. Previous studies have indicated that the aqueous extract of cinnamon and ginger contain higher concentration of total phenol and total flavonoid (Seidal et al., 2002).

**Table (3): Total phenols and flavonoids compounds of ginger, cinnamon powder and aqueous extracts**

Constituents	Ginger		Cinnamon	
	Powder	Aqueous extract	Powder	Aqueous extract
Total phenol (mg GAE/g)	5.75±0.37	1.21±0.04	10.79±0.92	1.15±0.13
Total flavonoids (mg QE/g)	1.29±0.15	0.38±0.07	1.10±0.08	0.41±0.06

GAE, gallic acid equavelant, QE, qurectin equavelant.

**Table (4): phenolic compound composition of ginger and cinnamon aqueous/aquatic extracts:**

Phenolic compounds	Ginger water extract (µg/g)	Cinnamon water extract (µg/g)
Chlorogenic acid	0.2589±0.005	-
Catachin	0.1239±0.005	-
Caffein	1.3939±0.001	-
Coffeic acid	0.2833±0.004	0.0867±0.006
Syringic acid	1.8312±0.003	0.0659±0.005
Coumaric acid	1.2578±0.007	0.0254±0.001
Vanilin	1.2022±0.006	0.0264±0.005
Ferulic acid	0.4024±0.004	-
Zingerone	33.2831±0.012	-
4'.7-Dihydroxyiso Flavone	1.9187±0.006	0.1699±0.001
Querectin	0.6806±0.003	0.2989±0.002
Cinnamic Acid	0.7777±0.001	11.2145±0.097
Sinapic acid	-	59.2233 ±0.031

#### **HPLC analysis of phenolic compounds in cinnamon and ginger aqueous extracts**

Amount of the different of phenolic compounds in ginger and cinnamon extracts by HPLC are presented in Table (4). Data revealed that the main phenolic compounds in cinnamon water extract were sinapic and cinnamic acids. Previous studies by **Klejdu and Kovacik, (2016)** whose reported that main phenolic compounds of cinnamon water extract was sinapic acid, cinnamic acid and other compounds. The present study revealed that ginger extract has different phenolic acid, the majority of them zingerone, 4'.7-Dihydroxyiso Flavone, Syringic acid, Caffeine, Coumaric acid and Vanilin. Also, the results by **Mao et al., (2019)** found that the phenolic compounds in ginger are mainly gingerols

#### **Effect ginger and cinnamon extracts consumption on body weight gain (BWG), feed intake (FI) and feed efficient ratio (FIR) of hyperlipidemic rats**

Data in Table (5) revealed that there was a significant increase  $P \leq 0.05$  of (BWG) of hyperlipidemic group (positive control) compared with negative control group. The increase BWG may be due to consume mor calories from fat lead to stored axcess on needs the body as fat within the fat cells and slowly accumulate over time

and results in wight gain. This study matched with a study conducted by **Amin and Nagy, (2009)**; **Mahmoud and Elnour, (2013)** they found that the rats fed on high fat diet for 6 weeks had a significant increase of body weight BWG compoared to rats fed on basal diet.

**Table (5): Effect of cinnamon and ginger aqueous extract on body weight gain, food intake and feed efficiency ratio of hyperlipidemic rats**

Group	Initianl body weight(g)	Final body weight (g)	Body weight gain (g)	Feed intake(g)	Feed efficient ratio(FER)
Control negative	123.6±8.4 <sup>a</sup>	156.8±8.2 <sup>b</sup>	33.2±5.3 <sup>c</sup>	97±0.89 <sup>a</sup>	0.33±.05 <sup>b</sup>
Control positive	121.25±9.4 <sup>a</sup>	193±18.9 <sup>a</sup>	71.7 ±25.1 <sup>a</sup>	90±3.28 <sup>a</sup>	0.79±.27 <sup>a</sup>
200mg ginger extract	129.25±11.01 <sup>a</sup>	169.5±6.2 <sup>ab</sup>	40.25±13.2 <sup>bc</sup>	95±0.89 <sup>a</sup>	0.42±.14 <sup>b</sup>
300mg ginger extract	121.8±10.1 <sup>a</sup>	170.8±10.3 <sup>ab</sup>	49±15.4 <sup>bc</sup>	95±1.89 <sup>a</sup>	0.51±.16 <sup>b</sup>
400mg ginger extract	123±11.2 <sup>a</sup>	169.6±10.2 <sup>ab</sup>	46.6± 13.3 <sup>bc</sup>	90±2.19 <sup>a</sup>	0.51±.14 <sup>b</sup>
200mg cinnamon extract	127.5±18.3 <sup>a</sup>	175.5±.19.4 <sup>ab</sup>	48±17.01 <sup>bc</sup>	96±1.67 <sup>a</sup>	0.49±.17 <sup>b</sup>
300 mg cinnamon extract	127±14.8 <sup>a</sup>	172±22.5 <sup>ab</sup>	45± 10.08 <sup>bc</sup>	95±0.63 <sup>a</sup>	0.47±.1 <sup>b</sup>
400 mg cinnamon extract	122.4 ±14.2 <sup>a</sup>	166.6±17.2 <sup>ab</sup>	44.2±13.4 <sup>bc</sup>	95±1.41 <sup>a</sup>	0.46±.14 <sup>b</sup>
100 ginger+100 cinnamon extracts	126.5±19.1 <sup>a</sup>	179.3±22.9 <sup>ab</sup>	52.8±8.5 <sup>b</sup>	96±1.26 <sup>a</sup>	0.54±.09 <sup>b</sup>
150 ginger+150 cinnamon extracts	132.8±21.04 <sup>a</sup>	175.2±19.9 <sup>ab</sup>	41±5.7 <sup>bc</sup>	95±1.09 <sup>a</sup>	0.42±.06 <sup>b</sup>
200ginger+200 cinnamon extracts	127.8±29.3 <sup>a</sup>	172.8±27.3 <sup>ab</sup>	45± 7.1 <sup>bc</sup>	95±0.63 <sup>a</sup>	0.47±.07 <sup>b</sup>

Each value represens the mean ± SD. Means with the different superscript letters in the same column were different significant at P≤0.05

From the results in the same table, it could be noticed that there was a significant decrease P≤0.05 in weight gain of group which consumed ginger and cinnamon water extracts and their mixtures of all concentration, while FI show no a significant different between all of the groups. The decrease in BWG may be due to phenolic compounds content in cinnamon and ginger. Phenolic compound in cinnamon and cinnamon extract reduced BWG of rats fed on high fat diet was observed by **Couturier et al., (2010)** and **Boque et al., (2013)**. The previous studies by **Gowri et al., (2017)** reported that consumption of cinnamon extract for 2 weeks reduces weight gain of obese rat.

### Effect of cinnamon and ginger aqueous extract on serum lipid profile of hyperlipidemic rats

The results in Table (6) showed a significant decrease  $P \leq 0.05$  in serum TC, TG, LDL, VLDL and AI of treated rat with different concentration of ginger and cinnamon water extract. But 400 mg cinnamon water extract revealed the lowest levels of TG, TC, LDL, VLDL and AI levels ( $67.33 \pm 7.9^{cd}$ ,  $144 \pm 7.2^{fg}$ ,  $99.67 \pm 5.8^d$ ,  $13.5 \pm 1.5^{cd}$  mg/dl and  $0.36 \pm 0.04^c$ ) respectively more than ginger extract ( $78.83 \pm 10.7^{bc}$ ,  $154.17 \pm 20.1^{ef}$ ,  $123 \pm 15.5^c$ ,  $15.8 \pm 2.1^{bc}$  mg/dl and  $0.44 \pm 0.05^{bc}$ ) respectively. While high levels mixture (200mg ginger+200mg cinnamon extract) showed no significant different with high level of cinnamon except for TC was lower than 400 mg cinnamon extract.

The hypolipidemic effect of ginger and cinnamon extracts were similar to the results obtained by **Shalaby and Sahfan, (2014)** and **El Rokh et al., (2010)**, who's reported that the ademonstration of aqueous extracts of cinnamon and ginger for 6 weeks decrease TG, TC when compared to positive control group. Rats' treatments by cinnamon for 60 days lead to decrease LDL, TG and total cholesterol (**Khan et al., 2003**). The decrease in TC may be due to reduction in dieatery fats and cholesterol absorption or increase in fecal excretion (**Tebib et al., 1994**). The lipid lowering effect of cinnamon may be due to polyphenolic compounds of cinnamon inhibiting hepatic HMG COA reduuctase (5-hydroxy-3-methylglutarly) coenzyme which is required for synthesis of cholesterol (**Amin, 2009**).

The results of HDL cholesterol revealed a significant decrease of HDL cholesterol in positive control group ( $11.67 \pm 1.2$  mg/ml) compared to negative control ( $24.33 \pm 4.9$ mg/ml). The previous results by **Shelaby and Shfanm (2014)** revealed that the rat fed on high fat diet for 6 weeks had significant decrease in HDL.

HDL cholesterol concentration was significantly higher in rats consuming different concentration of cinnamon and ginger water extracts and no significant different was observed between all groups. The high level of phenolic compound may be responsible for that increase HDL cholesterol. There are positive correlation between phenolic compound and HDL cholesterol (**Castro-Barquero et al., 2020**). Phenolic compounds in cinnamon lead to

activation peroxisome poliferatore receptore which increase HDL and decrease TG (Steiner et al., 2001). The improve in lipid profile of rats fed on cinnamon and ginger extract may be due to increasing antioxidant enzyme activity (Khan et al., 2003 and Vijaya Durga et al., 2013)

**Table (6): Effect of cinnamon and ginger aqueous extract on lipid profile of hyperlipidemic rats**

Groups	Triglyceride (mg/dl)	Cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	Atherogenic index
control-	60.33±5.8 <sup>d</sup>	51.67±6 <sup>i</sup>	24.33±4.9 <sup>c</sup>	15.83±1.8 <sup>g</sup>	12±1.1 <sup>d</sup>	0.42 ± 0.02 <sup>bc</sup>
control+	190.67±10.5 <sup>a</sup>	239.17±16.5 <sup>a</sup>	11.67±1.2 <sup>d</sup>	187.67±17.9 <sup>a</sup>	38±2.1 <sup>a</sup>	1.21± 0.03 <sup>a</sup>
200mg ginger extract	82.67±13.8 <sup>b</sup>	180.17±16.7 <sup>bc</sup>	31.5±1.5 <sup>ab</sup>	136.33±15.1 <sup>bc</sup>	16.5±2.7 <sup>b</sup>	0.41± 0.1 <sup>bc</sup>
300mg ginger extract	81.33±9.5 <sup>bc</sup>	162.33±19.8 <sup>de</sup>	29.17±1.1 <sup>ab</sup>	134.33±6.5 <sup>bc</sup>	16.3±1.9 <sup>bc</sup>	0.44± 0.05 <sup>bc</sup>
400mg ginger extract	78.83±10.7 <sup>bc</sup>	154.17±20.1 <sup>ef</sup>	28.67±1.3 <sup>b</sup>	123.5±15.5 <sup>c</sup>	15.8±2.1 <sup>bc</sup>	0.44± 0.05 <sup>bc</sup>
200mg cinnamon extract	75.83±6.6 <sup>bc</sup>	189±7.1 <sup>b</sup>	31.67±1.9 <sup>a</sup>	141.83±8 <sup>b</sup>	15.2±1.3 <sup>bc</sup>	0.38± 0.04 <sup>c</sup>
300mg cinnamon extract	74.33±10.07 <sup>bc</sup>	169.67±12.7 <sup>cde</sup>	29.67±0.8 <sup>ab</sup>	134.± 6.7 <sup>bc</sup>	14.9±2 <sup>bc</sup>	0.37± 0.05 <sup>c</sup>
400mg cinnamon extract	67.33±7.9 <sup>cd</sup>	144±7.2 <sup>fg</sup>	29.67±0.8 <sup>ab</sup>	99.67±5.8 <sup>d</sup>	13.5±1.5 <sup>cd</sup>	0.36± 0.04 <sup>c</sup>
Mix (100ginger+100 cinnamon extracts)	85.17±5.4 <sup>b</sup>	177.17±19.5 <sup>bcd</sup>	28.67±2.1 <sup>b</sup>	131.83±18.2 <sup>bc</sup>	17±1 <sup>b</sup>	0.48± 0.03 <sup>b</sup>
Mix (150ginger+150 cinnamon extracts)	76.5±17 <sup>bc</sup>	130.33±6.5 <sup>g</sup>	28.67±2 <sup>b</sup>	85.33±8.2 <sup>e</sup>	15.3±3.4 <sup>bc</sup>	0.42± 0.1 <sup>bc</sup>
Mix (200ginger+200 cinnamon extracts)	71.67±16 <sup>bcd</sup>	88.8±10.8 <sup>h</sup>	28.67±2.2 <sup>b</sup>	39.83±5.1 <sup>f</sup>	14.3±3.2 <sup>bcd</sup>	0.39± 0.1 <sup>bc</sup>

Each value represents the mean ± SD. Means with the different superscript letters in the same column were different significant at P≤0.05

### Effect ginger and cinnamon extracts on kidney function of hyperlipidemic rats

Data in Table (7) demonstrated that there were a significant increase in positive control group in their urea, creatinine and uric acid (47.5± 3.51<sup>a</sup>, 0.83± 0.1<sup>a</sup> mg/dl and 3.48± 0.32<sup>a</sup>) respectively compared with negative control group (33.67± 4.59<sup>d</sup>, 0.77± 0.14<sup>abc</sup> and 2.37± 0.06<sup>d</sup> mg/dl respectively). Rats which consumed (400 mg ginger water extract, cinnamon water extracts and mixture from (200mg ginger and 200mg cinnamon extract) showed a significant decrease of urea, creatinine and uric acid compared to positive

control. The highest decrease of urea was in group containig 400 mg cinnamon extract, while higher concentration of all extract and mixture showed no significant different of creatinine and uric acid between of them.. The decrease in uric acid may be due to antioxidant compounds which rich in cinnamon extract such as cinnamic acid. The reduction in urea was observed by **Sharma and Shukla, (2011)** reported that the rats treatment with ginger and cinnamon extract lead to decrease urea. Moreover, **Modarest et al., (2007)**, found that rats which received ginger extract decrease urea and showed little changes of creatinine compared to control group.

**Table (7): Effect ginger and cinnamon extracts on kidney function of hyperlipidemic rats**

Groups	Urea (mg/dl)	Creatinine (mg/dl)	Uric acid (mg/dl)
Control-	33.67± 4.59 <sup>de</sup>	0.77± 0.14 <sup>abc</sup>	2.37± 0.06 <sup>d</sup>
control+	47.5± 3.51 <sup>a</sup>	0.83± 0.1 <sup>a</sup>	3.48± 0.32 <sup>a</sup>
200mg ginger extract	40± 5.32 <sup>bcd</sup>	0.73 ± 0.05 <sup>abcd</sup>	2.84± 0.27 <sup>bc</sup>
300mg ginger extract	44.17± 4.16 <sup>ab</sup>	0.67± 0.04 <sup>cd</sup>	2.68± 0.28 <sup>bcd</sup>
400mg ginger extract	34.33± 9.09 <sup>de</sup>	0.62± 0.05 <sup>d</sup>	2.63± 0.16 <sup>bcd</sup>
200mg cinnamon extract	34.5± 6.34 <sup>cde</sup>	0.79± 0.12 <sup>abc</sup>	2.80± 0.16 <sup>bc</sup>
300mg cinnamon extract	34.5± 3.62 <sup>cde</sup>	0.70± 0.12 <sup>bcd</sup>	2.80± 0.23 <sup>bc</sup>
400mg cinnamon extract	30.83± 6.05 <sup>e</sup>	0.73± 0.07 <sup>abcd</sup>	2.64± 0.17 <sup>bcd</sup>
Mix (100 ginge+100 cinnamon extracts)	41.5± 3.27 <sup>abc</sup>	0.81± 0.09 <sup>ab</sup>	2.97± 0.19 <sup>b</sup>
Mix (150 ginger+150 cinnamon extracts)	40± 4.05 <sup>bcd</sup>	0.68 ± 0.05 <sup>cd</sup>	2.74± 0.72 <sup>bcd</sup>
Mix(200ginger+200 cinnamon extracts)	35± 4.00 <sup>cde</sup>	0.62± 0.1 <sup>d</sup>	2.49± 0.2 <sup>cd</sup>

Each value represents the mean ± SD. Means with the different superscript letters in the same column were different significant at P≤0.05

### Effect of ginger and cinnamon extracts on liver function of hyperlipidemic rats

Effect of ginger and cinnamon extracts on liver function is shown in Table (8). The results showed high fat diet increased ALT (55.17±0.3 IU/L) and AST (41.16±1, 92 IU/L) compared to normal control group that fed on standard diet (16±1.2 and 37±2.04) respectively. The increase in ATL and AST because high fat diet induced liver function disorder lead to increased release teansaminase from cell membrane to blood stream (**Deivanayagam**

et al., 2014). Previous results obtained by Hwang and Shim, (2000) reported that increased ALT and AST of rat's feed high fat diet compared to negative control group

**Table (8): Effect of ginger and cinnamon extracts on liver function of hyperlipidemic rats**

Groups	ALT (IU/L)	AST (IU/L)
Control	16± 2.9 <sup>gh</sup>	37± 5.02 <sup>b</sup>
control+	55.17± 0.75 <sup>a</sup>	41.16± 4.7 <sup>a</sup>
200mg ginger extract	47.17± 0.98 <sup>b</sup>	35.5± 1.04 <sup>b</sup>
300mg ginger extract	33.17± 2.4 <sup>c</sup>	34± 1.09 <sup>b</sup>
400mg ginger extract	28.33± 1 <sup>d</sup>	23.83± 1.83 <sup>d</sup>
200mg cinnamon extract	25.33± 5.1 <sup>de</sup>	30.5± 4.7 <sup>c</sup>
300mg cinnamon extract	24.33± 3.3 <sup>ef</sup>	24.5± 1.37 <sup>d</sup>
400mg cinnamon extract	22.5± 2.4 <sup>ef</sup>	22.33± 1.63 <sup>d</sup>
Mix (100ginger+100cinnamon extracts)	21.67± 3.7 <sup>f</sup>	23.5±1.04 <sup>d</sup>
Mix (150 ginger+150 cinnamon extracts)	18.33± 2.2 <sup>g</sup>	23.67±2.87 <sup>d</sup>
Mix (200 ginger+200 cinnamon extracts)	14.83± 1.4 <sup>h</sup>	23.5±3.14 <sup>d</sup>

Each value represents the mean ± SD. Means with the different superscript letters in the same column were different significant at P≤0.05

Different levels consuming of ginger and cinnamon extract and mixture of them decreased liver function. Moreover, cinnamon extract at 400 mg appeared lower level of ALT and ALT more than ginger extracts. Also, mixture at all concentration decrease liver function more than cinnamon and ginger extract alone. These results may be due to mixture of cinnamon and ginger content more active component (zingerone, 4'.7- Dihydroxyiso Flavone, chlorogenic acid, catachin, caffein and sinapic acid, cinnamic acid and querectin) these compunds have antioxidant effects. Our results are on line with Roussel et al., (2009) and Abdel-Azeem et al., (2013) reported that the reduction of liver enzyme with cinnamon and ginger extract may be due to antioxidant effect of cinamic in cinnamon and zingerone , catachin in ginger extract. Cinnamon supplementation revealed significantly reduced ALT enzyme acitivity of butter fed mice (Miah et al., 2022).

### Effect of ginger and cinnamon extracts on antioxidant enzymes of hyperlipidemic rats

Effect of ginger and cinnamon extracts on antioxidant enzymes are shown in Table (9). The Positive control group showed low significant levels of GSH, SOD, CAT and GPx activity with hyperlipidemic group. The rats feed high cholesterol diet have a significant decrease in SOD (Nagib, 2017). The group treated with 400mg ginger, 400 mg cinnamon and mixture of (200mg of ginger+200mg of cinnamon) showed higher levels of GSH and SOD. On the other hand, the best results of CAT and GPX was recorded of rats feed 400 mg of ginger and mixtutre (200mg of ginger +200 mg of cinnamon extracts). Increased antioxidant enzyme with increase concentration of extractions may be depends on the concentration of phenolic compounds because there are linear correlation between antioxidant power and phenolic concentration in plant extraction (Sönmez et al., 2005 and Rosenblat and Aviram, 2006)

**Table (9): Effect ginger and cinnamon extracts on antioxidant enzymes of hyperlipidemic rats**

Groups	GSH IU/L	SOD IU/L	CAT IU/L	GPX IU/L
control-	4.49±0.25 <sup>a</sup>	0.24±0.01 <sup>a</sup>	812.33±23.6 <sup>a</sup>	5.35±0.51 <sup>ab</sup>
control+	1.97±0.5 <sup>g</sup>	0.12±0.03 <sup>e</sup>	584±26.6 <sup>g</sup>	3.83±1.18 <sup>e</sup>
200mg ginger extract	3.44± 0.47 <sup>cd</sup>	0.19±0.009 <sup>c</sup>	737.5±75.3 <sup>cde</sup>	4.15±0.99 <sup>de</sup>
300mg ginger extract	3.71±0.63 <sup>bc</sup>	0.19±0.01 <sup>c</sup>	761.5±38.9 <sup>bcd</sup>	4.34±0.42 <sup>cde</sup>
400mg ginger extract	4.43±0.49 <sup>ab</sup>	0.20±0.01 <sup>c</sup>	789±6.3 <sup>ab</sup>	5.15±0.55 <sup>abc</sup>
200mg cinnamon extract	2.03±0.7 <sup>fg</sup>	0.17±0.01 <sup>d</sup>	705.5±4.7 <sup>e</sup>	4.52±0.52 <sup>bcd</sup>
300mg cinnamon extract	3.85±1.2 <sup>ab</sup>	0.19± 0.008 <sup>c</sup>	717.83±17.1 <sup>de</sup>	5.56±0.33 <sup>a</sup>
400mg cinnamon extract	2.88±0.23 <sup>de</sup>	0.23± 0.01 <sup>ab</sup>	637.83±41.1 <sup>f</sup>	4.73±0.41 <sup>bcd</sup>
Mix (100ginger+100cinnamon extracts)	2.61± 0.34 <sup>ef</sup>	0.19±0.006 <sup>c</sup>	692.16±40.1 <sup>e</sup>	4.58±0.61 <sup>bcd</sup>
Mix (150ginger+150cinnamon extracts.)	2.72±0.54 <sup>de</sup>	0.20±0.01 <sup>c</sup>	722.8± 3.7 <sup>de</sup>	5.19±0.66 <sup>ab</sup>
Mix (200ginger+200cinnamon extracts)	2.77±0.45 <sup>de</sup>	0.22± 0.01 <sup>b</sup>	776.5±41.4 <sup>abc</sup>	5.78±0.09 <sup>a</sup>

Each value represents the mean ± SD. Means with the different superscript letters in the same column were different significant at P≤0.05

### **Histological examination of Liver:**

Microscopically, liver of rats from group (1) revealed the normal histological structure of hepatic lobule (Fig. 1). On the other hand, liver of rats from group 2 showed focal hepatic necrosis associated with inflammatory cells infiltration (Fig.2). The results by (**Karam et al., (2018)**) Found that histological abnormalities change in liver tissue of rats feed high fat diet for 7 weeks. The rats treatment with 200mg ginger aqueous extract Fig (3) , mixture (100mg ginger+100mg cinnamon extracts) Fig (9) and mixture (200mg ginger+200mg cinnamon extracts) (Fig 11) observed no histopathological changes. Meanwhile, liver from group 4 revealed macrovesicular statuses of hepatocytes as shown in (Fig.4) and focal hepatic necrosis associated with inflammatory cells infiltration (Fig.5). Liver of rats from group 5 revealed macrovesicular steatosis of hepatocytes and mononuclear cells infiltration (Fig.5). However, examined sections from group 6 revealed no changes except macrovesicular steatosis of focal hepatocytes (Figs.6). Moreover, liver from group 7 revealed macrovesicular steatosis of hepatocytes (Fig.7). Sections from group 8 showed macrovesicular steatosis of focal hepatocytes (Fig. 8). Meanwhile, sections from group 10 showed macrovesicular steatosis of focal hepatocytes (Fig.10) and slight activation of Kupffer cells (Fig.10). From these results it could be noted that treated with ginger and cinnamon aqueous extract improve abnormality of histopathology of liver tissue and have protective effect of hyperlipidemia . Previous research by **Hassanen, (2010)**, found the rats treated with ginger and cinnamon reduced abnormality of histopathology of liver. Recent research by **Mousa et al.,( 2021)**, reported that treated rats with ginger lead to a positive change in liver histological.

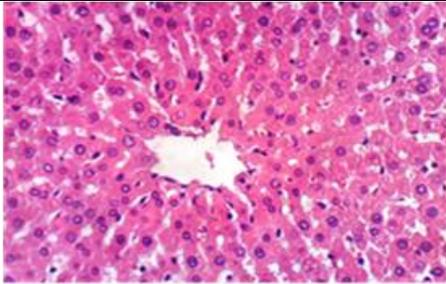


Fig. (1): Liver of rat from group 1 showing the normal histological structure of hepatic lobule (H & E X 400).

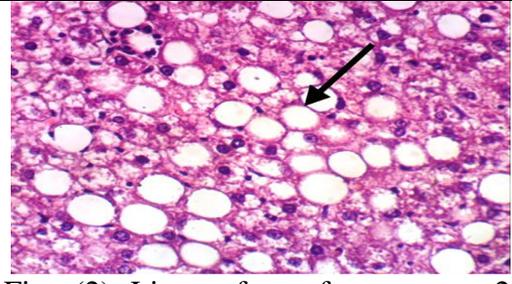


Fig. (2) Liver of rat from group 2 showing macrovesicular steatosis of hepatocytes and focal hepatic necrosis associated with inflammatory cells infiltration (H & E X 400)

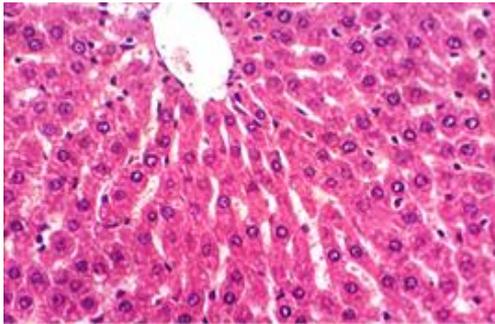


Fig. (3): Liver of rat from group 3 showing no histopathological changes

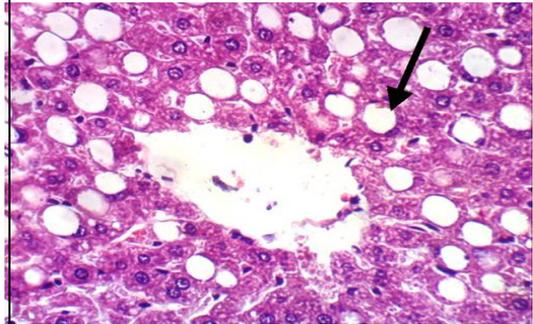


Fig (4): Liver of rat from group 4 showing macrovesicular steatosis of hepatocytes (H & E X 400)

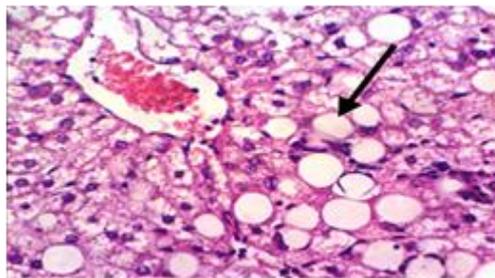


Fig. (5): Liver of rat from group 5 showing macrovesicular steatosis of hepatocytes and mononuclear cells infiltration (H & E X 400)

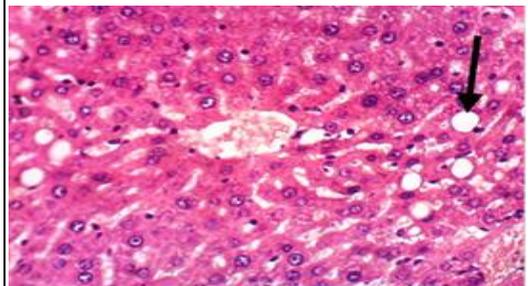


Fig (6): ): Liver of rat from group 6 showing macrovesicular steatosis of focal hepatocytes (H & E X 400)

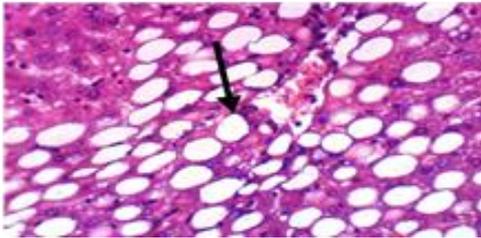


Fig (7): Liver of rat from group 7 showing macrovesicular steatosis of hepatocytes (H & E X 400)

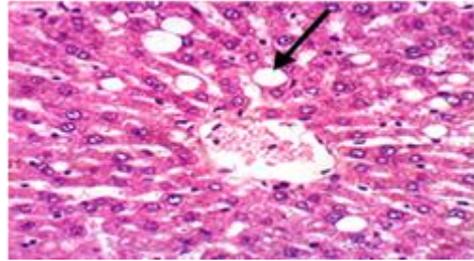


Fig (8): Liver of rat from group 8 showing macrovesicular steatosis of focal hepatocytes (H & E X400)

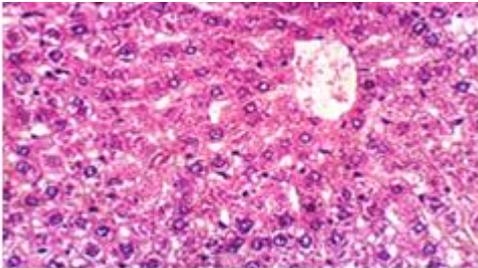


Fig (9): Liver of rat from group 9 showing no histopathological changes (H & E X 400)

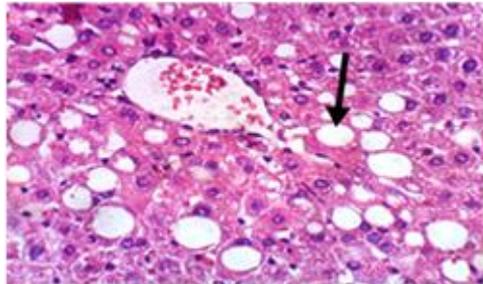


Fig (10): Liver of rat from group 10 showing macrovesicular steatosis of focal hepatocytes (H & E X 400)

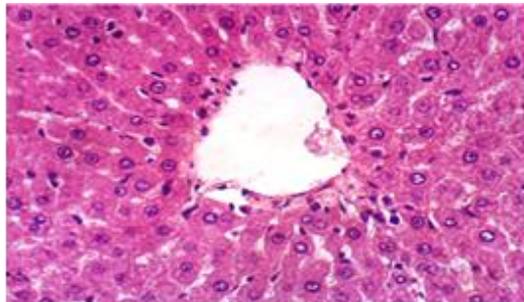


Fig (11): Liver of rat from group 11 showing no histopathological changes (H & E X 400)

## Conclusions

Data obtained in the present study showed that ginger, cinnamon extract and their mixture through 8 weeks has significantly improved the body weight and lipid profile in hyperlipidemic rats. Moreover, cinnamon water extract at high levels 400 mg revealed that hypolipidemic effect more than ginger extract and cinnamon is more effective in excess SOD and reduction urea, uric acid and ALT and AST more than ginger extract.

High levels of mixture (200mg ginger extract+200 mg cinnamon extract) have beneficial effect on TC, LDL, ALT more than cinnamon and ginger extracts alone and no histological of liver cell. The results suggested that consuming cinnamon water extract might have beneficial effects on hyperlipidemic rats.

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## دراسة مقارنة بين تأثير المستخلصات المائية للزنجبيل والقرفة ومخلوطهما على الجرذان التي تعاني من فرط دهون الدم

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## المخلص العربي

إجريت هذه الدراسة لمقارنة تأثير التركيزات المختلفة من المستخلص المائي للقرفة والزنجبيل المركز ومزيج بينهما على الجرذان المصابة بارتفاع في الدهون. إجريت الدراسة على عدد 66 من الجرذان الألبينو البالغين وزنهم من 120-140 جرام تم تقسيمهم الى إحدى عشر مجموعة. المجموعة الأولى تغذت على وجبة قياسية وتمثل المجموعة الضابطة السالبة. المجموعة الثانية تغذت على وجبة مرتفعة في محتواها من الدهون وتمثل المجموعة الضابطة الموجبة. المجموعة الثالثة والرابعة والخامسة تغذت على وجبة مرتفعة في محتواها من الدهون تحتوي على 200, 300, 400 مليجرام/100 جرام وجبة من المستخلص المائي للزنجبيل المركز. المجموعة السادسة والسابعة والثامنة تغذت على وجبة مرتفعة في محتواها من الدهون تحتوي على 200, 300 و400 مليجرام من المستخلص المائي للقرفة المركز. بينما تغذت المجموعة التاسعة والعاشر والحادية عشرة على وجبة مرتفعة في محتواها من الدهن مضاف إليها مخلوط مكون من (100 مليجرام مستخلص الزنجبيل + 100 مليجرام مستخلص القرفة المركز) ومخلوط مكون من (150 مليجرام مستخلص الزنجبيل + 150 مليجرام مستخلص القرفة المركز) ومخلوط مكون من (200 مليجرام مستخلص الزنجبيل + 200 مليجرام مستخلص القرفة المركز) وأستمرت التجربة لمدة 8 أسابيع. وأظهرت النتائج أن المستخلص المائي للزنجبيل والقرفة يحتوي على 1,21 مليجرام/جم و 1.15 مليجرام/جرام من المركبات الفينولية بينما أحتوى على 0.383 مليجرام/جرام و 0.604 مليجرام/جرام من مركبات الفلافونيدات. تشير النتائج الى أن مستخلص القرفة أحتوى على مستوى مرتفع من حامض السينابيك (  $0.03 \pm 59.22$  ) ميكروجرام/جرام) وحامض السيناميك (  $0.09 \pm 1121$  ) ميكروجرام/جرام) بينما أحتوى المستخلص المائي للزنجبيل على تركيز مرتفع من الزنجرون (  $01. \pm 33.28$  ) ميكروجرام/جرام). ويتضح أيضا من النتائج أن جميع المعاملات بعد ثمانية أسابيع سببت نقص معنوي في الجلسريدات الثلاثية (TG), الكوليستيرول الكلى, (TC), الليبوبروتين منخفض الكثافة-LDL), (c), الليبوبروتين منخفض الكثافة جدا (VLDL) ومعامل التصلب (AI) أكثر من المستخلص المائي للزنجبيل. ووجد أيضا أن التركيز المرتفع من المستخلص المائي للقرفة (400 مليجرام) يظهر نقص معنوي في TG, TC,

LDL-c, VLDL-c and AI

و (67.33±7.9, 144±7, 2, 99.67±5.8, 13.5±1.5) و  
0.04±0.36 ملليجرام/ديسيلتر) على التوالي.

ويتضح من النتائج أيضا أن هناك زيادة ذات دلالة احصائية في اليوريا والكرياتنين في الجرذان المرتفعة الدهون وعلى العكس من ذلك هناك انخفاض معنوي في نشاط الأنزيمات المضادة للأكسدة عند مقارنتها بالمجموعة الضابطة السالبة. ووجد أيضا أن التركيز المرتفع من المستخلص المائي القرفة أدى الى أعلى انخفاض في مستوى اليوريا (6.05±30.83 ملليجرام/ديسيلتر) وAST (1.63 ±22,33 وحدة دولية /لتر) وأعلى ارتفاع في نشاط SOD (0.23±0.01 وحدة دولية/لتر).

الخلاصة: تقترح النتائج أن استخدام المستخلص المائي للزنجبيل والقرفة لمدة ثمانى أسبوع لديهم تأثير خافض لدهون مصل الدم في الجرذان المصابة بارتفاع في الدهون. ويتضح من النتائج أن المستخلص المائي للقرفة له تأثير خافض لدهون مصل الدم أكبر من المستخلص المائي للزنجبيل بسبب احتوائه على تركيز مرتفع من حمض السينابيك وحمض السيناميك .

الكلمات المفتاحية: صورة دهون الدم، المركبات الفينولية ، الأنزيمات المضادة للأكسدة،  
أنزيمات الكبد- الفحص الهستوباثولوجى .