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# THE EFFECT OF GINGER (*ZINGIBER OFFICINALE*) ON SOME HORMONES LEVELAND LIPID PROFILE IN BLOOD SERUM OF MALE WHITE NEW ZEALAND RABBITS TREATED WITH CHOLESTEROL

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## Abstract

The present study was carried out to investigate the effects of oral administration of Ginger (*Zingiber officinale*) by which contain of active compounds that stimulate the necessary hormones and HDL-c to reduce the effect of added cholesterol to male white New Zealand rabbits diet (High fat diet HFD) to initiate and development of hypercholesterolemia. Thirty two male white New Zealand rabbits aged 9-11 months, 1500-2500 g had been divided randomly in to four groups (8rabbits/group), all groups had been given a standard ration with free water, first group had been orally drenched normal saline and considered as a control group, while the second group treated with 4g/kg of the dried rhizome, third group treated with 1% cholesterol added to rabbit's diet to initiate hypercholesterolemia, fourth group treated with 1% cholesterol added to rabbit's diet with4g/kg of the dried rhizome, the treatment for all groups continuous for 8weeks. The results showed positive effects as a significant increase ($P \leq 0.01$) in Adiponectin hormone and HDL-c, with decrease in level of lipid profile (except HDL-c), leptin and resistin hormone in rabbit's serum that treated with ginger. In contrast showed a negative effect as a significant decrease in Adiponectin and HDL-c in rabbits that given cholesterol with increase in level of leptin, resistin, lipid profile except HDL-c, while the results tend in rabbits that given cholesterol and with ginger near with normal concentration in control group.

***Key words:*** Ginger, hormones, lipid profile, blood serum

## Introduction

Hypercholesterolemia, which refers to elevated concentration of cholesterol in the blood, is a common cause of the atherosclerosis and related occlusive vascular disease that have come to represent a major cause of morbidity and mortality throughout the world (El Awady and Suddek, 2018). It is usually results from nutritional factors such as obesity and the nutrition with high fat diet, also hypercholesterolemia may be have an genetic cause (Bhatnagar *et. al*., 2008).

Moreover, adipose tissue, an inert organ that act as a temporary site for storage energy in the form of triacylglycerol, is also known to express and produce a number of secretions knowns as adipokines such as Adiponectin, Resistin and Leptin hormone ( Catta-Preta *et. al*., 2012). These hormones have an effective function to control the metabolism of fats. Imbalance of adipokines is a consequence of abnormal plasma hormone levels and contributes some diseases development including atherosclerosis and type II diabetes mellitus (Zhang *et. al*., 2015; Chen *et. al.,* 2016).

On the other hand, using of herbs to prophylaxis and treatment of the diseases is effective and with less adverse effect on the body (Abdul-Hussein, 2014). Active natural compounds especially from botanical sources such as spices have an important effect by their features on health. *Zingiber officinale* has been used in classical medicine in some countries such as Greek, China and in communal Arabic medical (Verma *et al.,* 2004).

Therefore, this study has been undertaken to investigate *Zingiber officinal* effect against induced hyperlipidemia, which lead to obesity and atherosclerosis and some adipokines levels.

Leptin hormone produced by adipose tissue, which classified as an endocrine organ after discovery of leptin, it has an important function in the regulation of weight by ruling diet intake and energy usage. High levels of leptin

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may be among those who are obese, but the efficiency of this hormone is low, it is due to resistance to leptin, while levels of this hormone decrease with a body weight declines (Al-Suhaimi and Shehzad, 2013); (Koleva *et. al*., 2013).

Adiponectin, also known as adipocyte complement-related protein of 30 KDa, was identified by different groups (Kadowaki and Yamauchi, 2005). Adiponectin hormone is an adipokine abundantly produced by adipose cells and recognized for itsanti-atherogenic, cardioprotective, anti-inflammatory and antidiabetic effects (Ohashi *et. al*., 2012).

Resistin hormone or 'resistance to insulin' was originally discovered in mice in (2001) and acquired its name for its ability toresist "interfere with"the action of insulin (Steppan *et. al*., 2001); at that time, it was proposed as a link between diabetes and obesity. Resistin hormone is also known as adipocyte-secreted factor (Schinke *et al*., 2004).

**Aims of the study**

The present study aimed to investigate

1- The effect of Ginger on the level of hormones adiponectin, leptin and Resistin in serum of the experimental normal or suffering from high cholesterol fed rabbits (HFD).

2- Lipid profiles level in blood serum of the experimental normal or suffering from high cholesterol fed rabbits (HFD).

## Materials and Methods

**Cholesterol**

Cholesterol was purchased from France (BDH) Company from the Chemistry department/ College of science/ University of Mosul, in the form of white crystalline powder, and was mixed with an ordinary diet for a period of 8 weeks (Dowell *et. al.,* 1996).

**Ginger**

The fresh ginger rhizomes was purchased from a spice dealer; then washed with water to remove adhering dirt. Ginger rhizomes were cut and chopped into smaller pieces. Under shade for 5 - 6 days, the chopped ginger rhizomes were dried, to prevent volatilization of its effective oils by direct sunlight. Air- dried samples are milled with the laboratory mill into powder- like particles (Jayashree *et. al*., 2014). The recommended daily dose of ginger was the equivalent of 4 g/kg body weight of the dried rhizome (Verma *et. al.,* 2004).

**Rabbits**

A total number of Thirty two adult males white New Zealand rabbits aged 9-11 months, and weighed 1500-2500grams were used in this study. The rabbits were obtained from College of Veterinary Medicine, Mosul University. Individual cages measuring 1.5m×1.0m×1.0m used to place the rabbits used in the research. The cages are characterized by their wire mesh floor and wooden frames. They were fed commercial concentrate diet only one week for the purpose of acclimatization. After 2 weeks of adaptation, rabbits were separated into groups.

**Standard ration**

The basal diet for rabbits (free of cholesterol) was prepared according to National Research Council (N.R.C., 1994), was prepared by Al- Ameen company for poultry feed trade in Mosul.

**The study protocol**

Thirty two, male rabbits were used in this study and were divided into four groups: group 1 included 8 male rabbits fed an ordinary diet for an experimental period of 8 weeks; group 2 included 8 male rabbits fed an ordinary diet mixed with 1% cholesterol powder at a dose of 200 mg/kg bodyweight for a period of 8 weeks; group 3 included 8 male rabbits fed an ordinary diet mixed with ginger powder, (4 g/kg of the dried rhizome) for 8 weeks; and group 4 included 8 rabbits fed an ordinary diet mixed with 1% cholesterol powder and were treated with ginger powder (4 g/kg of the dried rhizome) for 8 weeks.

**Kits for Analysis**

Commercial diagnostic kits for estimating serum Adiponectin, Leptin, Resistin hormone TAC were obtained from Elisa My BioSource company, USA. TG, TC, HDL-c kits were obtained from refletron company, Germany, while VLDL-c and LDL-c obtained from the mathematical equations

VLDL-c = TG/ 5

LDL-c= TC– HDL-c– TG/5

**Statistical analysis**

Statistical analysis were done using one way ANOVA analysis of variance using the General Linear Model, SAS software (SAS, 2004). Duncan was used to separate the means when significant differences exist. Means and standard deviations were calculated for all parameter. Difference were considered significant at $P \leq 0.01$.

## Results

The obtained results in table 1 showed significant increase in serum Adiponectin in ginger group, in contrast decrease significantly in cholesterol group, while in ginger treated group near the values of control group, Resistin and Leptin decrease significantly in ginger group, in

contrast increase significantly in cholesterol group, while in ginger treated group near the values of control group.

In table 2 TC, TG, LDL-c decrease significantly in ginger group, on the other hand HDL-c and increase significantly in ginger group and decrease significantly in cholesterol group, while in ginger treated group the all values near the values of control group.

## Discussion

The ability of ginger to raise the Adiponectin level may be caused by High content of $Mg^{++}$ (214 mg/100 g) (Stanisiere *et. al*., 2018), Cassidy *et. al*., (2009) indicate that $Mg^{++}$ raise adiponectin level when it taken by food richer with it, or its activity to raise adiponectin related to vitamin $B_3$ which stimulate Adiponectin secretion by stimulate the white adipose cells receptors and immune cells like monocytes and neutrophil, stimulate this receptors lead to fast increasing to produce Adiponectin (Plaisance *et. al*., 2009).

Ginger may be increase Adiponectin by its contain of linoleic acid which is most abundant fatty acid representing 52.7% of the total fatty acids content. Linoleic acid stimulate Adiponectin expression by white adipose cells also increase the activity of endothelial nitric oxide synthase which is anti- atherosclerosis (De clerq *et. al*., 2012); (Adeyeye, *et. al.,* 2014).

Anthocyanin compounds which present in ginger in adequate amount, accelerate Adiponectin production which increase thyroid hormones synthesis; specially $T_4$ hormone as a result of C- terminal globular reaction with receptors located in mitochondria of thyroid gland cells, this will give Adiponectin hormone sharing feature with thyroid hormones in some physiological functions like decrease body lipid sand increase lipid oxidation also body temperature regulation (Fernandez-Real *et al*., 2003) and according to relationship between Leptin and body lipids (Ouchi *et. al*., 2011), ginger shown to decreasing the level of Leptin by decreasing body lipids (Mahmoud and Elnour, 2013).

HFD lead to obesity (Sawkey, 2015) this will activate TNFα and IL-6 both of them inhibit expression of Adiponectin hormone in white adipose cells (Fasshauer *et. al*., 2003).

The previous data agreed with the results of studies have shown that leptin remains highly correlated to body fat mass and that it usually is coupled to be the antilog of adiponectin, increasing in level while the other is decreasing (Rea and Donnelly, 2004).

Saravanan *et al*., 2014 explained that leptin in HFD rats is increased while when treated orally with gingerol (active compound in ginger) once daily for 30 days showed significant decrease in leptin hormone compared with control.

High levels of resistin and leptin, occurring in obese persons by HFD, accelerate the development of hyperlipidemia and insulin resistance, whereas adiponectin seems to prevent this. (Ouchi *et al*., 2011).

Although the mechanisms of effective role of ginger on adipokines level have not been clarified, there are evidences from laboratory (in vitro) studies that the components of ginger may be increase the gene expression of some adipokines such as adiponectin (Isa *et al*., 2008)and inhibit the gene expression of resistin (Ahn and Oh, 2012), Also Attari *et al*., (2015) showed a significant decrease in leptin and resitin agreement with our study.

This decrease in serum resistin levels could be attributed to the weight loss that occurs in type1 diabetes, as resistin levels were positively and significantly correlated with the body weight, which is in agreement with that of Stroubini *et al*., (2009).

In addition, there is relationship between resistin hormone concentration and many inflammatory factors including interleukin-6 (IL-6), tumor necrosis factoralpha (TNF-a) and C-reactive protein (Silswal *et al*., 2005); (Stofkova, 2010), this markers increased also with high body lipids (Popko *et al*., 2010), so

**Table 1:** The Hormonal values in groups under study.

| No. | Groups | Adiponectinmg/L | Leptinp g/ml | Resistinp g/ml |
|---|---|---|---|---|
| 1. | Control group | 6.16±0.36 | 5.01±0.22 | 95.5± 4.5 |
| 2. | Ginger group | 10.88±0.7 | 2.81±0.86 | 35.5± 6.3 |
| 3. | Cholesterol group (HFD) | 4.12±0.45 | 6.10±0.22 | 175.3± 2.6 |
| 4. | Ginger and cholesterol group | 5.70±0.41 | 3.92±0.4S | 125.7± 5.8 |

The values is means ± SD, no. of rabbits/ group = 8
The no. followed by different letters means there is significant difference.

**Table 2:** The biochemical values in groups under study (mg/dl).

| No. | Groups | TC | TG | HDL-c | LDL-c | VLDL-c |
|---|---|---|---|---|---|---|
| 1. | Control group | 100.5±8.4 | 111±0.56 | 23.5±2.8 | 54.8±5.49 | 22.2±0.11 |
| 2. | Ginger group | 85.1± 3.7 | 90±2.01 | 36.05±2.5 | 30.6±0.8 | 18±0.4 |
| 3. | Cholesterol group (HFD) | 139± 10.6 | 142±6.5 | 11.6±2 | 109±2.8 | 28.4±1.3 |
| 4. | Ginger and cholesterol group | 119±4.3 | 120±2.17 | 19.7±2.7 | 75.3±1.17 | 24±0.43 |

The values is means ± SD, no. of rabbits/ group = 8
The no. followed by different letters means there is significant difference.

the data interpret the effect of HFD on increasing the level of resistin in HFD group.

Azuma *et al*., (2003) and Silha *et al*., (2003) have found that mean circulating resistin hormone levels in fat persons is increased about four folds compared with skinny persons; and also our results supported by Stroubini *et al*., (2009), who found that resistin hormone levels were increased in many experimental models of obesity and lowered after losing of weight. Moreover, de Luis *et al*., (2009) demonstrated that resistin levels were related to the total fat mass in patients with metabolic syndrome.

The datarepresented in table 1 showed significant increase in plasma TC, TG, LDL-C and VLDL-C with significant decrease in HDLC levels in HFD or hyperlipidemic rabbits. HFD that used to elevate the lipid profile parameters indicate its ability to elevate all parameters except HDL-C measured in this experiment, this results supported by the finding of EL-Sayed and Moustafa, 2016.

The levels of cholesterol are influenced by many factors such as the synthesis of cholesterol by liver, the excretion of cholesterol by bile and the absorption of cholesterol by intestine (Lopez *et al*., 1977). Z. *officinale* (Zanjabeel) was found to be have an effective role in lowering the level of serum TG, TC, VLDL-c and serum LDL-cin patients of primary hyperlipidaemia, by mechanisms include:

1. It inhibits of the enzyme for cholesterol synthesis, which named as hydroxymethylglutaryl CoA (HMG-CoA) reductase (Tanabe *et al*., 1993).

2. It impairs theabsorption of cholesterol and accelerates the excretion (Tanabe *et al*., 1993). It promotes the activity of enzyme in the catabolic conversion of cholesterol to bile acids in liver which named.

7- alphahydroxylase (Yamahara *et al*., 1985); (Murugaiah *et al*., 1999).

Furthermore, Adenosine monophosphate-activated protein kinase (AMPK) decreased fatty acid synthesis and increased fatty acid oxidation byinhibits the activity of acetyl-coA carboxylase (ACC) 1 and ACC-2 (Leeand Niemann, 1996) and accordingly, lower triglyceride concentrations.

The ability of ginger to decrease the TG may be due to the direct effect on Diacylglycerol acyl transferase because of high content of polyphenols compounds which have the ability to scavenge free radicles and inhibit LDL-c oxidation (Graf *et al*., 2013); (Rozanida *et al*., 2006).

HDL is a beneficial lipoprotein synthesized in intestine and liver, which protects the system from the pathogenesis of atherosclerosis (Xu *et al*., 2005). The HDL that considered the more important to the body due to its protective effect against LDL and cholesterol. The ginger extract was effective keeping the HDL in normal level and prevented it from reduction especially post addition of fat to feeding and there was no difference comparing to the normal level, and this agreed with Elshater 2009.

The important active component of ginger root is gingerol, which has appeared to stabilize adipocyte hormones, lipases and lipid profiles in high fat diet induced obese rats (Boissonneault, 2009). Also both TG and TC were reduced in group received ginger water foods (Sayed *et al*., 2020).

The effect of ginger on VLDL was noticeable and reduced the level pre addition of fat and prevented it to increase post addition of fat to the feeding. Reduced expression or activity of LDL-c receptor sites response to HFD treatment interpret the increase of LDL-c level. In another study decreasing the level of LDL-c may be an effective factor in decreasing the serum TC level in rats fed HFD (Rayner *et al*., 2010).

Ginger may be influence body weight or body composition through some mechanisms include (1) promoting catecholamine-releasing action which increase energy expenditure and thermo genesis (Mansour *et al*., 2012). (2) Increasing the lipolysis of white adipose tissue (Ahn andOh, 2012), (3) Decreasing intestinal absorption of dietary fat by inhibition of the lipase enzyme (Mahmoudand Elnour, 2013). Therefore, ginger treated HFD rats showed significant reduction in TG, TC, VLD-c and LDL-c level and increase in serum level of HDL-c as compared to control group. The decrease of lipids by ginger may be result from the suppression of the absorption of lipid and cholesterol by inhibiting the activity of pancreatic lipase. It is important to say that ginger extract effective to protect against hyperlipidemia, because it reduced the serum lipids and prevented them to increase even post addition of fat to feeding (Maralla *et al*., 2012).

## Conclusion

From our study, we can conclude that ginger is a good natural drug for it's an effective role in improving experimentally induced hypercholesterolemia in rabbits, it is fighting against increasing bad lipids by decreasing the related hormone Leptin and Resistin with increasing Adiponectin which have important role against increasing bad lipids.

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