

An In-Depth Analysis of the Lipid Lowering Effects of Saponin Extracts from *Ziziphus Sapina Christi* Leaves on Hyperlipidemic Rats

Raof Jabbar Maaroo^{1*}

¹University of Babylon, College of Nursing, Iraq

*Corresponding Author: Raof Jabbar Maaroo

University of Babylon, College of Nursing, Iraq

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Abstract: Background: Medicine plants, have become one of the most used and most important resources for treating high blood pressure and cardiovascular diseases. Their usage has increased tremendously in the contemporary period due to many factors as economic viability, easy accessibility, rapid effect, and last but not least minimal, side effects .

Aim: This study aimed to access the effect of Saponin extract from *Ziziphus Sapina Christi* on hyperlipidemic male rats.

Methods: In this study, thirty-six sexually mature male rats were used and divided into different groups: the C1 group was fed with normal feed containing 1.5% fat; the C2 group was fed with normal feed containing no fat and infused with 50 mg/kg saponin extract; the C3 group was fed with normal feed containing no fat and infused with 100 mg/kg saponin extract; C4 group was fed with normal feed that contains 1.5% fat and 50 mg/kg saponin extract, the C5 group was given normal feed that contains 1.5% fat and 100 mg/kg saponin extract. The C6 group was assigned as a control group that was receiving which received a typical forage without fats. Collection of blood samples were done after four weeks and eight weeks, respectively. Statistical analysis showed that the C1 group exhibited a significant increase in the means of Total Cholesterol, Triglycerides and Low Density Lipoprotein (LDL), and a significant decrease in the level of High Density Lipoprotein (HDL) as compared to the control and other groups. **Results:** the study results show a significant decrease in Total Cholesterol, Triglycerides, and LDL, with a significant rise in HDL in groups C2 to C5 as compared to the control and C1 groups; and these values decreased progressively with increasing dose duration, the more decrease being at the end of the dose period of eight weeks and the least being seen at the end of the dose period of four weeks. However, the study results indicated that the dose of 100 mg/kg of saponin extract for eight weeks was more effective at reducing the above parameters. **Conclusions:** This study reveals that saponin extracts from leaves of *Ziziphus Sapina Christi*, indicated reduction of lipid profile in hyperlipidemic rats and the concentration of extract used and dosing duration exerted a greater influence in the reduction of the above conditions in fat-diet-fed rats.

Keywords: Saponin Extract, Hyperlipidemia, *Ziziphus Sapina Christi* Leaves.

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INTRODUCTION

Cardiovascular diseases are an important health problem in the world [1], that many factors are associated with and cause such diseases, these factors include eating calorie foods, advancing ages, lack of exercise, and high genetic predisposition [2, 3].

Hyperlipidemia is regarded as the most dangerous factor for morbidity in cardiovascular diseases and raises human mortality rates [4]. A low concentration of lipids in blood serum was found to be

one of the dominant factors that prevent the development of atherosclerosis, thus reducing the incidence of cardiovascular diseases [5-7].

Many medicinal drugs help in the reduction of serum lipid components. These drugs decrease the percentage of low-density lipoprotein (LDL) by 20%-40% and may help moderately raise levels of high-density lipoprotein (HDL) [8]. The known and used drugs include niacin, fibrate, and 5-hydroxy-3-methyl glutary CoA reductase inhibitors. However, the side effects of these drugs, among many others, led to

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researchers turning towards natural substances that have the competence to reduce fat contents, having little or no side effects.

The use of medicinal plants in the treatment of high blood pressure and cardiovascular diseases has seen a considerable increase lately for their cheapness, availability, rapid effect, and most importantly, having very few side effects [9].

Sidr plant (*Ziziphus Sapina Christi*) represents one of the most popular medicinal plants in the Rhamnaceae family [10], and the chemical components of the Sidr plant contain many important medicinal substances, the most important being that its leaves have Saponins [11]. They also possess alkaloids, cyanogenic glycosidase, glucosinolates, phenolic compounds, sterols, and steroids. Saponin is a very important active compound in the Sidr leaves as it works by lowering cholesterol, enhancing immunity, and exerting an antimicrobial effect against the microbe that causes joint pain, thus reducing swelling and inflammation [13].

The scanty nature of studies on Sidr plant usage in fat components reduction necessitated the present study aiming to reveal the role of Saponin extract from leaves of the Sidr plant in reducing induced hyperlipidemia in laboratory animals.

METHODOLOGY

Thirty-six male white rats (*Rattus rattus*), aged eight to nine weeks and weighing between 190 and 200 g, were used in the study. They were kept in the animal house, and the temperature, humidity, ventilation, and hours of light and darkness were similar for all rats housed there. Their health condition was fine. The leaves of Sidr plants were used to choke the Saponin preparation as per method [14], using the continued extraction method with hot methanol. 20 g of dry sieved leaves were placed into the thumb of a Soxhlet device, connected to a 1L rounded flask, followed by adding 200ml of 95% methanol, and then extracted at 69°C for 6 hours. After that, the extract was concentrated with distillation at 65°C to get rid of alcohol. Butanol was added to the extract, and this mixture was allowed to settle in a separating funnel after shaking a few times. The upper layer contained butanol with Saponin, while the lower layer contained water. The water extract would be taken, and the last process would be repeated. Thereafter, the Saponin-Butanol layer is collected in a flask and then extracted concentrated by a rotary evaporator. The extract is then washed with 95% ethanol and further crystallized by diethyl ether to purified Saponins. The concentrations prepared were (100 and 50) mg/kg of total volume weight.

Animal Division:

There were six groups of animals, with each group having six animals. Each group was given an oral dosage for (four weeks, eight weeks). It included...

Group C1: There were fed with the standard diet mixed with 1.5% fat throughout the study period.

Group C2: The rats fed the standard diet without any percentage of fat that was then treated with oral administration of Saponin (50 mg/kg of body weight).

Group C3 represented rats fed a standard diet free of fats and treated orally with a dose of Saponin (100 mg/kg of body weight).

Group C4. The rats fed with the standard diet mixed with fat with 1.5% and a dose of saponin 50 mg/kg of body weight.

Group C5. The group of rats that ate the standard diet mixed with fat included:

1.5% as the required level, with a dose of saponin being 100 mg/kg of body weight.

Group C6. The control group received the standard diet devoid of any percentage of fat during the entire study period.

Animal Sacrifice and Blood Sample Collection:

The animals were dissected after being anesthetized with chloroform after the 31 day for the groups whose respective extracts consisted of doses of concentrations for a period of four weeks. For the animals with doses of extracts of concentrations for a period of eight weeks, they were dissected on the 57th day. Blood samples were drawn directly after sacrificing the animals by what is called an intracardiac puncture using medical syringes. 5 ml of blood were drawn and the blood samples were placed in clean test tubes free of anticoagulant and spun in a centrifuge at a speed of 3000 rpm for 15 minutes in order to obtain Blood serum was kept in plastic tubes at 20 deg C until utilized.

1. Determining of Lipid Profile

Determination of blood serum-cholesterol and triglycerides related to the various analyses prepared by kits of the French company Biomerieux were used.

HDL-cholesterol was determined after precipitation of VLDL and LDL with phosphotungstic acid and magnesium chloride.

LDL was calculated according to the equation of Friedewald.

$$\text{LDL Cholesterol (mg/dL)} = \text{Total cholesterol (VLDL + HDL)}$$

The value of VLDL was extracted as follows:

$$\text{VLDL Triglyceride} / 5$$

According to the manufacturer's instructions.

Statistical Analysis:

The fingerlings were randomized completely for further experimental design. The reactions were tested against LSD, or the least significant difference. The complete randomized analyze effect testing under the odds of 0.05 was applied in declaring significant results (SPSS).

RESULTS

1. Effect of Varying Concentrations of Saponin Extract of Sidr Leaves on Fat Components

Table 1 shows a substantial rise in concentrations of total cholesterol for the C1 group fed a diet containing 1.5% fat, reaching (186.25) against (97) for the control group. In contrast, there was a significant drop in total cholesterol concentrations occurring in the remaining groups, with readings of (67.25), (59.5), (80.5), (67.5) for groups C5, C4, and C32, respectively, whereas control C6 reached (97). Compared to groups C2, which does not differ from group C5, there is, however, a meaningful difference between the others.

From the results shown in the above table, a significant increase in triglyceride concentration in group C1 fed a diet formulated to contain 1.5% fat was found to reach (129) when compared against control group C6 (70). There was a significant decrease in the concentration of triglycerides in the rest, respectively, in

contrast to groups C5, C4, C3, C2, which reached (48.25), (36), (57.25) and (51.75) respectively, whereas the control group C6 reached (97). The intergroup comparisons were reported to show significant differences. In table 1, there is an increase in HDL levels for C1-treated animals fed with a 1.5% fat diet to (26.25); with values for control group C6 at (33). In contrast, the remaining groups exhibited an increase in HDL to (108.5, 121.5, 74.5, 85.5) for groups C5, C4 and C32, respectively, contrasted with control at (33). Intergroup comparison, however, indicated meaningful differences.

The same table exhibits a significant rise in LDL levels in the C1 group that consumed the feed containing 1.5% fat, which attained (121.25) in comparison to the control group (61.25), while a significant drop was seen in LDL levels in the rest of the groups, attaining (16.75), (11.25) (34) (28.5) for groups C5.4.3.2, respectively, in contrast to the control group, which reached (61.25). When contrasting the groups, the results indicated meaningful differences among them.

Table 1: Effect of different concentrations of saponin extract in fat components

Group	Cholesterol	Triglyceride	HDL	LDL
C1	186.25	129	26.25	121.25
C2	67.25	84.25	108.5	16.75
C3	59.5	36	121.5	11.25
C4	80.5	57.25	74.5	34
C5	67.5	51.75	85.25	28.5
C6	97	70	33	61.25
L.S.D	3.021	2.782	2.909	2.151

2- Interaction between Concentration and Duration of Dosing with Saponin Extract of Sidr Leaves and Its Effect on the Components of Fats

Total Cholesterol Concentration

The result in Figure (1) showed a significant rise in total cholesterol levels at both periods for group C1, which reached (199,173.5) for four weeks and eight weeks, respectively, when contrasted with control group,

C6, reaching (96.5,97.5) for four weeks and eight weeks, respectively. The total cholesterol levels for all the other groups were significantly lower when compared to the control group. In terms of intergroup comparison, the decrease was the greatest in group C3, where cholesterol levels were (54.5) and (64.5) for four weeks and eight weeks, respectively, when compared to group C4 that reached (89) and (77) respectively.

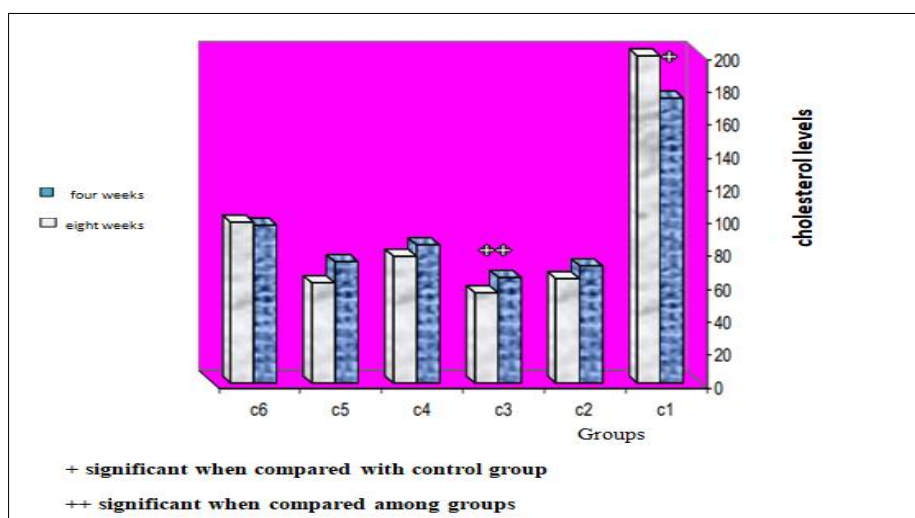


Figure1: Interaction between concentration and dosage of Saponin extract on cholesterol levels (LSD 4.273)

Triglyceride Concentration

The data in Figure (2) show that triglycerides levels for group C1 are significantly higher (109,149) at four weeks and eight weeks, respectively, against control group (71,69), whereas a meaningful decrease in triglycerides was found among the rest of the groups

compared to control group. Intergroup comparisons showed significance with a greatest decrease in group C3 treated with Saponin reaching 39.5 (32.5) at four weeks and eight weeks, respectively, relative to group C4, reaching (65, 49.5) at four weeks and eight weeks, respectively.

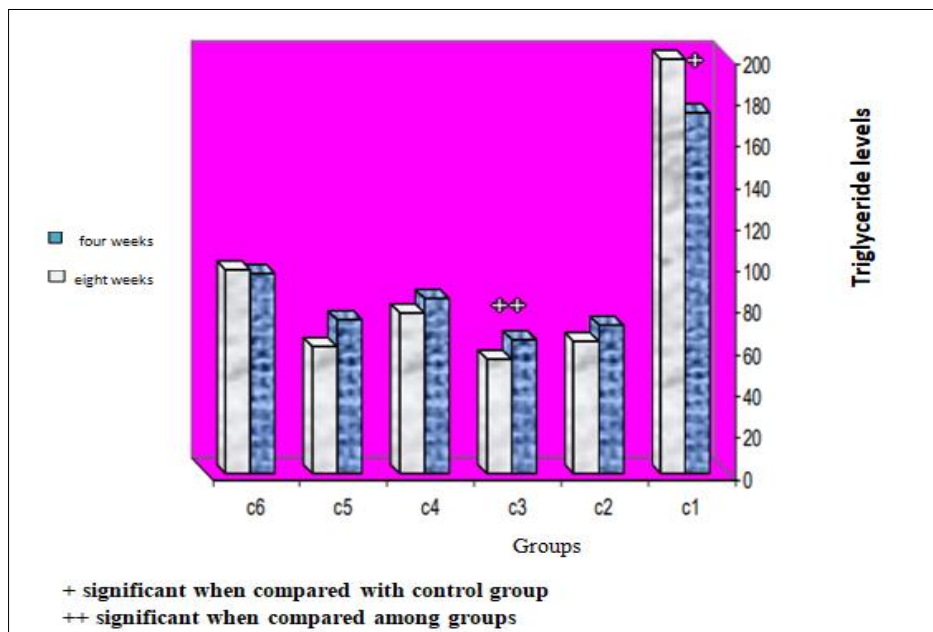


Figure 2: Interaction between concentration and dosage of Saponin extract on triglyceride levels (L.S.D 3.934)

HDL

From Figure (3), a meaningful decrease in HDL levels for group C1, which reached (23.5, 29) for four weeks and eight weeks, respectively, in contrast to the control group C6, which reached (32.5, 33.5) for four weeks and eight weeks, respectively. Whereas, the same figure shows a significant elevation of HDL level for the

rest of the groups in contrast to the control group. When comparing the groups, the results indicated a significant elevation, highest in group C3, which reached (115.5,127.5) for four weeks and eight weeks, respectively, in contrast to group C4, which reached (78,71), respectively.

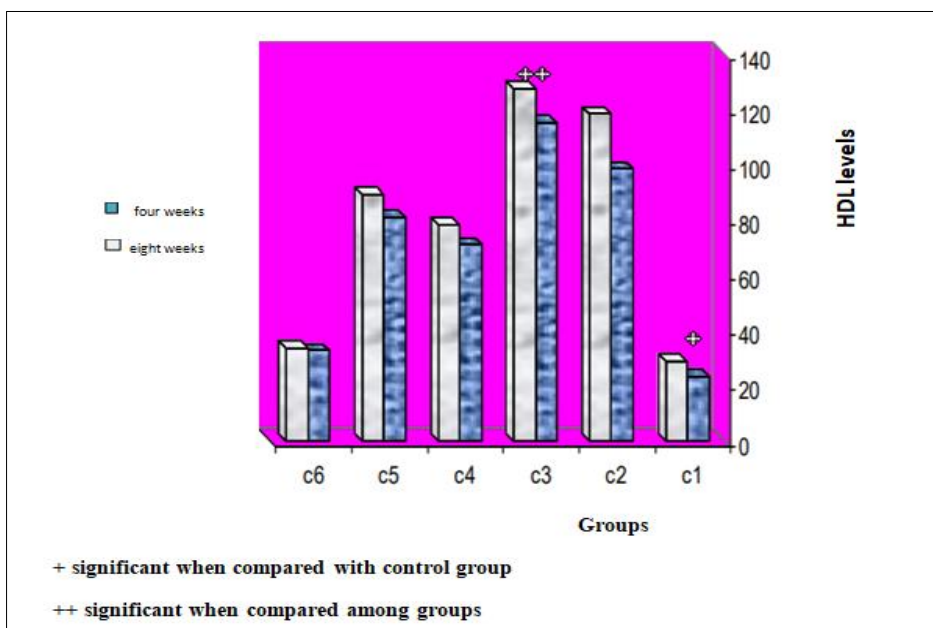


Figure 3: Interaction between concentration and dosage of saponin extract on HDL levels (L.S.D.4.114)

LDL

According to Figure (4), there was a significant increase in LDL levels for group C1, which reads (129,113.5) for four weeks, and eight weeks in contrast with the control group, which attained (61.5,61) for four weeks, and eight weeks, respectively. Whereas, the same figure indicated a significant drop in LDL levels for other

groups versus the control group. In the intergroup comparisons, the results demonstrated a significant depression which was steepest in group C3 recording (9,13.5) for four weeks and eight weeks respectively, when compared to group C4 values of (31.5,36.5) for four weeks and eight weeks respectively.

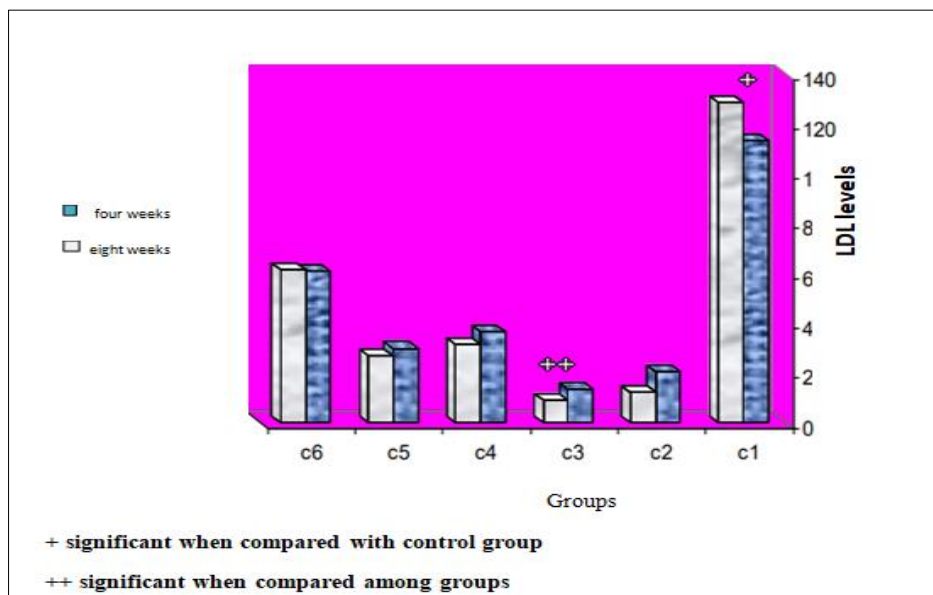


Figure 4: Interaction between concentration and dosage of Saponin extract on LDL levels (L.S.D 3.043)

DISCUSSION

Increased total cholesterol, triglycerides, and LDL levels were noted in group C1, after consumption of the standard diet that contained a percentage of fat, attributable to fat in the diet. Saturated fats increased blood levels of cholesterol and triglycerides [15]. Liver fat deposition is enhanced, which increases preparation or generation of greater amounts of Acetyl-CoA for the liver to convert into cholesterol and triglycerides [16]. Cholesterol and triglyceride abnormal elevations cause increased lipid components (hyperlipidemia), thereby promoting the development of cardiovascular diseases, inducing a path toward atherosclerosis [17]. Cholesterol is closely associated with LDL, which has been labeled as malignant proteins because they take part in cholesterol transport in the bloodstream. The results of this study, showing increased cholesterol and LD, prove an existence of direct link between them, which concur to the assertion [18].

The study found decreased HDL levels in group C1, resulting from high triglyceride levels, as raised triglyceride levels lower HDL levels via neutral fat exchange, and they also stimulate the building of small amounts of HDL protein [19]. There was also a remarkable decrease in cholesterol, triglycerides, and LDL levels for groups that received Saponin extract from Sidr leaves alone and for groups that received fatty feed and also received extract.

The decrease in cholesterol and triglycerides' concentrations results because Saponins decreases the levels of cholesterol and triglycerides as this compound finds bial-salt in the intestine, forming small micelles with cholesterol and triglycerides for facilitated absorption [20]. On the contrary, they decrease cholesterol and triglycerides concentration through preventing their reabsorption. The result of this study is in agreement with the study, wherein saponins are confirmed to reduce cholesterol and triglyceride by preventing their biosynthesis in liver cells, or inhibiting their molecular reabsorption in the small intestine [21].

Due to the direct relationship between Ch and LDL, a fall in Ch concentration caused a decrease in LDL concentration, as reported. Whereas the negative correlation between decrease in TG concentration and increase in HDL concentration has been demonstrated in many studies, a similar finding was also found in the results of the current study. In various studies, a decrease in TG level along with an increase in HDL concentration (TG/HDL) has been shown to decrease the coefficient of atherosclerosis, thereby also lowering the risks to the diseases [22, 23].

The above results show that the concentration of extract used and dosing duration exerted a greater influence in the reduction of the above conditions in fat-diet-fed rats, in which dosing of animals for eight uninterrupted weeks at 100% concentration of Saponin was found to evoke the highest reductions of the above

parameters. This can be attributed to the fact the 100% concentration contained more Saponin and thus exerted more significant effects with prolonged treatment, which shares a similar outcome with [24, 3].

CONCLUSION

This study reveals that Saponin extracts from leaves of *Ziziphus Sapina Christi*, indicated reduction of lipid profile in hyperlipidemic rats and the concentration of extract used and dosing duration exerted a greater influence in the reduction of the above conditions in fat-diet-fed rats.

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