Egypt. J. Chem. **Vol. 64,** No. 11 pp. 6529 - 6540 (2021)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Study of the effect of laurel plant (Laurus Nobilis) on some biochemical markers in diabetic mellitus rats

[a]Aser Ihsan Abdullah[*],[b] Saba Zeki M. AL-Abachi

[a,b]University of Mosul,College of Science, Department of Chemistry, Mosul, Iraq.

Abstract

The present study is aimed to introduce the effect of laurus nobilis extracts on blood glucose level, liver function, lipid profile, and body weight in diabetic rats. Three experiment was done for seventy- two albino male rats (150-200) grams were divided into twelve groups, in each study experiment rats were divided to four groups (6 rats for each) , first group treated with distilled water and served as control group, second group served as positive diabetic and treated with 100 mg/kg, BW single dose of alloxan. Third group treated with 250 mg\kg of oil, flavonoids and tannins extracted from Laurus nobilis, while fourth group was served as diabetic and treated with 250 mg\kg b. w of laurus nobilis extract, all groups were treated orally, the following results were evaluated, fasting blood glucose, triglyceride (TG), total cholesterol (TC), high density lipoprotein-cholesterol (HDL-c), low density lipoprotein-cholesterol (LDL-c), very low density lipoprotein-cholesterol (VLDL-c), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and body weight .After 4 weeks of treating by250 mg\kg BW bay leave extracts there was significant decrease in fasting blood glucose , TG, TC, LDL, VLDL, ALT, AST, ALP, and a significant increase in HDL and body weights.

***Keywords*:** Laurus nobilis; laurel plant; oils; flavonoids; tannins.

1. Introduction

The plant kingdom is rich in by-products which are characterized by their biological activity and physiological effect against incurable diseases of humans and other living organisms. The cultivation of medicinal and aromatic plants and herbs has spread in most parts of the world and their uses and characteristics have varied due to their pharmacological effectiveness and the speed of healing from disease without complications, either as whole herbs, powder or capsules[1].

Medicinal plants are Materials or preparations obtained from various group of plants or from the treated parts of the plant[2].

Various medicinal activities of herbal plants occur as a result of the presence of secondary metabolic compounds, including phenols, alkaloids, saponins, steroids, terpenoids and tannins. These compounds are widely distributed in plants that contain many properties such as antioxidant, antibacterial and anti-inflammatory [3].

Natural plant products are chemical compounds separated from plants, synthesized by following the primary or secondary metabolic pathways. And the study of natural products involves isolating these compounds in their pure form by Soxhlete extraction and chromatographic method، analysis of its composition use and purpose[4].

Diabetes mellitus is a chronic disease related to defect in glucose and lipid metabolism[5] .and it is one of the metabolic diseases characterized by high blood sugar levels [6]. Due to total or partial insulin deficiency [7].It take place when the body is unable to produce or to use enough of the insulin hormone effectively [8].as it includes defects in insulin secretion, insulin action, or both which lead to many complex and severe complications [5].

Treatment of diabetes mellitus has become more difficult because conventional oral anti-diabetic drugs are heterogeneous in their mode of action and cause undesirable effects such as hypoglycemia [9]. Therefore, it has become important to search for new and effective natural drugs against diabetes, due to the difficulty of producing current drugs in addition to the bad complication of these substances.

Many plant species like olive leaves, fenugreek, cloves, and Laurel plant have insulin enhancing activity in experimental studies. Laurel plant that have

*Corresponding author e-mail: aser.scp49@student.uomosul.edu.iq; (Aser Ihsan Abdullah).

Receive Date: 05 June 2021, Revise Date: 14 June 2021, Accept Date: 15 June 2021

DOI: 10.21608/ejchem.2021.79203.3889

an activity that enhances insulin secretion and help in the cure of diabetes. Laurel plant can enhance glucose metabolism in diabetic patients [5].where its activity relates to the presence of active compound such as eugenol, methyl chavicol, flavonoids, alkaloids, tannin, steroids, terpenoid and squalene [6].

Laurel plant is a plant that is widely used in the society as an alternative medicine, the presence of laurel plant is common, readily available and is expected to aid in introduction laurel plant as an alternative herb for health [10] .It is used for the treatment of eructation, epigastric bloating, impaired digestion and flatulence, used as diuretic and has many analgesic effects. The activity of laurel plant is not limited to the hypoglycemic effects, but also it improves lipid metabolism, enhancing liver and kidney function, as it lowers triglycerides, cholesterol, and low-density lipoprotein (LDL) cholesterol, and rises the value of high-density lipoprotein (HDL) cholesterol in patients with type 2 diabetes [5].

The aim of this current study was to evaluate the benefit effect of oils, flavonoids, and tannins laurel plant extract, on blood glucose, lipid profile, liver function and the effect on body weight in alloxan induced diabetic rats.

2. Materials and methods

2.1 Preparation of laurel plant (laurus nobilis)

Leaves of plant were purchased from local markets in Mosul, the leave were cleaned and dried at room temperature and grounded for (2 minutes) with the aid of using electrical grinder [11].

2.11 Extraction of Oils

Sixty grams of ground leaves powder were soaked in petroleum ether for (72 hours) then mixed with (300 ml) petroleum ether for (72 hours) by Soxhlet and filtered by using Buchner funnel and Whatman filter paper. The solvent was dried and concentrated by using rotary evaporator at (40˚C) the extract was kept in a darkish glass container at (4˚C)[11].

2.1.2 Extraction of Flavonoids

The flavonoids were extracted by taking the bagasse resulting from the oil´ extraction process then drying it from the effect of petroleum ether and soaking it with absolute ethanol for (72 hours) in the dark then mixed with absolute ethanol for (72 hours) and filtered by using Buchner funnel and Whatman filter paper. The solvent was dried and concentrated by using rotary evaporator at (40˚C) the extract was kept in a darkish glass container at (4˚C) [5].

2.1.3 Extraction of Tannins

The tannins were extracted by taking the bagasse resulting from the flavonoids´ extraction process then drying it from the effect of ethanol and soaking it with distilled water for (72 hours) in the dark then mixed with distilled water for (72 hours) and filtered by using Buchner funnel and Whatman filter paper. The water was dried and concentrated by using lyophilization device and the extract was kept in a darkish glass container at (4˚C) [12] .

2.2 Induction of Diabetes mellitus

Diabetes mellitus (DM) was induced in overnight fasting rats by using a single dose of alloxan (alloxan monohydrate) (100 mg / kg body weight). Each (100 mg) of alloxan was diluted in (1 ml) of normal saline after injection of alloxan (9). Rats were given (5%) glucose solution for (24hours) with drinking water to prevent drug-induced hypoglycemic mortality [13].

2.3 Experimental design

Three experiments have been done for Seventy two healthy albino male rats ageing between (12 and 14 weeks) and weighting between (150-200) grams were obtained from the animal house in the veterinary college of medicine / Mosul University / Iraq. Animals were randomly distributed and placed in special plastic cages (10 x 20 x 40 cm) covered with stainless steel wire, (6) animals were placed in each cage. Rats were housed under standard laboratory conditions, light and dark cycles of 12h, in a polypropylene cages and allowed free access to feed and tap water under strictly controlled pathogen free conditions with room temperature (25±2ºC), humidity (50±5%)[5].

In each experiment rats were divided into four group. All groups treated orally for 4 weeks:

Group one: represented as control group and rats have been given a distilled water and standard diet.

Group two: represented as diabetes group and rats have been injected by Alloxan (100 mg / kg body weight.

Group three: Rats have been given crude bay leave extract (oil, flavonoids and tannin) at dose 250 mg/kg body weight [13] .

Group four: diabetic rats have been treated by crude bay leave extract at dose 250 mg / kg body weight [13].

2.4 Collection of blood and biochemical analysis

After two week and at the end of experiment period the blood sample were collected by anesthetize the animals for a few seconds and then draw the blood from the Orbital sinus puncture using special capillary tubes, left stand in serum tubes for (30 minutes) to be coagulated. Serum samples were collected by centrifugation at (3000 rpm) for (15 minutes) at room temperature. The clear, non-haemolysed sera was separated and stored at (- 20°C) for determined biochemical analyses that include, blood glucose, cholesterol, triglyceride, HDL-C, LDL-C, VLDL-C, ALT, AST, and ALP [14].

2.4.1

Glucose, Cholesterol, triglyceride, ALT, AST and ALP were estimated in the laboratory by using (Biolabo/French) kit, based on enzymetic method whereas Estimation of HDL-c was done by using (Biolabo/French) kit, based on sedimentation method [15].

2.4.2

Calculation of VLDL-c Concentration was done by following the equation

VLDL-c Concentration= Triglyceride (mg/dl) /5.

Calculation of LDL-c concentration was done by following Friedewald equation

Concentration of LDL-c (mg/dl) = Cholesterol Concentration – HDL-c Concentration – VLDL-c Concentration[15] .

3. Statistical analysis

The data of this experiment calculated by using one-way analysis of difference ,the group differences calculated by using Duncan multiple range test, data are presented as mean± SD, the different letters investigate a significant difference (P<0.05)[13][13].

4. Results and discussion

The main target of antidiabetic plants is to reduce hyperglycemia and vascular complications risks, that can be carried through a number of mechanisms, due to the complexity of glucose metabolism.The backbone of antihyperlipidemic drugs is indicated by statins which inhibit 3-hydroxy-3- methylglutaryl-coenzyme A (HMG-CoA) reductase, reduces the formation of mevalonate, a precursor of cholesterol. In addition, statins can increase number of LDL receptors on hepatocytes which in turn lowers cholesterol [16][16]. Extraction of oil, flavonoids and tannins from laurel plant and identification their effect on healthy and diabetic albino male rats have been done at 3 different and separated experiments. First experiment explain effect of laurel plant oil to healthy and diabetic rats

The results in Table (1) revealed a significant increase (P<0.05) in cholesterol in diabetic group when compared with control group during the trial period (0, 2, and 4 weeks). Also in diabetic group which treated with oil extract when compared with oil group only at dose (250mg/kg BW).

The results indicated that there are no significant changes in oil group when compared with control group at 0 and 2 weeks, while there are a significant decrease (P<0.05) in cholesterol concentration after 4 weeks of administration.

Concentration of triglycerides increases significantly (p<0.05) in diabetic group when compared with control group during the trial period (0,2 and 4 weeks) also in diabetic group that treated with oil extract when compared with oil group at 4 weeks, and there are no significant change in triglyceride concentration between control and oil group at 0 week although a significant decrease ($P< 0.05$) after 2 and 4 weeks.

The comparison between diabetic with oil group and diabetic group notes that there are no significant change at 0 week, while there are a significant decrease (P<0.05) in cholesterol and triglyceride concentration after 2 and 4 weeks of treatment.

Table (1): Effect of oil and alloxan on Cholesterol and triglyceride concentration.

	Cholesterol mg/dl Mean± SD			**Triglyceride mg/dl Mean±SD**		
Groups(n=6)	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks
Control	81.7±2.2 a	79.8±1.0 ab	82.1±7.9 a	80±3.2 a	81.3±2.2 a	78±2.4 a
Diabetic	108±9.7 b	106.7±9.0 c	99.1±1.5 b	98.7±8.3 c	95.3±6.6 b	95±5.6 b
Oil 250mg /Kg	83.7±6.3 a	68.7±12.7 a	58.6±15.6 c	85.7±5.7 ab	70.2±13.9 c	45.3±4.4 c
Diabetic + Oil 250mg/Kg	104±7.3 b	87.7±10.3 b	73.5±9.1 a	91.7±6.3 bc	69.6±5.0 c	52.3±8.1 d

Different small letters in the table refers to a significant differences at (P<0.05) among the groups

Thus treatment of rats with oil extracted from laurel plant lead to decrease in cholesterol, TG, these results are in agreement with S.P.I.D results[13], also our results were consistent with results in other studies in which they observed that administration of the lemon essential oil for 8 weeks decreased the concentration of total cholesterol, LDL, and triglycerides after consuming it [17]. Further analysis of data resulted from the selected clinical trials showed that cumin (Cuminum cyminum L.) essential oil was predominantly used to treat diabetes and dyslipidemia [18].

The results in Table (2) shows a significant decrease (P<0.05) in HDL-c in diabetic group when compared with control group during the trial period (0, 2, and 4 weeks). Also in diabetic group which treated with oil extract when compared with oil group only at dose

(250 mg/kg BW). The results indicated that there are no significantly changes in oil group when compared with control group during the trial period (0, 2 and 4 week). The comparison between diabetic with oil group and diabetic group notes that there are a Significant increase at 2 and 4 weeks at ($P<0.05$) in HDL-c concentration.

Concentration of LDL-c was measured, and the results revered to a significant increase ($P<0.05$) in diabetic group when compared with control group during the trial period (0, 2, and 4 weeks). Also in diabetic group which treated with oil extract when compared with oil group only at dose (250 mg/kg BW) at 0 and 2 weeks.

The results indicated that no any significant change in LDL concentration occurred in oil group when compared with control group during the trial period (0, 2 and 4 weeks) as shown in Table (2).

Significant increase in VLDL-c concentration in diabetic group when compared with control group during the trial period (0, 2, and 4 weeks). And a significant decrease at ($P< 0.05$)between oil group compared with control group at 2 and 4 weeks, and a significant decrease in VLDL-c concentration ccur between diabetic with oil group compared with diabetic group at 2 and 4 weeks.

Table (2): Effect of oil and alloxan on HDL-c, LDL-c and VLDL-c concentration.

	HDL mg/dl Mean±SD			**LDL mg/dl Mean ± SD**			**VLDL mg/dl Mean ± SD**		
Groups(n=6)	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks
Control	38±4.1 a	37.7 ±1.4 a	37.6 ±2.6 a	27.7 ±5.6 a	25.4 ±0.3 a	28.8±9.9 a	16±0.6 a	16.3 ±0.5 a	15.6±0.5 a
Diabetic	21.4 ±2.5 b	18.6 ±0.5 b	17.9 ±1.7 b	66.8 ±6.4 b	69±8.0 c	62.0±3.3 b	19.7 ±1.7 b	19.1 ±1.3 b	19±1.1 b
Oil 250mg /Kg	35.1 ±8.9 a	36.5 ±3.2 a	40.9 ±4.0 a	31.4 ±5.3 a	18.2 ±6.8 a	25.3±1.0 a	17.1 ±1.2 ab	14.0 ±2.8 c	9.1±0.9 c
Diabetic+ Oil 250 mg/kg	19.6 ±3.9 b	25.3 ±3.3 c	31.5 ±5.1 c	66.0 ±9.4 b	48.5 ±12.2 b	31.1 ±11.8 a	18.3 ±1.3 bc	13.9 ±1.0 c	10.5±1.6 d

Different small letters in the table refers to a significant differences at ($P<0.05$) among the groups

In another study recommended that the L. nobilis tea consumption in healthy volunteers can improve blood lipid profile (HDL level increased and a small decrease in levels of LDL and triglycerides) and this implies a possible positive impact on the risk reduction of coronary heart disease [19]. Similar results were reported by Casamassima *et al* results. Whom investigated a substantial reduction in blood lipid profile, glycemic profile and liver enzymes, with decreased levels of LDL, ALT and AST, and increased HDL, has resulted from dietary incorporation of dried bay leaves meal [20].

The data in Table (3) investigated a significant increase ($P<0.05$) in ALT and AST in diabetic group compared with control group during the trial period (0, 2 and 4 weeks). Concentrations of ALT and AST increases significantly ($P< 0.05$) in diabetic group that treated with oil extract compared with oil group at dose (250 mg/kg.BW) at (0 and 4 weeks), and there was no significant change between the groups at 2

Weeks, also ALT and AST have non significantly change when oil group compared with control group at 0 and 2 weeks, but they decrease significantly at 4 weeks.

Comparison of ALT and AST between oil group and diabetic group shows that there concentration significantly decreased during the trial period (0, 2 and 4 weeks).

The ALP increases significantly ($P< 0.05$) in diabetic group compared with control group during the trial period (0, 2 and 4 weeks) and group that treated with oil extract compared with oil group at dose (250 mg/kg.BW).

The results indicated that there are no any significant change in ALP between oil and control group at 0 weeks, but a significant decrease occurred at 2 and 4 weeks.

A significant decrease occurred in ALP concentration between oil and diabetic group during the trial period (0, 2 and 4 weeks).

Our results were consistent with Mohammed *et al*, results which shows that the bioactive components in bay leaves restored the altered enzymes (ALT , AST and ALP)[21]. And with Esteghamati *et al*, notes which states that ALT and AST were significantly decreased in diabetic bay leaves treatment, and related to normal control group. In contrast diabetic group significantly higher level of enzymatic liver function test observed [22].

Table (3): Effect of Oil and alloxan on ALT, AST and ALP activities.

	ALT(U/L) Mean±SD			AST (U/L) Mean ± SD			ALP(IU/L) Mean ± SD		
Groups (n=6)	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks
Control	34.7±1.0 a	35.6±1.6 a	33.7±1.5 a	36±1.8 a	36±1.5 a	34±1.4 a	60.9±3.6 a	61.6±2.8 a	59.5±2.4 a
Diabetic	44.8±1.7 b	46.7±4.0 b	46.6±6.8 b	44.9±1.6 b	46.7±4.0 b	46.6±6.8 b	86.6±5.9 b	84.9±5.8 c	82.6±6.4 b
Oil 250mg /Kg	37.8±3.7 a	32. 0 ± 4.4 a	21.1±0.2 c	37.8±3.7 a	32. 0 ± 4.4 a	21.1±0.2 c	64.3±4.4 a	52.9±2.6 d	44.7±1.6 c
Diabetic+ Oil 250 mg/kg	45.7±3.6 b	39.7 ±12.7 ab	29.8±4.7 a	48.9±2.5 c	39.7 ±12.7 ab	29.8±4.8 a	88.2±5.5 b	70.9±2.2 b	54.8±3.3 d

Different small letters in the table refers to a significant differences at (P<0.05) among the groups

Results in Table (4) shows a significant increase (P<0.01) in glucose concentration in diabetic group when compared with control group during the trial period (0, 2, and 4 weeks), whereas when compared between oil and control groups noted that there are no significant change but when compared the diabetic with oil and oil groups we find that there is a significant increase between them during the trial period (0, 2 and 4 weeks).

Like these results Basak and Candan showed in an in vitro study that the major component of bay leaves essential oil such as 1,8-cineole, a-Terpinene 1-(S)-alfa pinene and R- (+)-limonene, capable to inhibit a-glucosidase activity , thus reduce the rate of glucose uptake [23].

According to body weight the results reported that there was a significantly decrease (p<0.05) in diabetic group compared with control group at 2 and 4 weeks. There is no significant changes oil group compared with control group at 0 and 2weeks, while the diabetic group that treated with oil obtained an improvement in body weight when compared with diabetic group after 2 and 4 weeks as shown in Table (4).

Table (4): Effect of Oil and alloxan on glucose concentration and body weight.

	Glucose mg/dl Mean± SD			Body weight gm Mean±SD		
Groups(n=6)	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks
Control	99±16.3 a	98.0±7.8 a	92.7±6.5 a	175±6.4 a	193.3±6.1 a	210.3±4.5 a
Diabetic	500.3±90.3 b	505.3±98.8 c	486.7±109.4 c	175.6±9.0 a	162.3±2.9 b	160±2.7 b
Oil 250mg /Kg	109.7±9.9 a	88.7±9.7 a	86.7±10.4 a	174.3±7.6 a	188.3±10.2 ac	202.7±7.4 d
Diabetic + Oil 250mg/Kg	440.3±80.2 b	266±29.1 b	206.7±16.0 b	176±6.3 a	183±4.8 b	188±2.9 c

Different small letters in the table refers to a significant differences at (P<0.05) among the groups

These results are in agreement with Mohammed *et al* results which states that the diabetic rats undergo loss of body weight when compared with rats in control group as a result of catabolic disorder [21].

Second experiment explain effect of flavonoids to healthy and diabetic rats.

Flavonoids are a large group of natural compounds found in fruits, vegetables, grains, bark, roots, stems, flowers, tea and wine. A variety of in vitro and in vivo experiments have shown that selected flavonoids exhibit anti-allergic, anti-inflammatory, antiviral and antioxidant activities [24].

The results in Table (5) revealed a significant increase (P<0.05) in cholesterol in diabetic group when compared with control group during the trial period (0, 2, and 4 weeks). Concentration of cholesterol increase significantly at 0 and 4 weeks in diabetic group which treated with flavonoids extract when compared with flavonoids group at dose (250mg/kg BW).

The results indicated that cholesterol concentration did not change significantly in flavonoids group when compared with control group at 0 and 2 weeks.

Concentration of triglycerides increase significantly (P< 0.05) in diabetic group when compared with control group during the trial period at (0,2 and 4 weeks).

Concentration of triglyceride increased significantly in diabetic group which treated with flavonoids extract compared with flavonoids at 0 and 2 weeks, while there are no any significant change at 4 weeks.

The results indicated that there are no significantly changes in flavonoids group when compared with control group at 0 week, while there are a significant decrease after 2 and 4 weeks in triglyceride concentration.

The comparison between diabetic with flavonoids group and diabetic group notes that there are a

significant decrease (P<0.05) between them at 4 weeks in triglyceride concentration, also a significant decrease in cholesterol concentration occurred between them during the trial period (0, 2 and 4 weeks) also cholesterol concentration decreased significantly (P<0.05) when comparison occurred between diabetic with flavonoids group and diabetic group during the trial period (0, 2 and 4 weeks).

Table (5): Effect of flavonoids and alloxan on Cholesterol and triglyceride concentration.

	Cholesterol mg/dl Mean± SD			**Triglyceride mg/dl Mean±SD**		
Groups(n=6)	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks
Control	81.3±3.1 a	75±6.4 a	82.9±9.7 a	86.9±2.5 a	86.2±5.5 a	82.9±5.0 a
Diabetic	103.3±6.0 c	95.4±4.5 b	98.2±6.7 b	101.3±4.8 b	103.4±5.9 b	103.2±6.8 b
Flavonoids 250mg /Kg	82.3±4.2 a	68.8±7.8 a	54.2±4.6 c	89.7±3.3 a	80.9±2.0 *c*	64.5±4.3 c
Diabetic + flavonoids 250mg/Kg	95.3±5.1 b	70.5±11.3 a	63.4±2.3 d	106.6±8.0 b	99.2±2.2 b	69.5±8.4 c

Different small letters in the table refers to a significant differences at (P<0.05) among the groups

The results in Table (6) shows a significant decrease (P<0.05) in HDL-c in diabetic group when compared with control group during the trial period (0, 2, and 4 weeks). Also in diabetic group which treated with flavonoids extract when compared with flavonoids group at dose (250 mg/kg BW).

The results indicated that there are no significantly changes in flavonoids group when compared with control group at 0 week while there are a significant increase at 2 and 4 weeks. The comparison between diabetic with flavonoids group and diabetic group notes that there are a significant increase at 2 and 4 weeks at (P<0.05) in HDL-c concentration.

Concentration of LDL-c was measured, and the results revered to a significant increase (P<0.05) in diabetic group when compared with control group during the trial period (0, 2, and 4 weeks). Also in diabetic group which treated with flavonoids extract when compared with flavonoids group at dose (250 mg/kg BW).

these results are in agreement with Al Chalabi *et al* results which they revealed a significant (P<0.05) increase in triglyceride, cholesterol, LDL, VLDL in diabetic rats compared with control and groups that treated with ethanolic extract, treatment of diabetic rats for 4 weeks by the ethanolic extract lead to a significant decrease all lipid profile in diabetic groups compared with control and groups that treated with ethanolic extract[5].

The results indicated that there were a significantly decrease (P<0.05) in LDL concentration in flavonoids group when compared with control group at 2 and 4 weeks as shown in Table (6).

Significant increase in VLDL-c concentration in diabetic group when compared with control group during the trial period (0, 2, and 4 weeks), and between flavonoids compared with control groups at 4 weeks, also between diabetic with flavonoids group compared with diabetic group at 4 weeks.

Table (6): Effect of flavonoids and alloxan on HDL-c, LDL-c and VLDL-c concentration.

	HDL-c mg/dl Mean±SD			**LDL-c mg/dl Mean ± SD**			**VLDL-c mg/dl Mean ± SD**		
Groups(n=6)	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks
Control	34.5±3.7 a	31.7±1.9 a	32.3±3.0 a	29.4±2.4 a	25.9± 4.9 a	34.0±7.0 a	17.3±0.5 a	16.9±0.9 a	16.5±1.0 a
diabetic	19.8 ±1.1 b	20.4±2.2 c	21.1±1.3 c	63.2±6.9 c	54.3±3.6 b	56.4±5.2 b	20.2±1.0 b	20.6 ±1.2 b	20.6±1.3 b
Flavonoids 250mg /Kg	31.7±2.3 a	37.0±2.7 b	35.8±1.7 b	32.8±6.4 a	15.4±9.9 c	5.46±4.0 c	17.9±0.70 a	16.2±0.4 a	12.9±0.8 c
Diabetic+ flavonoids 250 mg/kg	20.6±1.8 b	24.6±3.4 d	28.7±3.2 d	53.3 ±6.6 b	26.0±9.5 a	20.7±6.7 d	21.3±1.6 b	19.4 ±0.4 b	13.9±1.7 c

Different small letters in the table refers to a significant differences at (P<0.05) among the groups

These present results have shown that a concentration of cholesterol, TG, LDL and VLDL in diabetic groups treated with flavonoids extract of laurel plant have been reduced (Tables 5,6), the pest explanation of this results may be due to flavonoids and its derivatives that presents in laurel plant, participate in the management of lipids profile. An experimental study in rats reported that treatment diabetic rats with quercetin caused depression in the value of cholesterol and triglycerides [25], this effect due to inhibition of secretion of triglycerides from liver into blood ,treatment rats by alcoholic extract of laurel plant improve the insulin level in diabetic groups , reduce the activity of lipases

enzyme and leads to reduction in cholesterol level [5], as well as the decrease in concentrations of triglycerides, cholesterol and low-density lipoprotein could be related to the role of laurel plant in reducing liver enzymes that formed fatty acids or could be due to inhibiting the Acetyl-CoA Synthetase, which was an essential enzyme in the synthesis of fatty acids [26].

The data in Table (7) investigated a significant increase ($P<0.05$) in ALT, and ALP in diabetic group compared with control group and group that treated with flavonoids extract compared with flavonoids group at dose (250 mg/kg.BW) during the trial period (0,2 and 4 weeks).

AST increase significantly ($P< 0.05$) in diabetic group compared with control group during the trial period (0, 2 and 4 weeks). And group that treated with flavonoids extract compared with flavonoids group at dose (250 mg/kg.BW) at o and 2 weeks.

These results are corresponding with Al Chalabi *et al*, results in which they investigated a significant ($P<0.05$) increase in ALT AST and ALP activities in diabetic rats compared with control and groups that treated with alcoholic extract, but treatment of diabetic rats by ethanolic extract for 4 weeks lead to significant decrease in the liver function in diabetic groups compared with control. Also the results shows a significantly decrease ($P<0.05$) in ALT concentration in flavonoids group when compared with control group at 2 and 4 weeks and between diabetic with flavonoids group compared with diabetic group especially after 4 weeks of treatment[5].

AST concentration significantly unchanged when comparison occurred between flavonoids group and control group during the trial period (0,2 and 4 weeks) also there was no significant difference in ALP in flavonoids group compared with control group at 0 weeks whereas significant decrease occurred after 2 and 4 weeks, and significant decrease ($p< 0.05$) in ALP in diabetic with flavonoids group compared with diabetic group during the trial period (0, 2 and 4 weeks). these results means that there was significant decrease in the liver function in diabetic groups compared with control group.

Table (7): Effect of flavonoids and alloxan on ALT, AST and ALP activity.

	ALT(U/L) Mean±SD			**AST (U/L) Mean ± SD**			**ALP(IU/L) Mean ± SD**		
Groups(n= 6)	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks
Control	36.6 ±4.0 a	38.2±4.6 a	35.7±3.2 a	37.1 ±7.9 a	35.8 ±5.4 a	35.1±8.6 a	61.2 ±3.6 a	59.8±1.0 a	57.7±2.4 a
Diabetic	45.6 ±2.2 b	46.3±4.9 b	46.6±4.1 b	53.6 ±4.2 b	52.2 ±1.9 c	52.1 ±6.5 b	96.3 ±4.9 c	95.5±2.7 b	93.8±3.1 b
Flavonoids 250mg /Kg	35.1 ±2.9 a	26.8±3.8 c	21.9± 2.7 c	44.7±15 .3 a	35.3 ±7.6 a	27.3 ±5.6 a	61.8 ±4.0 a	51.8±3.2 c	37.6±5.1 c
Diabetic+ flavonoids 250 mg/kg	42.3 ±3.8 c	44.0±4.3 b	33.0±3.6 a	54.5 ±7.7 b	43.7 ±7.9 b	31.9 ±7.9 a	86.5 ±5.7 b	67.4 ±12.0 a	52.5±18. 6 a

Different small letters in the table refers to a significant differences at ($P<0.05$) among the groups

The present study also investigated that after 4 weeks of treatment by laurel plant flavonoids extract there was a statistical reduction in liver function marker that includes ALT, AST, and ALP activates in diabetic groups compared with control (Table 7), the possible mechanism of this results due to the antioxidant compounds in this extract works as a proof of the phenomenon of fat oxidation associated with diabetes and consequential them from necrosis and damage to the cells of the liver and thus regulate liver function[27]. These compounds inhibit hepatocyte apoptosis and exerted hepatoprotective role on experimentally induced diabetic rats by the anti-apoptosis action , recover liver histopathological disturbances, prevent diabetic liver damage by elevating and improving antioxidant enzyme activity which leads to decrease the liver injury markers such as ALT, AST and ALP activities [28].

Results in Table (8) shows a significant increase ($P<0.01$) in glucose concentration in diabetic group when compared with control group during the trial period (0, 2, and 4 weeks), whereas when compared between flavonoids and control groups noted that there are no significant change. When compared the diabetic with flavonoids and flavonoids groups we find that there is a significant increase between them during the trial period (0, 2 and 4 weeks). These results are in

agreement with other studies that illustrated a significant ($P<0.05$) increase in fasting blood glucose in diabetic groups as compared to control group and groups that treated by bay leave extract , but after 4 weeks of treatment by Laurel plant extract, a

significant (P<0.05) decrease occurred in blood glucose and in diabetic groups compared to control[5], similarly Cao et al attributed the significant decrease in fasting blood glucose in diabetic rat treated with flavonoids extract in (Table 8) , to the presence of various phenolic compounds such as flavonoids, alkaloids, glycosoide, coumarins, xanthenes, and procyanidins in these extracts, these compounds are able to prevent the depletion of endogenous antioxidants through scavenging free radicals and exhibits in tend to increase the amount of proteins involved in insulin signaling and glucose transport, also stimulates the insulin secretion from pancreas [29].

According to body weight the results reported that there was a significantly decrease (p<0.05) in diabetic group compared with control group at 2 and 4 weeks.

The reduction in initial body weight in diabetic groups compared control group and diabetic group treated with flavonoids extract , was related to the insulin concentration deficiency that leads to breakdown of protein and fatty acids, the deficiency of insulin hormone in diabetic groups causes excess degradation of protein which lead to increasing of amino acid levels in the blood , but treatment by bay leave flavonoids extract ,an increase in body weight occurred in diabetic groups , this results indicate that, this extract is very consequential in preventing protein degradation and weight loss by stimulating the insulin secretion [30].

There is no significant changes in flavonoids group compared with control group, while the body weight of diabetic treated with flavonoid groups obtained an improvement in body weight compared with diabetic group at 2 and 4 weeks as shown in Table (8). These results were identical with Al Chalabi *et al*, results. They notes that there was a decrease in final body weight in diabetic group compared with initial body weight of the same group, while the body weight of diabetic group treated with Laurel bay leave extract obtained an improvement in final body weight compared with initial body weight after 4 weeks of treatment.

Table (8): Effect of flavonoids extract and alloxan on glucose concentration and body weight.

	Glucose mg/dl Mean± SD			**Body weight gm Mean±SD**		
Groups	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks
Control	89.7±6.9 a	95.0±4.9 a	96.3±7.2 a	173.3±8.9 a	189±2.7 a	203.3±6.1 a
Diabetic	472.7±79.9 b	458.3±70.7 c	440.3±56.3 c	177±7.1 a	165±4.7 b	163.3±5.5 b
Flavonoids 250mg /Kg	94.7±4.2 a	86.3±5.9 a	77.7±3.7 a	175.7±6.6 a	186.3±5.6 a	200.3±4.0 a
Diabetic + flavonoids 250mg/Kg	548.3±43.6 c	392.3±41.1 b	352.0±33.8 b	180±3.2 a	174.7±5.2 c	192.7±4.9 c

Different small letters in the table refers to a significant differences at (P<0.05) among the groups

Experiment number 3 explain the tannin extract effect on healthy and diabetic rats.

The results in table (9) revealed a significant increase ($P< 0.05$) in cholesterol and triglycerides in diabetic group compared with control group during the trial period (0, 2 and 4 weeks). Also in diabetic group which treated with tannin extract when compared with tannin group at dose (250 mg/ kg.BW).

The results indicated that there are no significantly changes in cholesterol concentration in tannin group when compared with control group at 0 week, while there are a significant decrease after 2 and 4 weeks, and there are significant increase ($P< 0.05$) in triglyceride concentration when tannin group compared with control group at 0 week, and decrease significantly at 2 and 4 weeks.

The comparison between diabetic with tannin group and diabetic group notes that there are no significant change at 0 week, while there are a significant decrease after 2 and 4 weeks at (P<0.05) in cholesterol and triglyceride concentration.

The results in Table (10) shows a significant decrease(P<0.05) in HDL-c in diabetic group when compared with control group also in diabetic group which treated with tannin extract when compared with tannin group only at dose (250 mg/kg BW) during the trial period (0, 2, and 4 weeks).

The results indicated that there are no significantly changes in tannin group when compared with control group at 0 and 2 weeks.

Concentration of LDL-c was measured, and the results revered to a significant increase (P<0.05) in diabetic group when compared with control group. Also in diabetic group which treated with tannin extract when compared with tannin group only at dose (250 mg/kg BW) during the trial period (0, 2, and 4 weeks).

The results indicated that no any significant change in LDL concentration occurred in tannin group when compared with control group at 0 and 2 weeks, but a significant decrease occurred between them at 4 weeks as shown in Table (10).

Significant increase in VLDL-c concentration in diabetic group when compared with control group during the trial period (0, 2, and 4 weeks), and between tannin group compared with control group at 0 week but a significant decrease is noted VLDL-c when comparison occur occurred between tannin and control

group after 2 and 4 weeks, also a significant decrease occurred when diabetic with tannin group compared with diabetic group at 2 and 4 weeks.

Table (9): Effect of Tannins and alloxan on Cholesterol and triglyceride concentration.

	Cholesterol mg/dl Mean± SD			**Triglyceride mg/dl Mean±SD**		
Groups(n=6)	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks
Control	73.3±4.2 a	71.1±5.8 a	74±7.6 a	76.7±2.2 a	79.6±1.5 a	78.5±1.7 a
Diabetic	107±10.1 b	106.4±8.1 c	104.5±6.4 b	96.3±5.3 c	99.8±3.5 b	99.5±2.9 b
Tannins 250mg /Kg	79.3±1.4 a	63.0±5.6 d	50.1±4.8 c	84.5±9.9 b	69.6±10.3 c	59.6±6.2 c
Diabetic + Tannins 250mg/Kg	106.7±6.4 b	91.7±3.1 b	78.9±1.3 a	100.6±2.2 c	86.0±5.3 a	69.4±3.2 d

Different small letters in the table refers to a significant difference at (P<0.05) among the groups

Table (10): Effect of tannins and alloxan on HDL-c, LDL-c and VLDL-c concentration.

	HDL Mg/dl Mean±SD			**LDL mg/dl Mean ± SD**			**VLDL mg/dl Mean ± SD**		
Groups(n=6)	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks
Control	34.6±2.5 a	33.8±3.3 a	34.3±4.1 a	23.4±6.8 a	21.4±4.0 a	24.0±3.3 a	15.3±0.45 a	15.9±0.3 a	15.7±0.4 a
Diabetic	20.58±7.3 b	20.2±2.0 b	20.3±0.8 c	67.2±12.1 b	66.2±8.6 c	64.3±6.6 c	19.2±1.1 c	19.9±0.7 b	19.9±0.6 b
Tannins 250mg /Kg	35.7±3.7 a	34.7±1.9 a	37.8±1.7 b	26.8±2.3 a	14.4±8.3 a	8.8±0.6 d	16.9±1.9 b	13.9±2.1 c	11.9±1.2 c
Diabetic+ tannins 250 mg/kg	18.7±4.4 b	23.8±3.5 c	31.7±1.5 a	68.2±6.3 b	50.6±5.3 b	33.4±1.1 b	20.1±0.4 c	17.2±1.0 a	13.9±0.6 d

Different small letters in the table refers to a significant differences at (P<0.05) among the groups

Our study results was consistent with Matsumoto study results who states that Kaki-tannin deterred elevation of plasma total cholesterol, non-HDL cholesterol, triglycerides, and insulin in type 2 diabetic mice fed a high fat diet. Moreover, intake of kaki-tannin prevented fatty liver and induced the genes related to cholesterol metabolism [31].

The data in Table (11) investigated a significant increase (P<0.05) in ALT and ALP in diabetic group compared with control group during the trial period (0, 2 and 4 weeks). Also in diabetic group that treated with tannin extract at dose (250 mg/kg.BW) compared with tannin group during the trial period (0, 2 and 4 weeks). The AST increase significantly (P< 0.05) in diabetic group compared with control group at 4 weeks and diabetic group that treated with tannin extract compared with tannin group at dose (250 mg/kg.BW) at 2 weeks without significant change between them at 0 and 4 weeks.

Results revealed that comparison between tannin group and control group significantly unchanged, but significant decreases shown when tannin group compared with diabetic group at 4 weeks only.

Table (11): Effect of Tannins and alloxan on ALT, AST and ALP activities.

	ALT(U/L) Mean±SD			**AST (U/L) Mean ± SD**			**ALP(IU/L) Mean ± SD**		
Groups (n=6)	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks
Control	36.4±3.2 a	37.6±3.1 a	35.7±1.6 a	40.8±2.7 a	34.9±1.9 ab	31.7±2.9 a	56.5±2.8 a	49.5±2.9 a	49.4±3.6 a
Diabetic	49.1±4.7 c	45.5±5.5 b	40.0±1.1 b	46.2±4.4 ab	34.7±6.9 ab	42.9±8.4 b	87.9±4.3 b	77.4±8.5 b	56.7±7.3 b
Tannins 250mg /Kg	34.9±3.1 a	27.6±2.4 c	23.3±3.1 c	45.4±6.3 ab	33.3±3.3 a	30.8±2.1 a	60.3±1.9 a	49.8±6.3 a	34.9±4.8 c
Diabetic+ Tannins 250 mg/kg	43.5±2.7 b	36.6±4.2 a	25.6±2.7 d	48.9±3.2 b	39.0±3.8 b	31.0±2.3 a	88.7±5.4 b	70.5±5.1 b	53.4±3.1 ab

Different small letters in the table refers to a significant differences at (P<0.05) among the groups

Yuniarti and Lukiswanto showed that alloxan caused a significant increase in AST and ALT activity [32]. In this study, a significant decrease in the AST and ALT activity was observed in diabetic animals treated with the aqueous extract of bay leaves. Similarly, Gasparyan et al. observed that administration of bay leaves extract

lead to normalization of AST and ALT activities that indicated the hepatoprotective properties[33].

Results in Table (12) shows a significant increase (P<0.05) in glucose concentration in diabetic group when compared with control group during the trial period (0, 2, and 4 weeks), whereas when compared between tannin and control groups noted that there are no significant change. When compared the diabetic with tannin and tannin groups we find that there is a significant increase between them during the trial period at (0, 2 and 4 weeks).

According to body weight the results reported that there was a significantly decrease (p<0.05) in diabetic group compared with control group at 2 and 4 weeks. There is no significant changes when tannin group compared with control group during the trial period (0,2 and 4 weeks), while the body weight of diabetic treated with tannin groups obtained an improvement in body weight compared with diabetic group after 2 and 4 weeks as shown in Table (12).

Table (12): Effect of tannins and alloxan on glucose concentration and body weight.

	Glucose mg/dl Mean± SD			**Body weight gm Mean±SD**		
Groups(n=6)	0 week	2 weeks	4 weeks	0 week	2 weeks	4 weeks
Control	89.6±6.8 a	92.3±9.2 ab	88.3±6.8 a	178.7±8.5 a	189±10.3 a	203±7.1 a
Diabetic	405±34.9 b	381.3±26.4 c	366.7±34.6 c	180±1.8 a	172±5.9 b	165.7±4.0 b
Tannins 250mg /Kg	98.7±8.1 a	84.3±4.2 a	77±3.9 a	175±4.9 a	186.3±4.9 a	199.3±2.9 a
Diabetic + tannins 250mg/Kg	489.3±90.4 c	132±60.9 b	130.3±46.3 b	178±4.1 a	182.3±4.2 a	198±4.7 a

Different small letters in the table refers to a significant differences at (P<0.05) among the groups

Results indicated elevation in the level of blood glucose in diabetic group after induction of diabetic by alloxan with highly significant decrease in the blood glucose level in the diabetic animals treated with the aqueous extract of bay leaves. This result comes in agree with Khan et al. who noted that bay leaves reduces the level of blood glucose in diabetic people [34]. Also Aljamal explained that the antidiabetic activity of laurus nobilis related to the presence of polyphenols compound which affected the insulin sensitivity, glucose uptake and antioxidant status [35].

The results of this study showed a highly significant decrease in the body weight of alloxan diabetic rats compared to control animals. This weight loss may result from catabolic disorder. Similarly, continuous reduction in body weight of the diabetic rats was

observed by Nagy and Amin who attributed this to catabolic disorder on protein metabolism by retarding protein synthesis and stimulating protein degradation [36].

5. Conclusion

According to all of these results, the administered oil, flavonoids and tannin extracted from laurel plant are able to reduce blood glucose, cholesterol, and triglyceride, LDL-c, VLDL-c, ALT, AST and ALP
In diabetic albino male rats, also leads to increase value of HDL-c concentration and Body weight which reflect the importance and active role of laurel plant extracts as alternative medicine for treatment of type 2 diabetic and its complication.

Acknowledgments

Most sincere thanks and acknowledge to University of Mosul, College of Science, Department of Chemistry For the support.

References

[1] N.A.-L. Ali, Effect of adding different levels of crushed laurel leaves (Laurus nobilis) to the diet of broiler chickens on some physiological blood traits, EurAsian Journal of BioSciences 14(1) (2020) 449-452.
[2] O. Aina, L. Gautam, P. Simkhada, S. Hall, Prevalence, determinants and knowledge about herbal medicine and non-hospital utilisation in southwest Nigeria: a cross-sectional study, BMJ open 10(9) (2020) e040769.
[3] V. Verawati, D. Nofiandi, P. Petmawati, Pengaruh metode ekstraksi terhadap kadar Fenolat total dan aktivitas antioksidan daun Salam (Syzygium polyanthum (Wight) Walp.), Jurnal Katalisator 2(2) (2017) 53-60.
[4] K. Chahal, M. Kaur, U. Bhardwaj, N. Singla, A. Kaur, M. Kaur, U. Bhardwaj, N. Singla, A. Kaur, A review on chemistry and biological activities of Laurus nobilis L. essential oil, Journal of Pharmacognosy and Phytochemistry 6(4) (2017) 1153-1161.
[5] S. Al Chalabi, D. Majeed, A. Jasim, K. Al-Azzawi, Benefit effect of ethanolic extract of Bay leaves (Laura nobilis) on blood sugar level in adult diabetic rats induced by alloxan monohydrate,

Ann. Trop. Med. Publ. Health 23(16) (2020) SP231608.
[6] T. Widyawati, M.A. Pase, M. Daulay, I.B. Sumantri, Effect of Bay Leaf Ethanol Extract on Blood Glucose Level in Patients with Type 2 Diabetes Mellitus, 6th International Conference on Public Health 2019, Sebelas Maret University, pp. 613-617.
[7] O. Mansour, M. Darwish, G. Ismail, Z. Douba, A. Ismaeel, K. Eldair, Review study on the physiological properties and chemical composition of the Laurus nobilis, The Pharmaceutical and Chemical Journal, Coden 5(1) (2018) 225-231.
[8] J. Proboningsih, A. Joeliantina, A. Novitasari, D. Purnamawati, Complementary treatment to reduce blood sugar levels of DMT2 patients, International Journal of Public Health 9(3) (2020) 267-271.
[9] A.A. Ghadge, A.A. Kuvalekar, Controversy of oral hypoglycemic agents in type 2 diabetes mellitus: novel move towards combination therapies, Diabetes & Metabolic Syndrome: Clinical Research & Reviews 11 (2017) S5-S13.
[10] K. Harismah, Pemanfaatan Daun Salam (Eugenia Polyantha) Sebagai Obat Herbal Dan Rempah Penyedap Makanan, Warta Lpm 19(2) (2017) 110-118.
[11] ن.ع.ه. السامرائي, تقدير الفلا فونيدات في اوراق نبات الغار Bay Laurel ودراسة فعاليتها الحيوية, Tikrit Journal of Pure Science 22(7) (2018) 109-114.
[12] A.H.M. Muhayyidin, N.A. Ghazali, N.F.A. Bakar, W.A. Ibrahim, A. Sauki, Z. Hassan, Tannin Extraction from Bark of Rhizophora Mucronata Using Soxhlet and Boiling Techniques, Int. J. Adv. Sci. Eng. Inf. Technol. 8 (2018) 2525-2530.
[13] S.P.I.D. MALE, STUDY THE EFFECT OF BAY LEAF EXTRACTON THE SOMEBIOCHEMICAL PARAMETERS IN DIABETIC MALE RAT INDUCED BY ALLOXAN.
[14] A. Atta, M. Shalaby, I. Shokry, A. Ahmed, Interaction between oral hypoglycemics and antibiotics on blood glucose level of normal fasted and alloxan-diabetic rats [Egypt], Veterinary Medical Journal, Cairo Univ (1983).
[15] A.H. Wu, Tietz clinical guide to laboratory tests-E-book, Elsevier Health Sciences2006.
[16] S.C. Heghes, L. Filip, O. Vostinaru, C. Mogosan, D. Miere, C.A. Iuga, M. Moldovan, Essential oil-bearing plants from Balkan Peninsula: Promising sources for new drug candidates for the prevention and treatment of diabetes mellitus and dyslipidemia, Frontiers in Pharmacology 11 (2020) 989.
[17] H. Lee, M. Woo, M. Kim, J.S. Noh, Y.O. Song, Antioxidative and cholesterol-lowering effects of lemon essential oil in hypercholesterolemia-induced rabbits, Preventive nutrition and food science 23(1) (2018) 8.
[18] A. Hadi, H. Mohammadi, Z. Hadi, N. Roshanravan, M. Kafeshani, Cumin (Cuminum cyminum L.) is a safe approach for management of lipid parameters: A systematic review and meta- analysis of randomized controlled trials, Phytotherapy Research 32(11) (2018) 2146-2154.
[19] C. Chbili, M. Maoua, M. Selmi, S. Mrad, H. Khairi, K. Limem, N. Mrizek, S. Saguem, M. Ben Fredj, Evaluation of daily Laurus nobilis tea consumption on lipid profile biomarkers in healthy volunteers, Journal of the American College of Nutrition 39(8) (2020) 733-738.
[20] D. Casamassima, M. Palazzo, F. Vizzarri, R. Coppola, C. Costagliola, C. Corino, A. Di Costanzo, Dietary effect of dried bay leaves (Laurus nobilis) meal on some biochemical parameters and on plasma oxidative status in New Zealand white growing rabbit, Journal of animal physiology and animal nutrition 101(5) (2017) e175-e184.
[21] R.R. Mohammed, A.K. Omer, Z. Yener, A. Uyar, A.K. Ahmed, Biomedical effects of Laurus nobilis L. leaf extract on vital organs in streptozotocin-induced diabetic rats: Experimental research, Annals of Medicine and Surgery 61 (2021) 188-197.
[22] A. Esteghamati, D. Eskandari, H. Mirmiranpour, S. Noshad, M. Mousavizadeh, M. Hedayati, M. Nakhjavani, Effects of metformin on markers of oxidative stress and antioxidant reserve in patients with newly diagnosed type 2 diabetes: a randomized clinical trial, Clinical nutrition 32(2) (2013) 179-185.
[23] S.S. Basak, F. Candan, Effect of Laurus nobilis L. essential oil and its main components on α-glucosidase and reactive oxygen species scavenging activity, Iranian journal of pharmaceutical research: IJPR 12(2) (2013) 367.
[24] E.Z. Yassine, B. Dalila, B.S. El MansouriLatifa, S. Lebtar, A. Sanae, F. Abdellah, Phytochemical screening, anti-inflammatory activity and acute toxicity of hydro-ethanolic, flavonoid, tannin and mucilage extracts of Lavandula stoechas L. from Morocco, Int J Pharm Phytochem Res 8(1) (2016) 31-37.
[25] M. Rafieian-Kopaei, A. Baradaran, M. Rafieian, Oxidative stress and the paradoxical effects of antioxidants, Journal of Research in Medical Sciences 18(7) (2013) 628.
[26] F. Titilayo, S. Mojisola, H. Osheiza, Fermentation conditions and process optimization of citric acid production by yeasts, International Journal of Biotechnology 7(1) (2018) 51-63.
[27] V. Sánchez-Valle, N. C Chavez-Tapia, M. Uribe, N. Méndez-Sánchez, Role of oxidative stress and molecular changes in liver fibrosis: a review,

Current medicinal chemistry 19(28) (2012) 4850-4860.
[28] M.M. Alam, D. Meerza, I. Naseem, Protective effect of quercetin on hyperglycemia, oxidative stress and DNA damage in alloxan induced type 2 diabetic mice, Life sciences 109(1) (2014) 8-14.
[29] H. Cao, M.M. Polansky, R.A. Anderson, Cinnamon extract and polyphenols affect the expression of tristetraprolin, insulin receptor, and glucose transporter 4 in mouse 3T3-L1 adipocytes, Archives of biochemistry and biophysics 459(2) (2007) 214-222.
[30] K. Qian, S. Zhong, K. Xie, D. Yu, R. Yang, D.W. Gong, Hepatic ALT isoenzymes are elevated in gluconeogenic conditions including diabetes and suppressed by insulin at the protein level, Diabetes/metabolism research and reviews 31(6) (2015) 562-571.
[31] K. Matsumoto, S.-i. Yokoyama, Induction of uncoupling protein-1 and-3 in brown adipose tissue by kaki-tannin in type 2 diabetic NSY/Hos mice, Food and chemical toxicology 50(2) (2012) 184-190.
[32] W.M. Yuniarti, B.S. Lukiswanto, Altered Liver and Renal Serum Marker Enzymes in Alloxan Induced Diabetic Rats Treated with Phyllantus niruri, Journal of Applied Environmental and Biological Sciences 6(12) (2016) 94-98.
[33] G. Gasparyan, S. Tiratsuyan, S. Kazaryan, H. Vardapetyan, Effect of Laurus nobilis extract on the functioning of liver against CCl4 induced toxicity, Journal of Experimental Biology and Agricultural Sciences 3(2) (2015) 174-183.
[34] A. Khan, G. Zaman, R.A. Anderson, Bay leaves improve glucose and lipid profile of people with type 2 diabetes, Journal of clinical biochemistry and nutrition 44(1) (2009) 52-56.
[35] A. Aljamal, Effects of bay leaves on blood glucose and lipid profiles on the patients with type 1 diabetes, World Academy of Science, Engineering and Technology 69 (2010) 211-214.
[36] M. Nagy, K. Amin, Biochemical and histopathological analysis of Cystoseira myrica aqueous extract on alloxan induced diabetic rats, Biochem. Indian J 9 (2015) 81-91.