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Commiphora molmol (Myrrh) Modulates the Insulin Signaling in Skeletal Muscle of Diabetic Rats

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Abstract

Diabetes mellitus is a cluster of metabolic diseases evidenced by hyperglycemia and disorders in insulin secretion. The focus of this research was to look into the therapeutic effects of aqueous extract of *Commiphora molmol* (Myrrh) on alloxan-induced diabetic rats. 30 adult female albino rats were randomly divided into three groups (10 rats each): Normal control group (GI), untreated diabetic group (GII), and diabetic rats treated by oral administration of aqueous extract of Myrrh (0.5g/kg B.wt.) (GIII) for 30 days. Myrrh extract showed hypoglycemic and hypolipidemic effects, as well as amelioration of the oxidative stress in serum and muscle due to reducing malondialdehyde (MDA) and increasing the total antioxidant capacity (TAC) concentration. These effects were accompanied by a significant upregulation of muscular insulin receptor (IR), insulin receptor substrate-1 (IRS-1) and glucose transporters-4 (GLUT-4) genes expression. Aqueous extract of *Commiphora molmol* (Myrrh) has a potential therapeutic influence not only improves the glycemic status but also improves insulin signaling via restoring the oxidation state.

Keywords Diabetes. *Commiphora molmol*, MDA, TAC. Muscular gene expression

1. Introduction

Diabetes mellitus (DM) is the most predominant metabolic condition, affecting a vast number of people around the world. The fundamental cause of DM is the disruption of metabolic pathways which affect glucose and fat metabolism; these 2 key cellular substrates result in production of unhealthful metabolites [1] The diabetes can cause vascular problems, which can cause structural and functional alterations in tissues, as well as organ malfunction or failure [2]. However, beta-cell malfunction, reduced insulin quantity or sensitivity, or insulin resistance (IR), as well as apoptosis, mitochondrial dysfunction, oxidative stress, and inflammation, are all involved in the pathophysiology [1&3]. The insulin signaling cascade begins when insulin binds to the transmembrane insulin receptor (IR), which is followed by downstream actions that allow glucose to enter cells via glucose transporters (GLUT). GLUT-4 is one among these transporters, which, unlike other transporters, is insulin-dependent [4&5]. The first or major problem is assumed to be skeletal muscle insulin resistance, appearing decades before cell loss and hyperglycemia develop. In the postprandial state, in humans, muscle is the predominant site of glucose absorption. Muscle is responsible for eighty percent of glucose absorption under euglycemic hyper insulinemic circumstances [6]. The ability to metabolize fat is reduced in type 2 diabetics. The skeletal muscle oxidative capacity was found to be reduced when samples were taken. The insulin-resistant of skeletal muscle has metabolic capacity that be tuned toward esterified of fat instead of fat oxidation. A mismatch among intake of fatty acid and its oxidation can readily give rise to lipid storage in muscle, that lead to insulin resistance, as previously stated [7]. Maintaining glycemic control and preventing the initiation and progression of metabolic disorders are two of the most important therapy goals in DM management [8]. As a result, additional safe and effective medications and therapy techniques are needed to avoid numerous of the risk factors related with diabetes in the short and long term [9 & 10]. Several plant extracts have been proposed as having anti-diabetic effects. C. myrrha (Commiphora myrrha) has lowering effect of glucose and lipid, and antioxidant properties. C. myrrha extraction decreased high glucose level in diabetic rats by raising blood insulin levels. At obese rats, it also lowered weight growth and improved lipid profiles and hyperlipidemia [11]. Commiphora molmol, often known as 'myrrh' or Murr, is a species of Commiphora

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(in Arabic) [12]. It's an aromatic gum resin with a lot of bioactive substances like flavonoids, tannins, saponins, polyphenolic compounds, triterpenoids, alkaloids, saponins, and volatile oils, as well as furanodienes, which have a lot of medicinal applications and analgesic activity [13 &14]. As a result, the aim of the research was to view the reducing influence of Myrrh on diabetic albino rats that injected with Alloxan material on muscular insulin receptors and glucose transporter Phytochemical analyses of Myrrh resin will also be performed out in order to obtain a complete picture of the extracted plant elements.

2. Material and methods

2.1 Animals

Thirty albino rats (female) weigh 120-140 g were purchased from the Egyptian Organization for Biological Products and Vaccines (Helwan, Cairo, Egypt). Rats were kept in conventional cages (3 rats per cage) under standard conditions (12 h light/dark cycles, 50% humidity, and 28 °C 3). The rats will be fed a basal meal for 7 days throughout the adaption phase. There was plenty of food and water available. After examination by its study ethical council for animal research topic, the National Hepatology & Tropical Medicine Research Institute (NHTMRI) in Cairo, Egypt, accepted experiment protocol (approval number A5-2021).

2.2 Design of the study

Three groups of animals were assigned randomly (10 rats each): Rats served as

1- normal control (GI)
2- diabetic rats (GII) : (fasting blood glucose level greater than 300 mg/dl). Orally, these rats were given distilled water (1ml/kg body weight) and were left untreated.
3- Treated group (GIII) were diabetic rats treated orally by gavage with the extract of *Commiphora molmol* (*Myrrh*) (0.5g/ Kg b.wt) [15]. Rats were given a four-week assignment. The animals' weights were measured weekly.

2.3 Induction of Diabetes Mellitus

After fasting for 12 hours, a single intravenous a newly prepared alloxan injection (Sigma, USA) solution. The dose was 120 mg/kg weight of body was used to induce diabetes [16]. The glucose level of rats was tested using a glucometer 48 hours after administrating of alloxan, and those who have sugar levels less than 300 mg/dl were declared diabetic.

2.4 Plant extraction preparation

In Jeddah, Saudi Arabia, Commiphora molmol (Myrrh) was obtained from a local market. It's been washed, dried, and powdered to a fine consistency. Myrrh extract was made by dissolving 50 grams of plant resin powder in 125 ml of water without adding any suspending agents and storing it at 4 °C.

2.5 Blood collection and Muscle biopsy

Finally, the animals were weighed and anesthetized with urethane intraperitoneally. (99 percent, Aldrich). Urethane is given in the same rate, one gram per kilogram of body weight. Samples of blood were collected from the retro-orbital venous plexus after nightly fast. The samples were coagulated at 37°C for 15 minutes, after that, centrifuged for 15 minutes at 4000 RPM. rpm to extract the serum, which was then stored at -18°C. Betadine was used to sterilize the skin above the muscle, then 1 percent lidocaine was injected subcutaneously. A scalpel was used to make 2-cm incision, then used 5-mm Bergstrom biopsy needle to retrieve core muscle biopsy punch (Depuy Co.) [17]. Filter paper was used to dry the muscle tissue, which was then weighted and soaked in (phosphate buffer saline PBS,7.4 PH), For biochemical and gene expression tests, as well as histological exams, the muscle tissue was snap-frozen (at -80°C).

2.6 Biochemical analysis

2.6.1. Serum analyses

Glucose concentration was estimated by using the commercially available kit (Bio diagnostic, Egypt) (colorimetric method), while serum insulin levels were assessed by the enzymatic immunoassay (ELISA kit of rat insulin, Glory science Co., USA). The homeostasis model assessment of insulin resistance (HOMA-IR) and HOMA-B (an index for assessing β-cell function) were calculated with reference to Pickavance et al. [18] and Heald et al. [19], respectively. Glycosylated hemoglobin was assessed by the commercially kit (Spectrum, Egypt). Total cholesterol, triglycerides and high-density lipoprotein (HDL) were estimated by using the Bio-diagnostic kit (Egypt) (colorimetric method), however low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) has been calculated according to Mousavi et al. [20]. Serum levels measurements of malondialdehyde (MDA) as well as total antioxidant capacity (TAC) were carried out according to Miller et al. [21] and Jiang et al. [22].

2.6.2. Preparation of a Muscular Homogenizer for Determination of Lipid

Total lipid in muscle were performed according to the Folch et al. procedure [23] and the triglyceride (TG) levels according to the procedure of Foster & Dunn [24] then were estimated using a commercial assay kit (Bio-diagnostic, Egypt Egypt) by enzymatic colorimetric method.

2.6.3 Preparation of Muscular Homogenizer for Determination of Malondialdehyde (MDA)

Supernatants rich in Mitochondria were performed using frozen skeletal muscle as previously mentioned [25]. For skeletal muscle, it's around 20 mg. Remove

the desired components (connective tissues and fats) from the animal samples with a scalpel and dice it thinly. Ice cold potassium phosphate buffer (0.05 mM) solution (pH 7.3) was used as tissue lysis buffer which was added to 100 mg (wet weight)/ml to a chilled glass–glass homogenizer, then homogenize with ten strokes until sample is distributed. In a cooled Eppendorf tube, transfer the solubilized tissue. In a benchtop cold centrifuge, centrifuge the homogenate at 600 RCF for 10 minutes, then transfer the supernatant to a fresh tube. Freeze/thaw the homogenate supernatants twice in a dry ice/ethanol slurry, then separate them into tubes for batch analysis with the various assays and store at a temperature of 70°C. MDA was estimated using enzyme-linked immunosorbent assay (ELISA) [26].

2.7 Quantitative real-time polymerase chain reaction (q-RT-PCR)

2.7.1 RNA isolation

Total muscular RNA has been separated using RNeasy (QIAGEN Mini Kit) with the instructions of the manufacturer. RNA concentration has been estimated by spectrophotometrically using NanoDropND-1000 (Thermo Fisher Scientific, USA) and finally the purity of the isolated RNA has been checked.

2.7.2 Reverse transcription

Extracted RNA was used for cDNA synthesis reaction using the Reverse Transcription System (Promega, Madison, WI, USA). Total RNA has been incubated for 1 h at 42°C with RTase buffer (10×), deoxy nucleotide triphosphate (dNTP) mixture (10 mM), $MgCl_2$ (25 mM), oligo d(t) primers (shown in Table 1), avian myeloblastosis virus (AMV) reverse transcriptase (20 U/μL) and RNase inhibitor (20 U).

2.7.3 Quantitative real-time polymerase chain reaction (q-RT-PCR)

Q-RT-PCR has been carried out using ABI PRISM 7500 fast sequence detection system (Applied Biosystems, Carlsbad, CA, USA) under universal cycling conditions using gene-specific forward and reverse primers (10 μM), SYBR Green Master Mix (Applied Biosystems) and cDNA and nuclease-free water, The comparison threshold cycle method was used to calculate the relative transcription of the genes under consideration. The results have been adjusted to -actin, which was used as the housekeeping genotype control.

Table 1. Primer sequences used to Quantitative real-time polymerase chain reaction (q-RT-PCR)

Gene	Primer sequence	Accession Number
GLUT4	F: 5´CAAAGCATCGACCAGTGCTA3´ R: 5´TGGACAGCACTGACTTCCAG3´	XM_006246596.3
IR	F: 5´CAGCAAGCAGGTCATTGTTTCA3´ R: 5´TGGGTGGGTTTGGGCTCC3´	NM_017071.2
IRS1	F: 5´GGACTTGAGCTATGACACGGG3´ R: 5´GCCAATCAGGTTCTTTGTCTGAC3´	NM_012969.1
β-actin	F: 5´ATCATCACCTTTGCCGAGTC3´ R: 5´ACAGGTCACTGCCTTCCTTG3´	NM_031144.3

Glucose transporter 4 (GLUT4), insulin receptor (IR), insulin receptor substrate 1(IRS1).

2.8 Histological and morphological examinations

Muscular sections (three independent animals from each group) have been fixed in 10% Neutralize formalin buffer. Sections have been embedded paraffin, cut into 4-μm slices then stained by hematoxylin and eosin [27].

Muscular sections were fixed in 10% Neutralize formalin buffer (3 rats / group). Sections were embedded in paraffin, cut to slices (4-m), and dyed with hematoxylin and eosin [27].

2.9 Statistical analysis

The results have been expressed as mean ± SE. The Social Science Statistical Package (SPSS) version 23 (Chicago, USA) was used to carry out one-way analysis of variance (ANOVA), and the post-hoc-test, least significant difference analysis (LSD) to compare the studied groups. At $p < 0.05$, the difference was deemed statistically significant.

3. Results

3.1. Commiphora molmol (Myrrh) effect on body weight changes

In the end of research (30 days), the weight of untreated rats (GII) was showed significant ($p<0.0001$) lowering compared to other groups. Significant higher increases ($p<0.0001$) in body weight were found in control (GI) and treated with herbal extract (GIII) (Figure.1).

3.2. Biochemical analyses

In comparison to normal animals, diabetes caused by alloxan in animals (GII) results in a considerable increase in fasting glucose and glycated hemoglobin of roughly 4.8 and 1.7 folds, respectively, while serum insulin and HOMA- β% were dropped by 2.2 and 28 folds ($p <0.0001$) (Table 2). Furthermore, when diabetic rats (GII) were compared to normal rats, there was a substantial increase ($p < 0.001$) in HOMA-IR, which reached nearly 2 folds. When diabetic rats were given myrrh for four weeks (GIII), all of these measures were normalized ($p <0.0001$). Surprisingly, glucose and insulin levels, as well as HOMA-IR, were

all significantly lower (p <0.01) than in normal rats (GI) by 10, 19, and 27%, respectively. However, glycated hemoglobin and HOMA- β% were still 1.2 times higher than normal (p < 0.01).

When compared to the normal group, Alloxan intraperitoneal injection caused an imbalance in the oxidative status, as evidenced by a substantial elevate in serum MDA (p <0.001) and significantly reduce in serum TAC (p <0.002) (Figure 2,3). In comparison to the diabetic group, administration of the *Myrrh* extract improved their levels.

Alloxan significantly elevated serum levels of TC and TG, as well as LDL-C and VLDL-C, as compared to control rats, according to the results provided in (Figure 4). The serum levels of these parameters in *Myrrh* treated rats were much lower than in the diabetic rats but were still high as compared with the normal rats. When comparing diabetic untreated group to normal group, the amount of serum HDL-C was become 30% lower in untreated group. The Myrrh extract was used to normalize the decrease.

Table (3) demonstrates that total lipids, triacylglycerol, and MDA levels in muscle tissue of diabetic rats (GII) were elevated significantly by 3.1, 1.9 and 2.6 compared with normal rats (GI). Aqueous *Myrrh* extract was administered to diabetic rats (GIII), which significantly lowered these increases to levels comparable to normal rats.

Table (2). Significance of serum glucose, insulin, HOMA- β and HOMA-IR index as well as HbA1c concentrations of the various groups (expressed as Mean±SE).

Parameters / Groups	Control group (GI)	Diabetic group (GII)	Treated group (GIII)
Glucose mg/dl	**92±2.1** [a]	**437±16.5** [b]	**83±2.6** [c]
% change versus -ve control	--	375%	-10%
% change versus +ve control	-79%	--	-81%
Insulin mU/l	**1.93±0.03** [a]	**0.87±0.03** [b]	**1.56±0.04** [c]
% change versus -ve control	--	-55%	-19%
% change versus +ve control	122%	--	79%
HOMA- IR%	**0.44±0.01** [a]	**0.94±0.02** [b]	**0.32±0.01** [c]
% change versus -ve control	--	114%	-27%
% change versus +ve control	-53%	--	-66%
HOMA- β%	**24.89±1.85** [a]	**0.86±0.06** [b]	**33.02±4.06** [c]
% change versus -ve control	--	-97%	32%
% change versus +ve control	2795%	--	3739%
Hb AIC %	**5.01±0.09** [a]	**8.7±0.17** [b]	**6.01±0.1** [c]
% change versus -ve control	--	74%	20%
% change versus +ve control	-42%	--	-31%

Each group had ten rats. The significance of each group is denoted by a different superscript letter. At p < 0.05, the mean difference is significant.

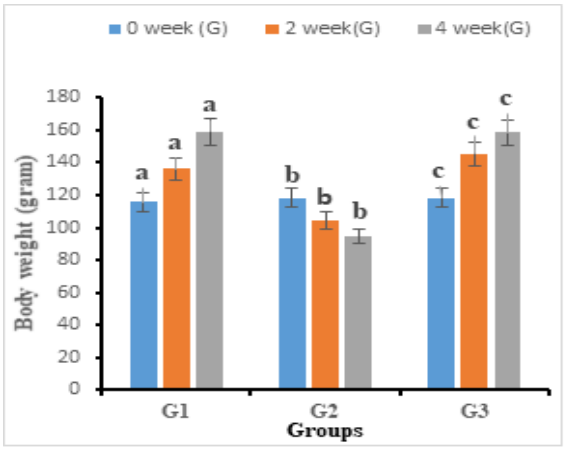

Fig. 1. Commiphora myrrh resin extract effect of on rats' weights. Rats were given basal diet for control (GI) and diabetic group (GII); myrrh (500 mg/kg bw) and basal diet were administered for treated group (GIII) for 4 weeks; and weekly body weight measured of rats. Values presented as Mean±SE. Various letters means significant difference (p < 0.05) between groups

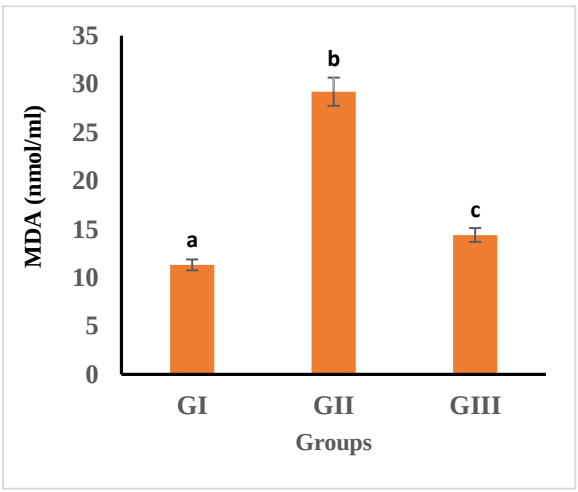

Fig. 2. Serum MDA: Malondialdehyde in the different studied groups. The data was presented as Mean SE. ANOVA was used to analyze the data, followed by LSD. At p<0.05, the mean difference is significant. Each group had 10 rats.

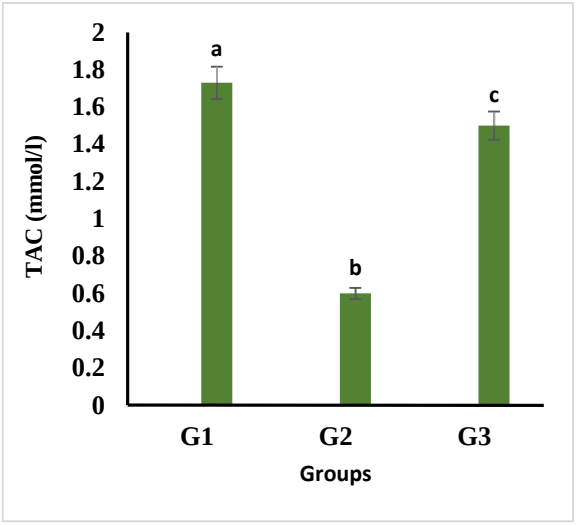

Fig. 3. TAC: total antioxidant capacity of the various studied groups. The data was presented as Mean SE. ANOVA was used to analyze the data, followed by LSD. At $p<0.05$, the mean difference is significant. Each group had 10 rats.

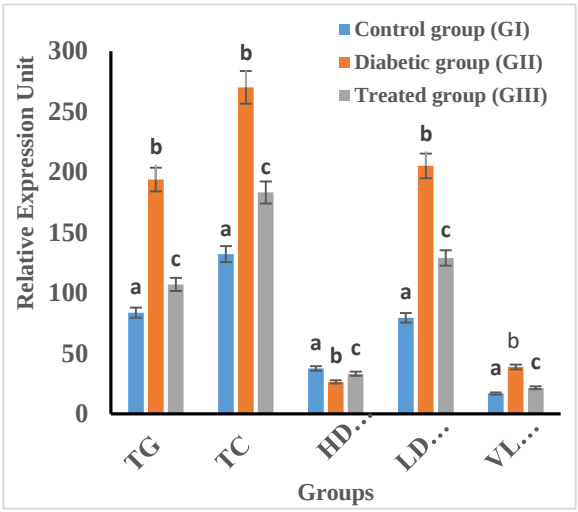

Fig. 4. TG: Triacylglycerol, TC: Total cholesterol, HDL-C: High density lipoprotein-cholesterol, LDL-C: Low density lipoprotein-cholesterol, VLDL-C: very Low-density lipoprotein-cholesterol in the various studied groups. Data were given as Mean ± SE. The analysed data were carried out by using ANOVA followed by LSD. At $p<0.05$, the mean difference is significant. Each group had 10 rats.

Table (3). Significance of Total lipid, Triglyceride and Malondialdehyde of Skeletal muscle in the various experimental groups (Mean ± SE)

Parameters / Groups	Control group (GI)	Diabetic group (GII)	Treated group (GIII)
T Lipid of muscle tissue mg/g	**17.1±1.2 [a]**	**54.5± 2.5 [b]**	**29.7±1.5 [c]**
% change versus -ve control	--	219%	74%
% change versus +ve control	-69%	--	-46%
TG of muscle tissue mg/g	**4.52±0.19 [a]**	**8.53± 0.29 [b]**	**5.62±0.28 [c]**
% change versus -ve control	--	90%	25%
% change versus +ve control	-47%	--	-34%
MDA of muscle tissue nmol/mg protein	**6.24± 0.2 [a]**	**16.2± 0.2 [b]**	**7.5 ± 0.3 [c]**
% change versus -ve control	--	160%	20%
% change versus +ve control	-62%	--	-54%

Each group had 10 rats Various superscript letters mean significance among groups
At $p<0.05$, the mean difference is significant T lipid: Total lipids, TG: Triacylglycerol, MDA: Malondialdehyde

3.3 Gene expression

Table (4) showed that alloxan decreased the transcription of the IR, IRS-1, and GLUT4 genes in muscle ($p < 0.002$) when compared to normal rats. When diabetic groups were given aqueous Myrrh extract, gene expression was improved ($p < 0.0005$) compared to the untreated rats, but it was still significantly down-regulated when compared to the normal rats

Table (4). Significance of muscular Insulin Receptor (IR), muscular Insulin Receptor substrate 1 (IRS1), muscular Glucose transporter 4 (GLUT4) concentrations in the various groups (Mean±SE).

Parameters / Groups	Control group (GI)	Diabetic group (GII)	Treated group (GIII)
Insulin Receptor of muscle tissue (IR)	**1.01±0.01 [a]**	**0.4±0.1 [b]**	**0.81±0.05 [c]**
% change versus -ve control	--	-60%	-19%
% change versus +ve control	150%	--	103%
IRS1 of muscle tissue	**1.04±0.03 [a]**	**0.32±0.06 [b]**	**0.79±0.09 [c]**
% change versus -ve control	--	-77%	-44%
% change versus +ve control	225%	--	147%
GLUT4 of muscle tissue	**1.01 ±0.01 [a]**	**0.32 ±0.1 [b]**	**0.79 ±0.05 [c]**
% change versus -ve control	--	-68%	-22%
% change versus +ve control	216%	--	147%

Each group had 10 rats Various superscript letters mean significance among groups
At $p<0.05$, the mean difference is significant

3.3. Histological analysis

The pathology of the normal animal showed no tissue alteration, the normal histological structure of muscle bundles and no tissue alteration was demonstrated in the diabetic and treated animals.

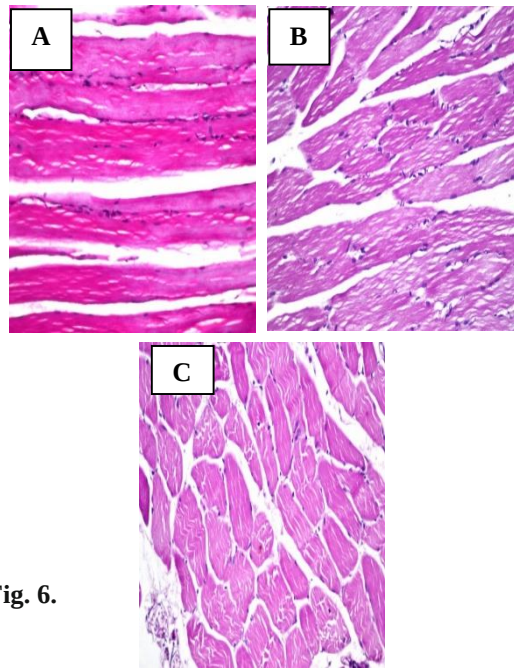

Fig. 6.

Photomicrographs of skeletal muscle sections of normal group (A), diabetic group (B) and *Myrrh* treated group (C). There was no histopathological alteration showed in 3 groups (Hematoxylin and Eosin, x640)

4. DISSCUSION

Type 2 Diabetes Mellitus is more frequent and is approaching epidemic proportions. Insulin deficiency and the failure of the pancreas cell to release insulin correctly [28], both of which are important aspects in the etiology of type 2 diabetes mellitus, are two critical features in the disease's pathophysiology [29]. The function of fatty acid metabolism in the progress of insulin resistance and diabetes mellitus type 2 is well established. Ectopic fat accumulation, or fat deposition in non-adipose tissue is now thought to be a key hallmark of the disease. The impact of mitochondria in lipid metabolism and insulin resistance in type 2 diabetes, particularly in muscle tissue, has recently attracted attention. Because skeletal muscle is responsible for the bulk (>80%) of insulin-stimulated body glucose clearance, it plays a major role in the pathogenesis of glucose intolerance. In diabetic and non-diabetic patients, there is a lot of evidence that an increase in plasma FFA via intravenous lipid infusion causes muscle insulin resistance to increase. Several hypotheses have been proposed to explain the process that leads to FFA-related issues. Insulin resistance is associated to increased triacylglycerol buildup in skeletal muscle (intramyocellular lipid, IMCL). [30, 31].

In addition to the lack fasting fat oxidation, insulin resistant patients' skeletal muscle is Featuring so-called metabolic inflexibility' [32]. As a result, when fasting, healthy people depend on fat oxidation and easily switch to carbohydrate oxidation when insulin is stimulated. This flexibility, however, is lost in insulin resistant (diabetic) state. Plants insulin sensitivity is positively related to their metabolic flexibility [33].

Since olden period, medicinal herbs have been employed as an origin of cures. Traditional medical treatment has turned to the resins of *Commiphora* species to treat obesity. Obesity has become a major health concern that raises the risk of a variety of diseases, including diabetes mellitus [34].

The aim of this research was whether *Commiphora myrrha* has any antihyperglycemic properties in alloxan-induced diabetic rats. Alloxan causes diabetes by triggering fast loss of pancreatic beta cells, resulting in hyperglycemia [35]. Diabetes mellitus increases the formation of free radicals as a result of glucose auto-oxidation [36]. In biological systems, free radicals are generated as a result of the interaction of biomolecules with molecular oxygen [37,38]

The findings demonstrate that daily dosages of Commiphora Myrrha dropped mean blood glucose levels in a dose-dependent approach comparison to diabetes control, with the (0.5 g/Kg) *Commiphora Myrrha* doses lowering the levels of blood glucose down to a more manageable ranges through 4 weeks of therapy [39].

The existence of furanoses quiterpenes as antioxidant properties in the plant, as described in a recent study, could be one explanation for this. Antioxidants are preventative molecules that restrict the production of reactive oxygen species (ROS), that cause cell harm. *Myrrh* is widely used plants in Arabia, it is usually referred to as "Balsam of Mecca" to emphasize its prominence in Arab culture [40]. Complications of diabetic like microvascular and macrovascular diseases are caused by chronic hyperglycemia. Furthermore, while smaller doses of alloxan (120 mg/kg body weight) cause partial lack of pancreatic beta cells, albino rats contain surviving beta cells, allowing regeneration [41].

As a result, it's probable that comparable substances present in leaf extracts will help to adsorb ROS and boost pancreatic beta cell regeneration. By scavenging free radicals, myrrh treatment reduced oxidative stress. *Myrrh* reduces MDA levels, according to the findings of the study. In addition, *Myrrh* extract increased nuclear factor-erythroid 2 (Nrf2) and glutathione (GSH) levels while decreasing MDA levels [42]. the reduction of oxidative stress in rats treated with *Myrrh* with a dose-dependent elevate in TAC level through a reduce in the activities of MDA

antioxidant enzyme [43]. Eugenol, Thumbergol [44], tannins, sterols, and Isoprenoids (Terpenoids) [45] which have antioxidant properties, contribute to myrrh's antioxidant capacity.

According to Ramesh and Saralakumari [46], Commiphora myrrha can increase the sensitivity of insulin and postpone the progress of insulin resistance in diabetic animals, as well as exacerbate antioxidant status, and perhaps utilized as an adjuvant treatment to patients that have insulin resistance.

Mithila and Khanum [47] discovered that Myrrha extract reduced glucose levels considerably. Guggulsterones, plant bioactive steroids derived from *Commiphora Myrrha*, have antiobesity and antihyperlipidemic properties, and *Myrrha* has been utilized to treat obesity and hyperlipidemia. according to Shen et al. [48]. Manalil et al. [49] claims that a nontoxic polyherbal formulation containing *Commiphora* has hypolipidemic and anti-atherogenic properties.

In this study, *molmol* extract had a powerful hypolipidemic impact, lowering cholesterol levels, triglycerides, and low-density lipoprotein cholesterol in obese hyperlipidemic animals. The anabolic steroids (guggulsterones) have gotten the greatest attention because of *Commiphora molmol* resin's powerful hypolipidemic action [50]. Alloxan-induced diabetes is associated with a significant loss of weight, which was also observe in our research. Treatment of diabetic rats with herbal extract greatly diminished weight loss, however it did not return to control levels. Accelerated muscle wasting and tissue protein decomposition can lead to weight loss in diabetics. After treatment with *C. myrrha* extract, the body weight of alloxan-induced diabetic rats elevated considerably. They theorized that this could be caused by carbohydrate metabolism stimulation. This impact is due to an increase in insulin production, which is the primary regulator of glycogenolysis in muscle tissues [51].

5. Conclusion

This study reveals that an aqueous extract of C. molmol (Myrrh) may be a therapeutic supplement for type 2 diabetics, as it improves hyperglycemia via restoring insulin signaling. The hypolipidemic and antioxidant properties of Myrrh were used to improve muscular insulin signaling.

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