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Original article

THE PROTECTIVE EFFECTS OF *ELETTARIA CARDAMOMUM* ESSENTIAL OIL EXTRACTED AGAINST DECADRON INDUCED ON PANCREATIC TISSUES IN RATS (*RATTUS NORVIGICUS*)

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Abstract

Background. Decadron is used to treat a wide range of disorders and regulates various physiological systems in the body. Literature data indicate that the essential oils of *E. cardamomum* exhibit multiple biological effects, including antihypertensive, antioxidant, antimicrobial properties, and pancreatic tissue protection.

Purpose. This study aims to investigate the protective effects of *E. cardamomum* essential oils on body weight loss, hyperinsulinemia, hyperglycemia, and histopathological changes in the pancreas of rats induced by Decadron. Additionally, the chemical composition of the essential oils was characterized using GC-MS.

Methodology. Rats were divided into six groups (n=5): (1) control, (2) Decadron-induced diabetes (1 mg/kg, orally), (3) induced diabetes + low-dose *E. cardamomum* essential oil (50 mg/kg, orally), (4) induced diabetes + high-dose *E. cardamomum* essential oil (100 mg/kg, orally), and (5 & 6) two groups receiving essential oils alone (50 & 100 mg/kg, orally). Diabetes was induced by administering Decadron (1 mg/kg, orally) for 14 days. Body weight was measured, and histopathological examination of pancreatic tissues was performed.

Results. Decadron administration led to a decrease in body weight and an increase in glucose and insulin levels. Histopathological examination revealed hypertrophy of the islets of Langerhans, disintegration of pancreatic cells, and hemorrhage within pancreatic tissue. However, these pathological changes were mitigated by

E. cardamomum essential oil treatment. GC-MS analysis identified 29 volatile compounds in the essential oils.

Conclusion. Our findings suggest that cardamom oil may serve as an adjuvant in reducing elevated serum insulin and blood glucose levels in Decadron-induced diabetes.

Keywords: Decadron; *Elletaria cardamomum*; hyperinsulinemia; hyperglycemia; GC-MS; Eucalyptol; pancreas

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Introduction

Decadron belongs to the glucocorticoid family, which is used to treat a wide range of disorders and regulates many physiological systems in the body. They are known to be powerful drugs that can reduce inflammation and collaborate with the immune system to address a variety of medical issues. and have side effects on various organ tissues [1; 2]. Long-term administration of Decadron at high doses causes beta-cell hyperplasia, insulin resistance and beta-cell hypersecretion and the Decadron induced insulin resistance alone can't cause steroid-induced diabetes but pancreatic beta cell dysfunction also plays a crucial role in the development of new –onset diabetes caused by Decadron and the acute effect of Decadron reduces insulin secretion in both pancreatic islets and pancreatic beta cells through several mechanisms including oxidation, membrane depolarization and decreased glucose uptake [3-5]. On the other hand, Decadron has many undesirable side effects including laboratory-treated pancreatic tissues with Decadron, and the damage caused by Decadron has been reported in many studies, it causes damage and necrosis of the endocrine cells of the islets of Langerhans and shrinkage of the islets with degeneration of the acinar cells as well as hypertrophy of the pancreatic islets and congestion of blood vessels and the presence of gaps between the pancreatic cells and degeneration of the cytoplasm in addition to the harmful effects of Decadron on the function of the pancreatic endocrine cells which ultimately affect glucose balance [6-9].

The green cardamom, *Elettaria cardamomum* is considered the third most expensive and oldest type of spice in the world, which is referred to as "black gold" and is also called the "King of spices", it is one of the types of the Zingiberaceae family and this name is due to its distinctive smell and taste. In

addition, it is considered a monocotyledonous and perennial herbaceous plant [10; 11]. It is well recognized that plants are abundant in bioactive chemicals, which can be used as building blocks to create therapeutic and advantageous natural products. It is well known that plants develop secondary metabolites to guarantee the continual existence of their species [12; 13] .

Cardamom essential oil is one of the most utilized goods that are produced, and the fruits have been used for ages as a flavor and spice [10]. Data from the literature show that the essential oils of this plant have a range of biological consequences, like high blood pressure, antioxidants, gastroprotective, antimicrobial, antihyperglycemia, antispasmodic, laxative, anti-platelet-aggregation, anticancer activities and antibacterial [10; 14-16]. In order to reduce the harmful side effects of Decadron, many researchers have focused on isolating plant compounds to reduce these effects. The cardamom extract has been found to be a therapeutic effect in protecting the pancreatic tissue. Significant improvement in pathological changes and a decrease in guarantor tissue barriers with an increase in the number of Lankerhans islands [17].

Cardamom's important tasting components for oil consist of allo-aromadendrene, citronellal, linalool, α-and β-pinene, terpineol, and as well as limonene,1,8-cineole, and α-terpinyl acetate [18; 19]. Monoterpenes 1,8-cineole and ester α-terpinyl acetate, linalool, limonene, myrcene, α-pinene and terpinolene, which are accountable for the effectiveness among these essential oils in treating various diseases [15,20]. GC-MS analysis is among the best instruments to determine the components of essential oils [21]. Also thidentification of various metabolites of plant extracts [22; 23].

This study sets out to determine the bioactive compounds present in *Elettaria cardamomum* seed volatile oil extract and explore its protective effects against Decadron induced diabetes and damage of pancreatic.

Materials and methods

Plant material

E. cardamomum seeds were gathered from Basrah Governorate of Iraq from local marketplaces during September 2023 and kept in polyethelen bags then dried in room temperature without light.

Samples preparation and extraction of volatile oils

The samples were ground using an electric grinding machine from the German company Super Crest until fine particles were obtained. The samples were then stored in a dark-colored glass container and tightly closed at a temperature of 4°C until it is time to use them. To extract the volatile oil was done using a

Clevenger device. 25 gm of powdered sample was placed in a 1000 ml round beaker, 250 ml of distilled water was added to it and heated at 60-80°C for 4 hours. The volatile oil was collected in the device's condenser after evaporating it with water to form a white layer on the surface of the water. Then essential oils are separated from the water layer using a separating funnel, then placed in a tightly sealed dark glass bottle and kept in the refrigerator at 4°C until used.

GC-MS analysis

To determine the chemical compounds of the essential oil in the *E. cardamomum*, using GC-MS in the gas chromatography/mass spectrometry laboratory at the Basrah University in the Agriculture College, (device type SHIMADUZ - Japan, GC-MS, QP 2010 Ultra) and the capillary column type equipped with it (DB-MS). 5% phenyl, 95% methyl poly siloxane as a fixed phase; its length was 30 m and 0.32 m in diameter and the thickness of the stationary phase was 0.25 micrometers. The carrier gaseous flow rate was 72.4 mL/min. A sample was injected into the GC-MS at 280°C injection temperature. The operating status temperature of the GC-MS was determined, with a holding temperature of 50°C for 0 minutes at first, and then progressively increased at a faster pace of 150°C to 280°C as the ultimate temperature (holding 0 minutes). The mass scanning range (m/z) was 50-800 amu. By comparing the spectrum of the *E. cardamomum* essential oil with those of identified components kept, the components of the oil can be found in the NIST library (2005). The NIST library (2005) contains the oil's components, which were identified (Figure 1-6).

Experimental design

The present study was conducted: hyperglycemia was induced by oral administration of Decadron drug to rats for 14 days, followed by fasting for 24 hours. The blood glucose level of these rats was estimated after one week of Decadron administration and after 14 days, hyperglycemia was confirmed by blood samples collected from the tail tip using a blood glucose meter. Animals with blood glucose level equal to or greater than 200 mg/dl were declared hyperglycemia and were used in the entire experimental group and rats' weight was measured both first and again. (7, 14 and 21 days) as well as at the end of the method of experimentation. Therefore, thirty male rats were randomly divided into six groups as shown: group 1: control group (n=5) no treatment. Group 2: dose with Decadron (orally, 1mg/kg) to induce diabetes for 1 month (n=5). Group 3: Diabetic animals were treated with essential oil of *E. cardamomum* (orally, 50 mg/kg) for 1 month (n=5). Group 4: Diabetic animals were treated with essential oil of *E. cardamomum* (orally, 100 mg/kg) for 1 month (n=5). Group 5: orally administered with essential oil only (50 mg/kg) for 1

month (n=5). Group 6: orally administered with essential oil only (100 mg/kg) for 1 month (n=5).

At the end of the experiment, the rats were anesthetized by chloroform inhalation and blood was taken straight from the heart, the serum was separated by centrifugation, and it was kept at -20˚C for biochemical examination.

Biochemical analysis

A sample of blood from each experimental rat was collected into serum separation gel tubes then the samples underwent a 10-minute centrifugation at 4000 rpm. After being separated, plasma was processed right away for biochemical analysis. and the plasma sample was analyzed for biochemical markers, including blood glucose levels and determination using diagnostic kit (from Biolabo SAS company) and insulin level determination using diagnostic kit (from Shinghai company) based on ELISA method using ELISA reader.

Histopathological examination

For histopathological study, pancreatic tissues were excised via thoracotomy and set in 10% formalin for 24 hours, then routine histopathological examination was performed, and the pancreatic tissue section was stained with hematoxylin and eosin stains and photographs were taken by LEICA ICC50 HD light microscope.

Statistical analysis

All data were expressed as mean ± SD. Statistical analysis was performed using SPSS software through analysis of variance (ANOVA) followed by multiple comparisons to compare all groups with the control group. A *p*-value of less than 0.05 was considered statistically significant.

Results and discussion

Essential oils compounds of *E. cardamomum*

The GC-MS analysis of *E. cardamomum* seed extract disclosed the presence of 29 phytochemicals compounds (Figure 1 and Table 1) that might enhance the plant's therapeutic qualities. The peak area, molecular formula, and retention time were used to confirm the phytochemical compounds identities. The active principles are shown in their corresponding retention time (RT), chemical formula, and peak area as a percentage (Table 1). Most of the chemical component's identification of *E. cardamomum* seeds represented essential oil, the results showed that the color of the extracted essential oils are transparent with a distinctive and wonderful smell. In addition, the percentage of extracted volatile oil was 21.96%. There were three distinct sesquiterpene components; alpha-Selinene, gamma -Muurolene and Nerolidol which represented 10.34%

of all the compounds in essential oil, and the 18 chemicals known as monoterpenes (52.20%). Our results support the conclusions of other investigations that monoterpenes are the main constituent of essential oils derived from cardamomum [24; 25]. Moreover, the three most prevalent monoterpene components are viridiflorole (11.8%), camphor (15.6%), and 1, 8-cineole (20.1%) [26].

Essential oil's fundamental components 1,8-Cineole (Eucalyptol) had the highest percentage (38.30%), followed by alpha-Terpineol (17.80%), α-Terpinyl acetate (11.38%), Linalool (10.35), Terpinen-4-ol (3.32%) and Linalyl acetate (3.17%), with other compounds beta-Pinene, beta-Myrcene, gamma. -Terpinene, Geraniol, alph-Thujene and alpha-Pinene (Table 1, Figure 1-6). Our results are consistent with Abdel-Hameed *et al*., (2023) for the two compounds eucalyptol (41.41%) and α-Terpinyl acetate (37.12%) [27]. In addition, the results agreed with researchers whose reported that the major compound in *E. cardamomum* was 1,8-Cineole [18; 19; 28-30],but the percentage of 1,8-Cineole was different between the researches, the major percentage recorded by Sultana *et al*., (2009) was 89.6% [29], while it was 28.4% and 10.7% in the study of (Menon, *et al*., 1999 and Singh *et al*., 2008) respectively compared with the percentage in our result which was 38.30% [28; 31]. Furthermore, our results are in line with those of other researchers who discovered myrcene, linalool, terpineol, α-pinene, β-pinene and α-terpinyl acetate [15; 20; 28] .

The researchers explained that the distinctive smell of the cardamom plant is due to the proportion of esters and 1,8-cineole (eucalyptol) and the high level of α-Terpinyl acetate compared to eucalyptol which also gives a superior aroma quality to cardamom essential oil, A few key flavor components of cardamom for oil are limonene, 1,8-cineole, α-terpinyl acetate, Citronellal, linalool, β-pinene, terpineol, and allo-aromadendrene [18,19,30]. In addition, it is clear from most of the works of researcher Pavarino *et al*., (2023) shows the most prevalent compounds are terpinyl acetate and 1,8-cineole, with around 30% and 40% of each, respectively and they are two main components of cardamom seed oil which are characterised by an abundance of oxygenated compounds which is consistent with our study [32]. According to Al-Zereini *et al*. (2022), out of 39 compounds, the majority 55.99 % was α-terpinyl acetate. Eugenol, Z-caryophyllene, geraniol, terpinen-4-ol, 1,8 cineole (8.82 %), linalool (6.99 %), and dihydrocarveol (6.06 %) [33].

The *E. cardamomum* essential oils' chemical makeup varies according to our findings, in addition to the quantity and ratio of active compounds. These variations may result from varying essential oil hydrodistillation techniques,

growing environments, or a diversity of plant sources. Geographical variations, physiological variables, and genetic factors could all be contributing factors to these differences [34-36]. Environmental characteristics that need to be considered include weather, soil, time of year for harvest, and drying method, conditions of storage, as well as the part of plant tissue being assessed [37-40]. Additionally, Farhat *et al*. (2001) demonstrated significant seasonal variations in the oil's composition [41].

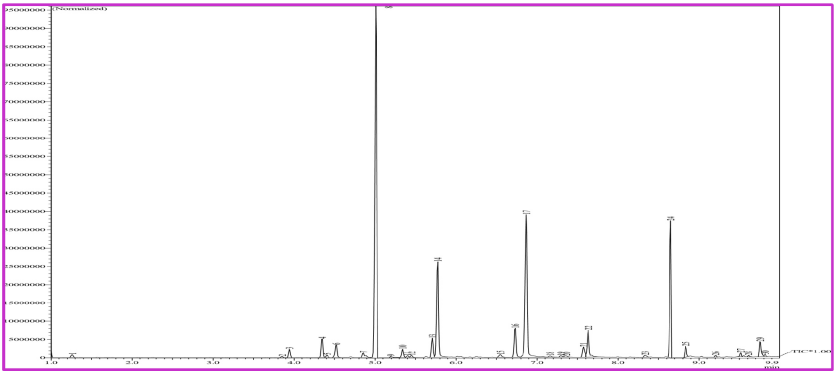

Fig. 1. Illustrates the active compounds of essential oils in *E. cardamomum* plant using GC-MS analysis.

Table 1.

Essential oil compounds in *E. cardamomum* using GC-MS

Peak	Chemical compounds	Chemical formula	Retention time	Percentage %
1	Dodecaethylene glycol	$C_{24}H_{50}O_{13}$	1.263	0.34
2	alpha- Thujene	$C_{10}H_{16}$	3.853	0.12
3	alpha-Pinene	$C_{10}H_{16}$	3.943	0.81
4	4(10) Thujene or Sabinen	$C_{10}H_{16}$	4.346	1.90
5	beta-Pinene	$C_{10}H_{16}$	4.408	0.25
6	beta-Myrcene	$C_{10}H_{16}$	4.521	1.48
7	Bicyclo[4.1.0]hept-2-ene, 3,7,7-trimethyl-, (1S-cis)-	$C_{10}H_{16}$	4.856	0.82
8	1,8-Cineole or Eucalyptol	$C_{10}H_{18}O$	5.011	38.30
9	tert-Butyl carbanilate	$C_{11}H_{15}NO_2$	5.194	0.18
10	gamma.-Terpinene	$C_{10}H_{16}$	5.340	1.01
11	cis-beta- Terpineol	$C_{10}H_{18}O$	5.401	0.23
12	trans-Linalool oxide (furanoid)	$C_{10}H_{18}O_2$	5.452	0.25

13	Terpinolen	$C_{10}H_{16}$	5.708	1.87
14	Linalool	$C_{10}H_{18}O$	5.772	10.35
15	delta -Terpineol	$C_{10}H_{18}O$	6.547	0.46
16	Terpinen-4-ol	$C_{10}H_{18}O$	6.730	3.32
17	alpha- Terpineol	$C_{10}H_{18}O$	6.868	17.80
18	trans-Carveol	$C_{10}H_{16}O$	7.160	0.37
19	cis-Geraniol	$C_{10}H_{18}O$	7.295	1.55
20	Neral	$C_{10}H_{16}O$	7.358	0.24
21	Linalyl acetate	$C_{12}H_{20}O_2$	7.631	3.17
22	delta.-Terpineol, acetate	$C_{12}H_{20}O_2$	8.335	0.29
23	alpha.-Terpinyl acetate	$C_{12}H_{20}O_2$	8.648	11.38
24	Geranyl acetate or Acetic acid, geraniol ester	$C_{12}H_{20}O_2$	8.835	1.00
25	Terpinyl propionate	$C_{13}H_{22}O_2$	9.203	0.16
26	alpha-Selinene	$C_{15}H_{24}$	9.515	0.33
27	gamma.-Muurolene	$C_{15}H_{24}$	9.610	0.15
28	Nerolidol	$C_{15}H_{26}O$	9.754	1.68
29	(3E,7E)-4,8,12-Trimethyltride-ca-1,3,7,11-tetraene	$C_{16}H_{26}$	9.817	0.18
				100.00

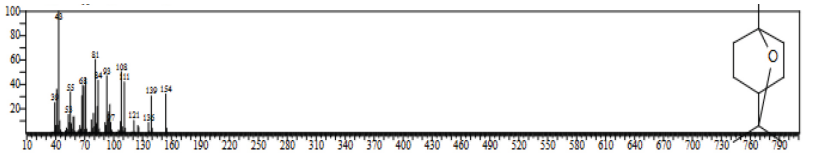

Fig. 2. Standard GC-MS spectra of the Eucalyptol

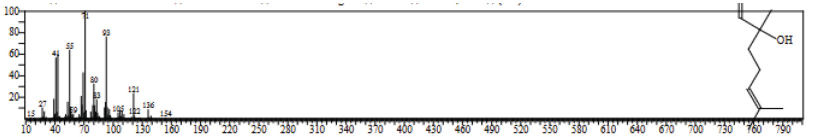

Fig. 3. Standard GC-MS spectra of the alpha-Terpineol

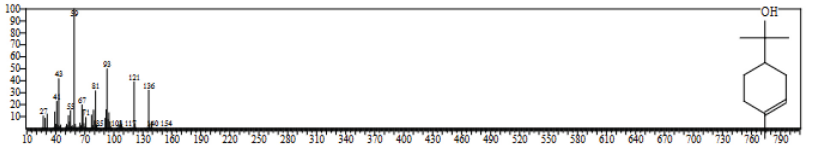

Fig. 4. Standard GC-MS spectra of the alpha-Terpinyl

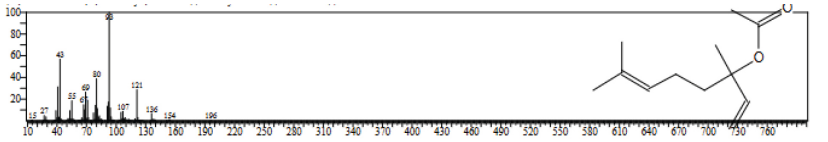

Fig. 5. Standard GC-MS spectra of the Linalool

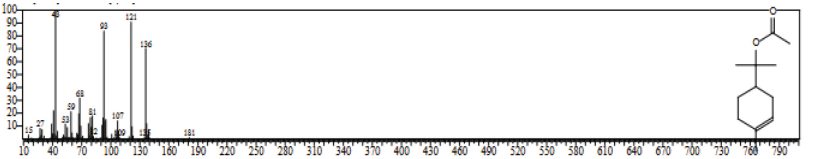

Fig. 6. Standard GC-MS spectra of the Linalyl acetate

***E. cardamomum* essential oil reversed decadron induced alternation of body weight**

The results showed that the group with diabetes induced by Decadron experienced a significant decrease ($p<0.05$) in body weight from the 7 days until the end of the experiment, similar to the other groups treated with *E. cardamomum* essential oil whose increased weights were significantly ($p<0.05$) (Table 2).

These findings are comparable to those of Kepta *et al.* (2021) who indicated that this decrease in weight indicates the proteolytic effect of Decadron [42], and our results are also consistent with the study of (Albu-Mhamed, 2013; Al-Hraishawi, 2012) [43; 44]. A theory proposed in favor of the present findings on body weight loss is that Decadron caused time and dose dependent weight and muscle loss in rats due to upregulation of muscle myostatin [45]. Franco *et al*., (2006) showed that the reason for the decreased body weight is the prevention of glucose entry into cells, which leads to weight loss after acute treatment with the drug [46]. While our results were consistent with the study (Elamin & Dousa, 2013; Shinde *et al*., 2017) conducted on rats to evaluate the effect of *E. cardamomum* on blood glucose, the researchers noted an improvement in the rate of decrease resulting from the development of diabetes caused by alloxan [47; 48]. Also, the study (Adanma, 2019) on the effect of the aqueous extract of *Citrus* on diabetic rats, the results showed an increase in body weight after treatment with the aqueous extract at very high concentrations [49]. The increase in body weight is attributed to the role of active compounds that stimulate beta cells to secrete insulin, which enhances the structural state of fats and proteins, which are the primary source of energy, in addition to the ability of active compounds to control the metabolic activity of carbohydrates.

It was found that flavonoids lead to controlling body weight and adipose tissue and regulating the metabolism process [50; 51].

Table 2.

Effects of Decadron and essential oil of *E. cardamomum* administration on diabetes rats body weight (g) (mean ± SD)

Groups	0 day	7 days	14 days	21 days	30 days	44 days
control	144.00 ± 3.36	149.25 ± 3.59	157.25 ± 2.50	163.50 ± 2.51	169.75 ± 2.50	0
Decadron	148.00 ± 2.16	133.00 ± 4.32	120.25 ± 4.19	103.25 ± 11.78	81.25 ± 11.08	0
Decadron + *E. cardamomum* (50 mg/kg)	143.50 ± 7.18	131.75 ± 9.46	118.50 ± 1.29	132.50 ± 4.50	147.75 ± 7.76	160.50 ± 6.35
Decadron + *E. cardamomum* (100 mg/kg)	146.00 ± 4.08	137.50 ± 5.06	121.50 ± 2.08	137.50 ± 7.93	153.50 ± 6.61	165.00 ± 5.59
E. cardamomum (50 mg/kg)	144.25 ± 3.40	148.75 ± 3.77	156.00 ± 2.44	160.25 ± 2.98	165.50 ± 3.11	0
E. cardamomum (100 mg/kg)	146.75 ± 1.70	151.50 ± 2.38	156.50 ± 1.29	163.50 ± 1.29	176.00 ± 2.58	0
L.S.D.	4.685	5.722	3.670	6.342	6.574	4.280

Cardamom oil attenuated hyperglycemia and hyperinsulinemia caused by Decadron

The present study showed that Decadron induced diabetic rats showed significant ($p<0.05$) increase in blood glucose and serum insulin levels compared to the control group (Figure). Cardamom oil administration of *E. cardamomum* oil at both doses (50 and 100 mg/kg) attenuated the effects of Decadron, significantly ($p<0.05$) reducing serum insulin levels when compared to Decadron induced diabetic rats. The higher dose (100 mg/kg) of *E. cardamomum* oil showed a better effect on glycemic parameters levels than the lower dose (Table 3).

This result is consistent with the study of Sultana *et al*., (2024) which reported that when given to normal rats, decadron induces insulin resistance as evidenced by increased blood glucose and insulin levels [52]. Consistent with the high blood glucose-lowering effect of Decadron and the increased insulin levels associated with Decadron treatment in rats, Shittu *et al*., (2021) observed a significant increase in blood glucose levels in Decadron treated rats and reported that the adaptive response of pancreatic islets to hyperglycemia leads to elevated insulin levels [53]. The increase in insulin levels may be an adaptive response of the pancreatic islets to hyperglycemia. In one study, it was reported that glucose stimulated insulin secretion in rats given Decadron involved increased expression of the connexin protein (CX36) while the glucose trans-

porter (Glut2) remained unchanged [54; 55]. The mechanism of action of these extracts in reducing blood glucose and insulin levels is not yet known, but the parts of the plants used have an anti-hyperglycemia role, which in turn is consistent with many studies, including the study by Ashokkumar *et al*., (2020) which proved that the *E. cardamomum* plant extract has the ability to reduce blood glucose levels due to its biological activity based on its active chemical compounds [10]. As it contains the active compounds 1,8-cineole, which is the main compounds in the extract, it has shown promising potential in improving high blood glucose. Recent reports have confirmed the ability of 1,8-cineole to reduce blood glucose levels in mice by activating glyoxalase [56-58].

Table 3.

Effect of decadron and essential oil (*E. cardamomum*) on glucose and insulin levels in diabetes rats (mean ± SD)

Groups	Glucose (mg/dl)	Insulin (µIU/ml)
control	152.47 ± 12.60	12.92± 0.57
Decadron	241.78 ± 24.59	17.43± 0.92
Decadron + *E. cardamomum* (50 mg/kg)	226.39 ± 5.33	12.90± 0.94
Decadron + *E. cardamomum* (100 mg/kg)	156.29 ± 38.56	14.77± 1.29
E. cardamomum (50 mg/kg)	197.82 ± 31.46	13.60± 1.27
E. cardamomum (100 mg/kg)	158.38 ± 33.88	15.65± 0.44
L.S.D.	27.12	1.55

Essential oils of *E. cardamomum* seeds alleviate the histological changes in pancreatic tissues caused by decadron

In the present study, the results observed in figure (7 A-F) in the pancreas of diabetic rats showed that Decadron induced many alterations in comparison to the pancreatic control group. These changes comprised hypertrophy of the islets of Langerhans with disintegration of some pancreatic cells and the presence of areas of hemorrhage between the cells of the pancreatic tissue. Most of the cells of the islets of Langerhans appear to have dark pyknotic nuclei and some of them are ruptured, especially the peripheral ones with infiltration of inflammatory cells and separation of the islets from the pancreatic visceral tissue.

While the results of microscopic examination of the tissue sections of the diabetic pancreas treated with volatile oil (50 mg/kg) showed histological changes represented by the pancreatic visceral tissue still containing degeneration acinar cells and tissue disintegration with slight bleeding as well as separation of the islets of Langerhans from the exocrine tissue, beta and alpha cells also appear disorganized within the islets with infiltration of inflammatory cells. However, the

high dose of essential oil reversed the effects of Decadron and showed a similar histological result to the control group, as the islets of Langerhans regained their normal cellular structure although some gaps still existed between the endocrine cells and these cells were in the form of twisted ropes. It is also noted that the histological structure of the exocrine part of the pancreas consists of cells arranged in the form of more regular pancreatic acini with small spaces separating them.

Microscopic examination of the pancreatic tissue treated with essential oil (50 mg/kg) showed that the islets of Langerhans had a normal structure with a proliferation of endocrine cells and the islets were surrounded by a capsule composed of loose connective tissue in addition to the acinar cells appearing as pyramidal cells with a peripheral nucleus and a slight infiltration of some inflammatory cells within the islets with the presence of slight hemorrhage in sites between the pancreatic acini. Moreover, the histological diagnosis of the pancreatic tissues in rats treated with volatile oil (100 mg/kg) showed normal histological structure with cells arranged in the form of twisted ropes with a doubling of beta cells. The pancreatic visceral tissue is surrounded by a capsule composed of loose connective tissue and includes pyramidal- shaped acinar cells with clear boundaries with a dark spherical nucleus and slight vacuolization in one of the secretory cells. The histological structure of the interlobular duct also appears with wide and large cavities lined with simple cuboidal epithelial tissue in addition to fibrous tissue barriers between the secretory cells extending into the capsule. These results were similar to those of Mawout *et al*., (2020) and Kepta *et al*., (2021) who confirmed that the endocrine pancreas is inactive in the Decadron and furthermore [42; 59]. Decadron-induced insulin resistance leads to hyperinsulinemia which in turn stresses the beta cells in the islets of Langerhans and thus leads to reduced endocrine activity of the pancreas and then hypertrophy of the islets of Langerhans. The observed effect of Decadron on pancreatic tissue was consistent with the results of Mahmoud *et al*., (2022) who observed an increase in the size of the islets and areas of hemorrhage between the endocrine cells and most of the cells with hollow cytoplasm [60]. These observed changes may be due to decreased peripheral insulin activity which causes compensatory changes in the endocrine pancreas [61; 62]. It has been suggested that one of the main causes of steroid-associated diabetes is pancreatic beta cell dysfunction. However, the mechanism isn't fully understood but several different studies have investigated the effects of various doses of Decadron on the pancreas and metabolic alterations have shown comparable outcomes [63-66].

The present study provides evidence that the essential oils of *E. cardamomum* seeds exert cytoprotective effects against the Decadron induced adverse effects

on pancreatic tissues with the results showing restoration of the normal structure of pancreatic islets as well as the appearance of cords of regular islet cells. Our study agreed with Attia *et al*., (2023) who showed that the aqueous extract alleviated the histopathological changes induced by tamoxifen possibly through antioxidant, anti-inflammatory and lipid-lowering effects besides reducing free fatty acid levels [17]. *E. cardamomum* is one of the most popular species with several pharmacological properties that exhibit antioxidant and anti-inflammatory effects and exhibit beneficial hypoglycemic effects [67-70]. Several studies have revealed several active components in the aqueous extract of *E. cardamomum* L. that prevent oxidative stress and inflammation [67; 71-74].

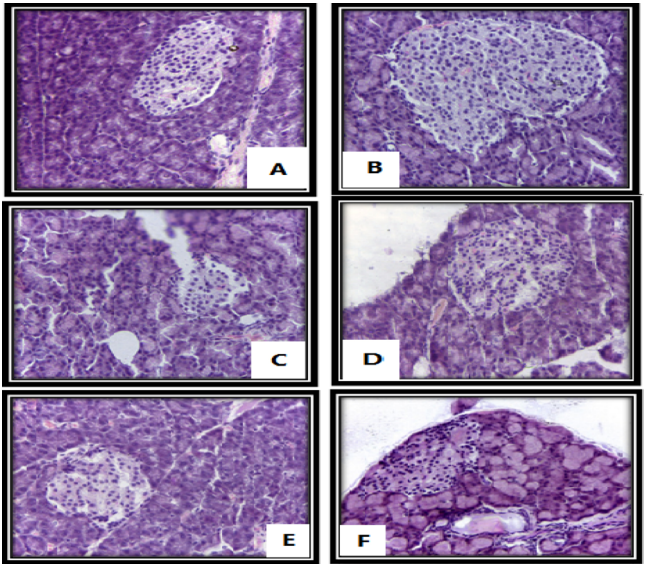

Fig. 7. photomicrographs of H & E-stained pancreatic sections from distinct experimental groups. Control groups is shown (A) islets of Langerhans are round and scattered among the cells of the pancreatic acini and the cells are arranged in branched cords. Decadron groups (B) show dilation of the ialets of Langerhans and their separation from the pancreatic visceral tissue. Decadron and essential oil (50 mg/kg) groups (C) shows separation of the islets of Langerhans from the exocrine tissue and the cells appear disorganized within the islets. Decadron and essential oil (100 mg/kg) groups (D) shows islets of Langerhans with normal cellular structure and cells in the form of coiled rops. EC essential oil (50 mg/kg) groups (E) show islets of Langerhans with normal structure with cells spread and the islets are surrounded by a capsule. EC volatile oil group (100 mg/kg) (F) shows the normal histological structure of the islets of Langerhans with multiplication of beta cells.

Conclusion

To our knowledge, this study demonstrates the protective effect of *E. cardamomum* essential oil against Decadron induced diabetes. We showed that the volatile oil of *E. cardamomum* seeds could attenuate hyperinsulinemia, hyperglycemia, body weight loss and histological changes in the pancreas induced by Decadron. This indicates the promising potential of *E. cardamomum* seed essential oils in preventing the adverse effects of Decadron and suggests that cardamom oil could be used as an adjuvant hypoglycemic agent in diabetes, especially Decadron induced diabetes.

Ethics committee conclusion. All procedures performed on rats were in accordance with the ethical standards of the Ethics Committee of the Institutional Review Board of University of Basrah – College of Science.

Conflict of interest information. All authors declare that there are no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Zahraa Abd Alreda Jabbar: conceptualization, methodology, software, validation, investigation, resources, visualization, project administration.

Karim H. Al-Derawi: conceptualization, validation, writing-original draft preparation, writing-review and editing, supervision.

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