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The antioxidant of *Anethum graveolens* (Dill) on some biochemical parameter in blood serum of male rats

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Abstract---Liver toxic is an acute effect of paracetamol (500 mg/kg) Consequently, we investigated how paracetamol toxicity affected liver cell enzymes in this study aspartate aminotransferase (GOT) and alanin aminotransferase catalyzes (GPT), Glutation (GSH) and total protein ,glucose , liver and body weight of male rats that drenched *Anethum graveolens* (Dill) . were used in this research 40 adult male rats, weight 172-311 gm, age 8-12 weeks, isolated in a environment at temperature 25°C in an animal house in university of karbala ,They were given food, male rats were divided into four groups (G). (G1) the control group has gaves the food and normal saline 0,9% only, (G2) injection of paracetamol 500 mg/kg body weight (B.W). (G3) injection 100 mg/kg B.W *A. graveolen* extract + 500 mg/kg B.W of paracetamol. (G4) given 150mg/kg B.W of flavonoid compound extracted + 500 mg/kg B.W of paracetamol. The present study found ability of Dill and flavonoid extract to antioxidant and protective liver enzyme against the paracetamol overdose by significant decrease GPT, GOT, glucose.

Keywords---*Anethum graveolens* (Dill), flavonoid, paracetamol.

Introduction

Medicinal plants (alternative plants) are types of plants used at herbalism. These plants considered a rich source of active secondary metabolism compounds which can be used in drug synthesis and development (1) active secondary metabolites

compounds are any compound in plants as polysaccharide, flavone, terpenoid and phenol (2).

Southern Europe is home to *A. graveolens*, an indigenous member of the Umbelliferae family. It grows as an annual plant in the Mediterranean southern Asia and central. (3), It has been used for more than 5,000 years as a means of a well-liked aromatic spice and herb. It was employed as a milk secretion stimulant and a treatment for gas and indigestion. Additionally, it is used as a wound healer, antiemetic, anticonvulsant, anticramp (in youngsters), to strengthen the stomach, and to improve hunger. (4).

Consist of a large group of polyphenolic compounds have antioxidant effects in biological systems (5), according to chemical structure are classified in to flavones, flavonols, flavanones, catechine. isoflavones anthocyanidins, chalcones. Poor absorption of these compound may be because the Formation of a complex with another substance and phenol moiety breakdown by bacteria in the gastrointestinal tract , which prevent absorbtion , due to the presence of sugar moieties, which increase their hydrophilicity, are scarcely absorbed from the small intestine (6).

Antioxidant enzyme defense mechanisms that shield cells from cellular free radicals and repair and prevent antioxidant the formation of oxidative stress damaged molecules can help avoid oxidative stress damage, Antioxidant enzymes are essential for shielding cells from reactive oxygen species' (ROS) damaging effects. (7). ROS leads to oxidation the lipid, DNA and protein under normal conditions (8). Under most oxidation stress conditions, Malondialdehyde enzyme (MDA) is a product which is considered as a marker of peroxidation damage of cell, ROS and free radicals reactions with membrane lipids causing lipid peroxidation (9). The first line of defense against free radical damage is the antioxidant system, which is essential for maintaining wellbeing and optimum health. (10). A common antipyretic and analgesic, paracetamol can cause liver damage if used in excess is primarily broken down via conjugation with glucuronide and sulphate in the liver (11,12), Hepatic cytochrome P-450 breaks down some paracetamol into a hazardous metabolite. is produced that has been linked to paracetamol's hepatotoxicity (13) , In the United States, United Kingdom, and America, 60 percent of acute liver cell failures requiring orthotropic liver transplantation are caused by paracetamol, either alone or in combination with other medications. (14), In the United States, United Kingdom, and America, paracetamol is to blame for 60% of acute liver cell failures necessitating orthotropic liver transplantation, either alone or in combination with other medications.(15).

Material and method

1- plant collection

The plant *A. graveolens* purches from Karbala city/ Iraq at 10/3/2022 during the flowering stage, were dried at air , Plant material was mechanically ground into a powder and used right away (16).

2- Soxhlet Extraction: For 22 hours, 60 grams of *A. graveolen* were placed in a thimble with 160 ml of 70% methanol in a flask round. The extract was then evaporated using a rotary evaporator at 45°C (17 and 18)

3- Secondary metabolism screen study :

3-1 : Saponins

The swirling of the extract aqueous solution for a prolonged period of time caused foam to form (19).

3-2: Phenols

Test for lead acetate, precipitate formed after adding 0.5 ml of a 1 percent lead acetate solution to 5 milligrams of dill extract.

3-3: Glycosides

After dissolving 0.5 mg of dill extract in 1 ml of water, aqueous NaOH solution was added. creation of the color yellow.

3-4: Tannins

added 5 ml of distilled water to 5 ml of oil extract , the mixture heated at 80-100 °C for 10 minutes in water bath apparatus , after being filtered , added 5 drops of 1 % ferric chloride , the dark green color (20) .

3-5: Alkaloids:

The gathered filtrate was mixed with Wagner reagent, which is a solution of potassium iodide and iodine, reddish-brown precipitate formation (21).

3-6: Flavonoids:

4mL of extracts were combined with 1.5ml of 50% methanol. After mixing, 5–6 drops of concentrated HCl were added, and the mixture was heated with magnesium metal till red color was created. Flavonoids are present when a color is red. (22).

4: Exrtraction of flavonoids compound from *A. graveolen*.

Twenty grams of dried dill methanol extract were placed in a reflex for eight hours with 400 ml of 2M hydrogen chloride solution. After the filtrate had been cooled, it was moved to a separator funnel where the glycon moiety was extracted using 100 ml of ethyl acetate alcohol .The obtained ethyl acetate layers were washed with distilled water (D.W.) to remove excess acid, and then dried using rotary evaporator equipment at 40°C for 20 minutes. (23).

4- Experiment Design:

40 adult male rats, weight 172-311 gm, age 8-12 weeks, isolated in a environment at temperature 25°C in an animal house ,They were given food, There were four groups of rats. (G). (G1) the control group has injection the food and normal saline 0.9 % only, (G2) 500 mg/kg B.W. of paracetamol is injected, (G3) injection 100 mg/kg B.W *A. graveolen* extract + 500 mg/kg B.W of paracetamol. (G4) given 150mg/kg B.W of flavonoid + 500 mg/kg B.W of paracetamol.

5- Biochemical tests

Blood were drawn by cardiac puncture technique were then centrifuged apparatus at 3000 rpm for 10 min to separate the blood serum. The blood serum

was stored at 40°C until enzymes assays were carried out, blood bled at 30 days, .serum total protein concentration (24). And glucose (25).

5-1- The assay method for GOT and GPT is the synthesis of the glutamate oxaloacetate and glutamate pyruvate enzymes, which facilitate the transfer of the amino group from alanine to oxoglutarate. A kit approach was used to measure GOT and GPT (Reitman-France colorimetric method, linear chemical, S.L., Spain). (26 ,27).

5-2 : Glutathione (GSH) Assay (µmol/ L).

Tris Buffer Solution:

A concentration of 50 mmol. was prepared by dissolving 6.057 gm. of Tris hydroxyl methyl aminoethan in 900 ml. of distill water . and add 0.0292 gm. of Ethylenediaminetetraacetic acid (EDTA) at 0.1 ml., complete the volume to 1 L. of distill water,with acidic substrate (pH 7.6) the solution was stored in the refrigerator until use (28).

Results and Discussion

1- Phytochemical study:

The findings of the chemical compounds screen analysis were used to identify the active phytochemical compounds in the extract of *A. graveolen* shown in table (2). were positive results for Phenol , Glycoside, Alkaloid Flavonoid Saponin and Tannins.

Table (1) phytochemical screen of *A. graveolen* extract

Compounds	extract
Saponin	+
Phenol	+
Glycoside	+
Tannins	+
Alkaloid	+
Flavonoid	+

Oxidant Assay 3

Table (2) GOT, GPT and GSH enzyme Percentage for Rat Groups Treated with the Study concentrations level (U/L)

Parameter Treatment Groups	GOT	GPT	GSH
Control	88.91	45.21	2.29±7.41
G2	122.34 ^a	82.87 ^a	1.23 ^a
G3	99.8 ^b	78.76 ^b	2.01 ^b
G4	102.88 ^b	55.76 ^b	2.22 ^b
LSD	0.17		

Significant altering signified by a little letter

)a) denotes a notable increase(

)b) signifies a notable decline(

p≤ 0.05

Table (3) Protean and glucose Percentage for Rat Groups Treated with the Study Concentrations level mg/dl

Parameter Treatment Groups	Protean (mg/dl)	Glucose (mg/dl)
Control	5.76	0.186
G2	4.99 ^b	0.202 ^a
G3	5.99 ^a	0.190 ^b
G4	7.98 ^a	0.88 ^b
LSD	0.14	

Significant altering signified by a little letter.

(a) denotes a notable increase.

(b) signifies a notable decline.

p≤ 0.05

Table (4) weight of body and the liver weight Rat Groups

Parameter Treatment	weight of body gm	liver weight gm
Control	31.76	2.99
G2	25.22 ^b	1.99 ^b
G3	27.99 ^a	2.22 ^a
G4	30.01 ^a	2.89 ^a
LSD	0.15	

Significant altering signified by a little letter.

(a) denotes a notable increase.

(b) signifies a notable decline.

p≤ 0.05

Result

Paracetamol (500 mg/kg) showed hepatotoxicity after 24 hours evident from biochemical measure of research, the level of liver enzyme in rats G2, GOT (122.34IUL) and GPT (82.87 IUL) indicate significant increase as compared with control and also G3 GOT (99.8 IUL) and GPT (78.76 IUL) and G4 GOT (102.88 IUL) and GPT (55.76 IUL) revealed significant decrease compared with control table (2)

Level of liver GSH enzyme in rats G2 (1.23 IUL) reveal significant decrease as compared with control, G3 (2.01 IUL) indicate significant increase as compared with G2.

The result in table (3) reveal significant decrease in G2 compared with three groups. the level of protean in male rats G2 , (4.99 mg/dl) and also G3 protean (5.99 mg/dl) and G4 protean (7.98 mg/dl) revealed significant increase compared with control and G2, While the level of glucose in male rats in G2 (0.202 mg/dl) indicate significant increase as compared with control, and also G3 (0.190 mg/dl) and G4 (0.88 mg/dl) revealed significant decrease compared with control and G2 .

The result in table (4) reveal significant decrease in G2 compared with three groups. the weight of body in male rats G2 , (25.22 gm) and also G3 (27.99 **gm**) and G4 (30.01 **gm**) revealed significant increase compared with control and G2, While the liver weight in male rats in G2 (1.99 **gm**) indicate significant decrease as compared with control, and also G3 (2.22 **gm**) and G4 (2.89 **gm**) revealed significant increase compared with control and G2 .

Discussion

The goal of the current study was to examine the antioxidant and protective effects of *A. graveoles* extract and flavonoids on liver enzyme damage caused by paracetamol. An accidental height dose of the commonly used painkiller and antipyretic medication paracetamol causes severe liver cell destruction. It is known that the cytochrome P450 pathway transforms a portion of paracetamol into the hazardous metabolite N-acetyl-Pbenzoquinamine (NAPQI) [29]

Paracetamol caused significant increase in GPT and protean (30) , It is well known that toxins like paracetamol cause enough damage to the hepatic parenchyma cells to lower the level of total plasma protein content (31), and that the toxicity of paracetamol is accompanied by an increase in the GPT, GOT enzyme, and glucose levels and decrease by taking a paracetamol dose, Uric acid and total protein are caused. (32) .

The significantly increase of Alanine aminotransferase ALT Aspartate aminotransferase AST Enzymes in the paracetamol-treated group showed that a paracetamol overdose had a hepatotoxic effect on parenchymal cells (33). This increase may be brought on by ROS-induced liver cell memory loss and the release of these enzymes into the serum. [34].

Overdosing on paracetamol causes liver glutathione (GSH) depletion (due to the conjugation of glutathione with NAPQI to form mercapturic acid), which then causes an increase in the lipid peroxidation enzyme by drawing hydrogen from a polyunsaturated fatty acid. This damage to the liver cells is the result of the paracetamol overdose.. **(35,36)** Rat hepatocytes are damaged by ROS produced as a result of paracetamol overdoses.

This outcome is consistent with the findings of (37) who showed that paracetamol toxicity happens when it is taken in large doses. Elevated plasma liver enzymes were a sign of damaged liver cells. (38).

However, the giving of *A.graveoles* extract and flavonoid Additionally, paracetamol has stopped the rise in GOT, GPT enzymes and glucose, prevented the decrease GSH enzymes and total protein. The experiment showed that flavonoid and Dill increased antioxidant enzyme activity and worked to effectively scavenge free radicals. Because flavonoids have the ability to scavenge electrons of ROS for this reason is considered antioxidant (39). Have an antioxidant effect at intracellular OR extracellular antioxidant act inhibition xanthine oxide activity that has turns of xanthine oxide product to xanthine dehydrogenase (40). The flavonoid significant increase in GSH level may be due to the activation of the enzyme γ Glutamyl cysteine synthesis (GCS) or increased resistance Glutathione synthesis or this compounds may activate γ - Glutamyl transe peptidase (41). Eventually, the GSH enzyme converts hydrogen peroxide into water (H₂O)(42) .

Because glutation peroxidase enzyme antioxidant that scavinig the super oxygen, super oxide and hydrogen peroxide, as well as the ability to stop the production of ROS or free radicals (43). Compare with study (44) show Malondiadehyde (MDA) levels in fatigued animals rats decrease when oral inject of rutin compound (15.30,60 mg/kg) B.W. for 7 days and increases the activities of the super oxide dismutase and GPx enzyme .

The presence of phenolic compounds and essential oil in *A. graveolens* has been reported [45]. Polyphenols compounds are able to neutralize ROS or free radicals prevent singlet and triplet oxygen, and break down peroxides. The present study (46) showed that dill aqueous extract is a source of antioxidants that may be employed to limit cellular damage and reduce biological oxidative stress by scavenging ROS activity of the oxidative stress. Strong antioxidant components found in dill aqueous extract function as an extracellular ROS neutralizer.

Dill's abundant polyphenols and volatile oil components have antioxidant properties and support healthy renal function. Indicated the ability of the dill extract to protect hepatocytes from oxidative stress damage caused by paracetamol overdose. Decrease of bilirubin of total protein and albumin levels in protected rats revealed endoplasmic reticulum cells and stabilized biliary cell function leading to protein synthesis and bile acid [47].

Conclusions

The present research the Dill and flavonoid extract has antihebatotoxic that may minimize effect generated by hebatotoxic paracetamol.

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