Biological study of sweet fennel fruits on regeneration of liver cells

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الملخص العربي

دراسة بيولوجية لثمار الشمر الحلو لتجديد خلايا الكبد

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الملخص باللغة العربية

أمراض الكبد هي الأكثر انتشارا بين أمراض المصريين، والأكثر خطرا على حياتهم وأعمالهم منذ زمن بعيد، أثبت العلماء أن مركب الانيثول الموجود في الشمر المصري وفي كثير من دساتير الأدوية الأوروبية يستخدم لعلاج امراض الكبد، كما أثبتت الدراسات العلمية آن للشمر تأثيراً قاتلاً لبعض أنواع البكتيريا ولهذا يستخدم لإيقاف الإسهال المتسبب عن البكتريا. وفى هذه التجربة تم استخدام ٦٠ فأرا من سلالات الألبينو (سبراجو داولي) والتي قسمت إلي ٤ مجموعات بكل مجموعة ١٥ فأرا كالتالي: **المجموعة الأولي :** المجموعة الضابطة السالبة Control negative تم تغذيتها علي الغذاء الخالي من التلوث أو الإضافات. **المجموعة الثانية :** وتم حقنها `برابع كلوريد الكربون مع الغذاء القياسي بدون إضافات(المجموعة الضابطة الموجبة). **المجموعة الثالثة:** وتم تغذيتها علي الغذاء القياسي مضافا إليه تركيزات من الشمر الحلو هو ٥% - ١٠% - ١٥ % **المجموعة الرابعة:** وتم حقنها برابع كلوريد الكربون مع تغذيتها على الغذاء ا لعادي مضافا إليه تركيزات من الشمر الحلو ٥% - ١٠% - ١٥ %.

النتائج التي تم الحصول عليها يمكن تلخيصها في ما يلي : -

التركيب الكيميائي لثمار الشمر: يحتوي الشمر (السنوت) على زيوت طيارة وأهم مركبات الزيت مركبي الانيثول (Anethole) والفينشون (Fenchon) وتعود الرائحة المميزة للسنوت إلى المركب الأخير. كما يحتوي على مركب الاستراجول (Estragole) بالإضافة إلى فيتامينات أ، ب، ج ومعادن الفسفور والكالسيوم والكبريت والحديد والبوتاسيوم ويتميز الشمر الحلو بارتفاع نسبة الانيثول بقدر كبير عن الشمر المر مما يجعله مرغوبا من دول أوروبا كما يعزى إلى هذا المركب التأثير الواقي للكبد. وفيما يلي أهم النتائج : -

تأثير الشمر علي وظائف الكبد فقد أوضحت النتائج الأتي: بالنسبة للمجموعة الضابطة الموجبة لوحظ حدوث ارتفاع ذو دلالة إحصائية في مستوي إنزيمات الكبد AST (S.GPT) ALT,(S.GOT)) بتأثير رابع كلوريد الكربون في المجموعات T2 وT6 و مقارنتا بالمجموعة الضابطة السالبة وT1. .مما يوضح التأثيرات الضارة لرابع كلوريد الكربون علي وظائف الكبد وحيث بلغت ALT و AST أعلي القيم مع T2 كما أعطت المعاملة T1 قيم منخفضة من كل من و ALT و AST . وأظهرت النتائج أن التغذية على الشمر الحلو لها تأثيرا وقائيا للكبد وحيث أعطت T4 قيما منخفضة من ALT و AST عن كل من T2 . كما أظهرت النتائج أن التغذية على الشمر بنسبة ٥%أعطي أفضل النتائج من ALTو AST في حين أن زيادة تركيز الشمر تؤدي إلى زيادة كل منهما.

الالبيومين:أوضحت النتائج وجود فروق معنوية بين المجموعات المختلفة حيث أعطت كل منT1 اقل قيم الالبيومين في حين أعطت المجموعة T2 أعلي القيم .بالنسبة للتركيزات لا يوجد فروق معنوية. وهناك تأثير معنويا بين التركيزات والمجموعات فسجلت المجموعة الأولى (المجموعة الضابطة السالبة) وكانت اقل قيمة(٢,٨) عند تركيز ٥% .

البليروبين: اختلف تأثير المعاملات للمجموعات الأربعة معنويا فيما بينها في البليروبين الكلى والمباشر وغير المباشر. وقد أعطي المجموعة الضابطة السالبة T1 اقل قيم البليروبين الكلى والمباشر (٠,٢٥ و ٠,١٤) في حين أعطت T2أعلي القيم 5.8 . وقد أدت التغذية بالشمر الحلو لوقاية كبد الفئران التي تم حقنها برابع كلوريد الكربون وأدت إلى

خفض قيمة البليروبين الكلى والمباشر وقد أعطت T1 (الضابطة السالبة)اقل قيم في البليروبين الغير مباشر وقد لوحظ ارتفاعا طفيفا في قيم البليروبين بزيادة تركيز الشمر في غذاء الفئران.

الكولسترول:أظهرت النتائج أن T3 قد خفضت من قيمة الكولسترول حتى مقارنة ب T1(الضابطة السالبة) وذلك بفضل استخدام الشمر الحلو والذي يحتوي على نسبة مرتفعة من الانيثول. في حيت سجلتT2 أعلي قيم الكولسترول بتأثير كل من الحقن ب رابع كلوريدالكربون أدت المعاملة بالشمر الحلو في T3 في الحصول على اقل قيم في LDL . كما أعطت المعاملة ب١٠% من الشمر الحلو اقل قيم LDL تليها التغذية علي ٥% من الشمر الحلو . تم الحصول على اقل قيم من LDL (٤٢) بواسطة المجموعة T3 عند التغذية على١٠% من ثمار الشمر الحلو في عليقة الفئران .أما في الكولسترول عالي الكثافة أعطت T2 اقل قيم (٤٧,٣) في حين أعطت T3 أعلي قيم HDL (٧٤,٩) ولم يكن هناك تأثيرا ذو دلالة إحصائية لتركيزات الشمر في العلقة على هذه الصفة . في حين سجلت ت٣ عند التغذية على ١٠% شمر في العلقة أعلي قيم HDL (٧٧)

الدهون الثلاثية :سجلت أعلي قيم الدهون الثلاثية بواسطة المجموعة T2 (85.33) في حين حققت T3 اقل القيم (٥٥,١١) .

التوصيات

إضافة الشمر الحلو إلى الطعام كونه مادة وقائية للكبد ويؤدي إلى تجديد خلايا الكبد المصابة وذلك بإضافة الشمر الحلو بنسبة ٥% إلى معظم الأطعمة التي يمكن إضافته لها.كما توصي الدراسة إلى بذل المزيد من الدارسات في استخدام الشمر في الطعام واستخلاص المواد الفعالة لاستعمالها في مجال الغذاء كمواد حافظة طبيعية وكواد مجددة لخلايا الكبد

Abstract:

Only one strain of common fennel (*Foeniculum vulgare* Mill.) was cultivated in Egypt for the national and international purpose. The cultivar yields big fruits and reasonable percentage of essential oil with particularly high estragole content, but it is poor in fenchone which is an important constituent of the fennel essential oil. Sixity albino male rats (Sprague Dowely strain) of an average weight 120 ± 10 g were divided into 20 groups each group contains 5 rats. Group1:Control group (control negative) 5 rats were fed on basal diet for 30 days. Group 2 : Control group(5 Rats which were induced by CCl_4) (control positive)5 rats were fed on basal diet for 30 days. Group3: 5 rats were fed on basal diet containing sweet fennel 5%, 10% and 15%. Group4: 5 rats were fed on basal diet containing Bitter fennel 5% ,10% and 15%. The results revealed that hepatoprotective effect of sweet fennel was very obvious ,where the rats treated with CCl4 but received S.F (T4) indicated lower value of ALT & AST which significantly differed with T2 and T4 of treated rats with CCl4 of S.F the result revealed that fennel had better effect at 5%where Concerning the effect of fennel concentration , the result revealed that fennel had better effect at 5%where ALT & AST value was over all fennel varieties, while increasing level of fennel led to increase ALT & AST.

Key words: Fennel, Sweet fennel, regeneration, Bilirubin, Foeniculum Volgare ,Albumin, ALT, AST,HP,HDL,LDL, Triglyceride

Introduction:

Afify *et al.*,(2011) reported that, fennel is a plant belonging to the *Umbelliferae* (*Apiaceae*) family, known and used by humans since antiquity. Because of its flavor, it was cultivated in the countries surrounding the Mediterranean Sea. Fennel is one of the oldest field crop used by the Egyptian for medicinal purposes. Most of the area cultivated with fennel is located in Mid-southern Egypt (mainly, Elfayom, Menia and Assiut Governorates). The total area cultivated with fennel in Egypt was 2209 feddan in 2006 which produced 3446 tons of ripe dry seeds. Assiut Governorate cultivated about 86% of this area **(A. E. B., 2007).** The liver plays a vital role in fighting infections, particularly infections arising in the bowel. It does so by mobilizing part of the body defenses mechanism called macrophage system. The liver contains half of the body supply of the macrophages (known as kupffer) which literally destroy any bacteria that come into contact with them. If the liver is damaged in any way its ability to fight infections is impaired(**DAA,2000**) Chemicals that cause liver injury are called hepatotoxins. These chemicals often cause subclinical injury to liver which manifests only as abnormal liver enzyme tests. Carbon tetrachloride CCl_4 has been widely used in animal models to investigate chemical toxin – induced liver damage. The most remarkable pathological characteristics of CCl_4 induced hepatotoxicity are fatty liver, cirrhosis and necrosis, which have been thought to be resulted from the formation of reactive intermediates such as trichloromethyl free radicals (CCl_3+) metabolized by the mixed function cytochrome p 450 in the endoplasmic reticulum **(Recknagel *et al.,* 1989*).*** Usually, the extent of hepatic damage is assessed by the increased level of cytoplasmic (ALT,AST ,and ALP), thus leads to leakage of large quantities of enzymes into the blood circulation .This was associated by massive centrilobular necrosis, ballooning degeneration and cellular infiltration of the liver **(Gowri *et al.*,2008). Telci *et al.*,(2009*)*** reported that the essential oil content and composition varies during the different

maturation stages of *F. vulgare*. The essential oil content was reported to decline with fruit maturity. The content of trans-anethole, the main component, varied between 81.63% and 87.85%. Fennel has been used as food and medicine with long history in central Europe and Mediterranean region as well as in China. It is also a flavor food with health value. Numerous compounds including trans-anethole, estragole, fenchone, sesquiter penoids, coumarins and polyphenolics were isolated from this plant, most of which exhibited significant bioactivities. The fennel has potential beneficial therapeutic actions in the management of bacterial and fungal infections and colic pain. Both the fruit and whole plant of this plant might be the source of chemical and biological materials in future. For furtherutilization of this plant, systematic phytochemical and biological mechanic studies are needed **(Lee, 2004*).* Telci *et al.*,(2009*)* reported that the essential oil content and composition varies during the different maturation stages of *F. vulgare*. The essential oil content was reported to decline with fruit maturity. The content of trans-anethole, the main component, varied between 81.63% and 87.85%. Fennel has been used as food and medicine with long history in central Europe and Mediterranean region as well as in China. It is also a flavor food with health value. Numerous compounds including trans-anethole, estragole, fenchone, sesquiter penoids, coumarins and polyphenolics were isolated from this plant, most of which exhibited significant bioactivities. The fennel has potential beneficial therapeutic actions in the management of bacterial and fungal infections and colic pain. Both the fruit and whole plant of this plant might be the source of chemical and biological materials in future. For furtherutilization of this plant, systematic phytochemical and biological mechanic studies are needed **(Lee, 2004*).* Telci *et al.* , (2009*)* reported that the essential oil content and composition varies during the different maturation stages of *F. vulgare*. The essential oil content was reported to decline with fruit maturity. The content of trans-anethole, the main component, varied between 81.63% and

87.85%. Fennel has been used as food and medicine with long history in central Europe and Mediterranean region as well as in China. It is also a flavor food with health value. Numerous compounds including trans-anethole, estragole, fenchone, sesquiter penoids, coumarins and polyphenolics were isolated from this plant, most of which exhibited significant bioactivities. The fennel has potential beneficial therapeutic actions in the management of bacterial and fungal infections and colic pain. Both the fruit and whole plant of this plant might be the source of chemical and biological materials in future. For furtherutilization of this plant, systematic phytochemical and biological mechanic studies are needed **(Lee, 2004*).*** Fennel was known as excellent sources of nature antioxidants and contributed to the daily antioxidant diet (**Shahat *et al.,* 2011).** The volatile oil of fennel showed strong antioxidant activity in comparison with butyrated hydroxyanisole and butylated hydroxytoluene (**Singh *et al.,* 2006). Choi and Hwang *(2004*)** reported that essential oil of fennel had hepatoprotective activity against carbon tetrachlo-ride (CCl_4) which induces liver injury in rat's model as it decreases levels of serum AST, ALT, ALP and bilirubin. Fennel contains several types of phenolic and flavonoids that is known as anti-oxidants and had strong free radical scavenging. It is one of the most effective antioxidants in the food industry. Lately, chemical composition of fennel demonstrated the presence of anethole as the most potent antioxidant **DE *Martinol et al., (2009*).** Presumably, fennel functions as an antioxidant, stops the propagation of the peroxidative chain reaction, by inhibiting 5-hipoxigenase ***Miguel et al., (2010*).** Antioxidant defense mechanisms are important for the protection of cells and tissues against oxidative damage. The major endogenous antioxidant enzyme-systems include superoxide dismutase, catalase, selenium-dependent glutathione peroxidase, glutathione peroxidase, and glutathione reductase. The major non-enzymatic endogenous antioxidants include glutathione and vitamin E **(Abd El-Ghany *et al.,* 2012)**. **Rezq,(2012),** revealed that significant increase in the activities

of liver enzymes (AST, ALT and ALP) in feeding rats with high fat-diet. These elevations in liver enzymes may be attributed to their release from the cytoplasm into the blood circulation after rupture of the plasma membrane, cellular damage. This result confirmed by histo-logical changes of liver sections of positive control rats, which showed congestion of hepatic sinusoid, vacuolization of hepatocytes and necrosis of spo-radic hepatocytes as well as fatty changes of hepa-tocytes. ***Rather et al.,(2012)*** indicated that The essential oil extracted from the fruits of *F. vulgare* exhibited antibacterial effect against foodborne pathogens such as *Escherichia coli*, *Bacillus megaterium* and *Staphylococcus aureus* (***Mohsenzadeh, 2007)***, *Listeria monocytogenes* and *S. aureus* (**Dadalioglu and Evrendilek, 2004 and Cantore *et al.*, 2004).** Aqueous and organic extracts of *F. vulgare* have been reported to show antibacterial activity against some bacterial strains (**Kaur and Arora, 2008).** The seed essential oil of *F. vulgare* has also been reported to possess antibacterial activity against some human pathogenic bacteria. Ethanol and water extracts of *F. vulgare* have shown activity against Campylobacter jejuni and Helicobacter pylori ***(Mahady et al., 2005).*** The fennel essential oil has been reported to exhibit antifungal effect. The fennel essential oil and its seed extracts have been reported to exhibit anti mycobacterial and anti candidal albicans activity (***Abed, 2007*****, Pai *et al.,* 2010**).The essential oil of *F. vulgare* has also been reported to reduce the mycelial growth and germination of Sclerotinia sclerotiorum and as such could be used as bio fungicide alternative to synthetic fungicides against phytopathogenic fungi (**Soylu *et al.,* 2007).** The essential oil of *F. vulgare* has been reported to show complete zone of inhibition against *Aspergillum niger*, *Aspergillum flavus*, *Fusarium graminearum* and *Fusarium moniliforme* at 6 µl dose (**Singh *et al.,* 2006).** Estragole and trans-anethole are the major constituents of the essential oils of bitter fennel chemotypes *(Foeniculum vulgare* Mill. var. vulgare) (***Gross et al., 2002*****).** In addition to estragole, the European Food Safety Authority

(EFSA) compendium indicates transanethole as a substance of possible concern for human health presentin *F. vulgare* Mill. **(EFSA, *2012*).** For trans-anethole the joint FAO/WHO Expert Committee on Food Additives (JECFA) derived a temporary acceptable daily intake (ADI) of 0–2.0 mg/kg bw ***(JECFA, 1998),*** which can be used to define whether exposure resulting from proposed uses and use levels will be safe.

MATERIAL AND METHODS

1-MATERIAL

1-1.Investigated samples: Investigated samples consisted of sweet fennel. Fennel items have been bought from Royal Company for medicinal products and prepared for chemical analysis, which are suggested for treatment of liver disorder from the fennel. The chemical composition are reported as shown in (Table, 1)

Table (1):Chemical composition of sweet fennel .

Fennel oil(%)	
Component	Sweet fennel
Trans-anethole	83.1
Fenchone	4.7
Estragole	3.5
a-Pinene	3.4
Limonene	3.7

Carbon Tetrachloride CCl_4 and Paraffin oil. Carbon tetrachloride CCl_4 has been used as toxic chemical for liver injury according to **Passmore and Eastwood,(1986).**

METHODS:

2-1. Preparation of Fennel : The fennel seeds used were purchased from Royal Company for medicinal products, El-Haram St. Gizza .

2-2 Grouping of Experimental Animals (rats) : The rats were divided into four groups as following :

Group1:Control group (control negative) 5 rats were fed on basal diet for 30 days.

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Group3: 5 rats were fed on basal diet containing sweet fennel 5%.

Group3: 5 rats were fed on basal diet containing sweet fennel 10%.

Group3: 5 rats were fed on basal diet containing sweet fennel 15%.

Group4: 5 rats were fed on basal diet containing Sweet fennel 5%.

Group4: 5 rats were fed on basal diet containing Sweet fennel 10%.

Group4: 5 rats were fed on basal diet containing Sweet fennel 15%.

Introduction of the liver disorders in experimental animals (rats). Rats were housed in wire cages in a room maintained at 25±2 ^{O}C and kept under normal healthy conditions. All rats were fed on basal diet for one week before starting the experimental for acclimatization. After one week period, the rats were divided into eight groups. **Jayasekhar *et al.*,(1997)**

Biochemical Analysis:

Determination of liver functions

Determination of Serum Glutamate Oxalo acetate Rensaminase (AST) or (GOT). Determination of GOT was carried out according to the method of **Henry (1974) and Yound (1975).**

Determination of Serum Glutamate Pyruvate transminase (ALT):

Determination of GPT was carried out according to the method of **Henry (1974) and Yound (1975).**

Determination of Serum Bilirubin and Serum Albumin: Serum bilirubin and Serum Albumin were determined according to **(Young , 2001) .**

Determination of Serum Lipids :

Determination of Total Cholesterol (TC)and of High density lipoprotein cholesterol (HDL-c): The principle use of total cholesterol and HDL-c were determined according to **Allain , (1974)** .

Statistical analysis: Statistical analysis were performed by using computer program statistical package for CoStat programe ,and compared with each other using Least Significant Differences. All obtained results were tabulated. Statistical analysis has been achieved using CoStat Program according to **Gomez and Gomez (1984) .**

Results and discussion:

Table(2):Effect of sweet fennel concentrations on liver function at different treatments.

	T1	T2	T3	T4		T1	T2	T3	T4	
Fennel conc.	ALT					Total bilirubin				
5%	36.00	116.33	27.67	65.67	61.42	0.25	0.290.92	0.25	0.33	0.44
10%	38.67	112.67	25.67	63.67	60.17	0.24	00.89	0.29	0.36	0.44
15%	36.67	121.00	31.33	65.33	64.33	0.25	0.92	0.24	0.41	0.46
Mean	38.11	116.27	28.22	64.89		0.25	0.91	0.26	0.37	
LSD	A 3.2		B 2.4		AB 7.6	A 0.01		B NS		AB 0.02
	AST					Direct Bilirubin				
5%	42.00	124.00	35.00	73.70	68.67	0.16	0.47	0.13	0.21	0.24
10%	45.30	120.30	32.30	67.00	66.25	0.11	0.60	0.13	0.23	0.27
15%	46.00	127.70	37.70	74.30	71.42	0.15	0.58	0.16	0.19	0.27
Mean	44.44	124	35	71.67		0.14	0.55	0.14	0.21	
LSD	A 2.8		B 1.3		AB 4.5	A 0.05		B 0.02		AB 0.02
	S .Albumin					Indirect Bilirubinin				
5%	2.80	5.5	2.8	5.0	4.03	0.09	0.45	0.12	0.13	0.20
10%	2.80	5.4	2.7	5.1	3.99	0.13	0.29	0.16	0.12	0.18
15%	2.80	6.3	2.9	5.5	4.38	0.10	0.34	0.08	0.23	0.19
Mean	2.8	5.8	2.8	5.2		0.11	0.36	0.12	0.17	
LSD	A 0,2		BNS		AB 0.3	A 0.02		B NS		AB 0.04

The data presented in Table (2) showed the effect of the four groups treatments, three concentrations of sweet fennel on ALT (serum Glutamate Pyrovic Transaminase (S, GPT) or ALT). The data of ALT indicated that CCl_4 caused a significant depression on liver functions which led to increase ALT values. Exposure to high concentrations of carbon tetrachloride (including vapor) can affect the central nervous system, degenerate the liver, where ALT reached 116.27with positive

control (T2).While rats of control negative (T1) exhibited low value of ALT (38.11) and untreated rats with CCl_4 and received S.F showed the lowest value of ALT (28.2) . The hepatoprotective effect of sweet fennel was very obvious , In this connection, Essential oils as natural sources of phenolic components, attract investigators to evaluate their activity as antioxidants or free radical scavengers. Fennel (*Foeniculum vulgare* Miller) belongs to the family apiaceae. It was demonstrated, that the oils of fennel had antioxidant capacity. Also, it has been reported that fennel volatile oil has a potent hepatoprotective action against carbon tetra chloride (CCl_4) induced liver injury in rats. **Özbek *et al,* (2004).** The effect of the interaction between the treatments and fennel concentration exhibited highly significant where the values of ALT varied significantly, rats fed with basal diet plus 10% of S.F (T3) showed the favorable value of ALT (25.76) , in the contrary , the highest ALT value (121) was produced by rats CCl_4 + 15% of T2.

Data presented in Table (3) showed highly significant damage on liver with administration of CCl_4 were T2 exhibited high value of AST (116.67) The rats administrated with CCl_4 exceeded negative control (T1 (44.44) and T3 (35). in the activities of ALT and AST in blood might be due to the increased permeability of plasma membrane or cellular necrosis of liver. **Rao (2006),** this showing the stress condition of the treated animals. Moreover, GGT activity is a marker of hepatobiliary injury, especially cholestasis and biliary effects and shows high sensitivity with a low false negative rate in humans. **Sheehan *et al.,* (1979).** On the other, favorable and good results of sweet fennel treatments (T3) may duo to the active substance anethol and low content of the Estragole content. In this connection, **(Tognolini *et al*., 2007**) stated that, a nethole also prevented thrombin induced clot reaction at concentrations similar to fennel oil. The fennel oil and anethole were tested in rat aorta with or without endothelium and displayed comparable NO-in dependent vaso relaxant activity at antiplatelet concentrations which have been proved to be free from cytotoxic effects in vitro. Furthermore, both *F. vulgare* essential oil and anethole (100 mg/kg oral administration) provided significant protection towards ethanol induced gastric lesions in rats.

Table (3):Effect sweet fennel concentrations on cholesterol and triglyceride at different treatments.

	T1	T2	T3	T4		T1	T2	T3	T4	
Fennel conc.	S. Cholesterol					LDL				
5%	123.3	136.7	123.3	128.7	130.2	55.0	88.3	51.3	78.0	68.17
10%	125.0	132.0	119.0	114.3	127.4	53.7	86.7	42.0	72.3	63.67
15%	122.3	140.3	120.3	139.0	132.0	53.0	92.0	44.7	85.0	68.67
Mean	123.6	136.3	120.9	138.7	129.9	53.89	89.00	46.0	78.44	66.83
LSD	9.2	NS	5.6			9.68	5.05	5.93		
	HDL					serum triglyceride				
5%	68..3	48.3	72.0	59.3	62.00	60.0	85.3	60.3	73.7	69.83
10%	71.3	45.3	77.0	61.3	63.75	51.3	85.3	53.0	67.0	64.17
15%	69.3	48.3	75.70	60.0	63.33	56.3	85.3	52.0	74.3	67
Mean	69.7	47.3	74.9	60.2		55.89	85.33	55.11	71.67	
LSD	**3.2**	**NS**	**1.9**			**4.08**	**NS**	**2.5**		

The obtained data in Table (3) illustrated the serum albumin in different treatment groups, different fennel and their interaction. It was clear from Table (2) that there were high significant S. Albumin values in negative controlT1, T3 (Sweet fennel) which gave 2.8 while the heights value of S. Albumin was obtained by T2 (CCL4+Basal Diet) . The most hepatoprotective effect was related to using S. F in diet regime where T3 decreased Serum Albumin value 2.7 when infected rats were fed with sweet fennel. Slight but significant increases were recorded with using 10% of fennel (over all fennel varieties) where it gave S. Albumin value 5 but no significant differences were found between 5%&10% of fennel concentration. This may reveal that, sweet fennel and its active constituents (anethole) which have a hepatoprotective property. **(JECFA, 1998).** Data recorded in Tables (3) presents the effect of sweet fennel on Total Bilirubin, direct bilirubin and indirect bilirubin in deferent treatment groups . Significant differences were reported between the four treatment groups in total bilirubin, direct bilirubin and indirect bilirubin. The values of total and direct bilirubin had the same trend where T1 (control negative) which

have the lowest values of Bilirubin 0.25 and 0.14.In the same time data indicated clearly that administration of Sweet fennel in diet regime of rats whether treated with CCl_4 or un treated, hepatoprotective effect due to sweet fennel addition reflected in small values of bilirubin T3(sweet fennel and T4(CCl_4+sweet fennel) gave0.26, 0.37 &0.14,0.21 for total direct bilirubin respectively, Concerning indirect bilirubin the values of T1(negative control 0.11) followed by T3 (0.12, and 0.17 T4 The concentration of fennel addition in diet regime had insignificant effect on bilirubin. The optimum concentration was found to be 5%, and slight increases in bilirubin values were observed with increasing fennel concentration 10% and 15%. The interaction between the eight groups and the fennel concentration had no significant effect on total bilirubin direct and indirect bilirubin values.

The tabulated data presented the values of serum cholesterol as affected by the four treatment groups which exhibited high effect on this trait. The rats of T3group (Sweet Fennel) recorded the best value of serum cholesterol (120.9) and was superior to T1 (negative control 123.6) without significant differences. All the rest treatments recorded high and significant differences comparing to the negative control (T1). Iten, (2004). In respect to fennel concentrations, there were insignificant effects on serum cholesterol. Significant effects were attributed to the effect of the interaction between the four treatments groups and the fennel concentration addition in diet regime ,the lowest value of serum cholesterol was 114.3 due to T4 at 10 % sweet fennel concentration without significant differences with T1 (negative control). Application of sweet fennel additives in diet regime of rats led to cause clear depression in LDL recording the lowest value of LDL (46) with T3 followed by T1 (negative control 53.89) . Administration of fennel concentration caused significant differences where application of 10% fennel additive recorded the lowest value of LDL(71.04) followed by 5% (63.67) then 5%(68.17) . The data of HDL recorded the lowest value (47.3) with T2 while the heights one were recorded with T3 (74.9). Fennel concentration additives in rat diet regime hadno significant effect on HDL values. The interaction between the eight groups treatment and fennel concentration had high significant on HDL values whereT3 (feeding with sweet fennel) at 10% of fennel , exhibited the heights of HDL 77. Table (3) presented the values of serum triglycerides as affected by the eight treatment groups which

exhibited high effect on this trait. The heights value of TG was reported by T2 (positive control) 85.33 while the lowest value of TG recorded with T3 (55.11).The concentration of fennel addition in diet regime had insignificant effect on TG. Significant effects were attributed to the interaction between the four treatments groups and the fennel concentration addition in diet regime , were significant and the lowest value of TG was 51.3 with T 1 (negative control) at 10% of sweet fennel concentration.

Table (4):Effect sweet fennel concentrations on HB at different treatments.

	HB				
	T1	**T2**	**T3**	**T4**	
5%	12.3	11.6	13.1	9.80	12.2
10%	12.6	11.3	13.3	10.1	11.9
15%	12.4	12.1	12.5	10.0	11.8
Mean	**12.4**	**11.7**	**13.00**	**10.7**	12
LSD	**0.5**	**NS**	**NS**		

The obtained data in Table (4) illustrated the HP values in different treatment groups, different fennel concentrations and their interaction. It was clear from Table (4) that there were high significant differences among HP values ,where T3(sweet fennel) gave the highest value (13) followed by T1(12.4). It was no significant effect due to the concentration of sweet fennel, slight increases was found with application of 5% fennel concentration without significant difference with 10&15% fennel. The effect of the interaction between the treatments and fennel concentration exhibited in significant effects where the values of HP for rats fed with basal diet plus 10% of S.F (T3) gave (13.3) .

Recommendation:

It is highly recommended to add sweet fennel fruits to food as a hepatoprtective material led to regeneration the injured liver. Sweet fennel is the optimum fennel variety as an effective hepatorotective. The addition of sweet fennel fruits at 5% to food is the more effective fennel concentration as an additive in diet regime .More scientific research efforts are needed to extract the effective materials to provide a source of drugs from the environment which was originally Egyptian source.

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