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Abstract:

The current investigation was carried out to examine the possible potential protective effects of ethanolic extract of annona fruit against trichloroacetic acid induced liver cancer. After completing the preparation of annona fruit extracts, the HPLC conditions of phenols were estimated for each extract separately. The biological experiment used twenty- four albino rats. The weight of male rats was about 130± 10g. After the adaptation period, the rats were divided into four groups (6 rats each). One of them was considered as a negative control and another positive control (Trichloroacetic acid group). The remaining groups were divided into two groups consisting of mixture annona extracts at levels 100 and 150 mg / kg. Blood samples were collected to assays the levels of liver functions (ALT, AST, ALP, BIL, TP, ALB and GLB), kidney functions (creatinine and urea), and oxidation stress (CAT, GPX and MDA). Liver tissues were collected for inflammation markers analyses (IL6, AFP, COX2 and PGE2) and histopathology anylasis. The study results were as the fallowing: all liver cancer protected by annona extracts groups marked a significant improvement in liver functions, kidney functions, oxidation stress, inflammation markers and histopathological results when compared them with the unprotected liver cancer control group (+ve). Therefore, this study recommends that the insertion annona fruit in diets for liver cancer patient because its hepatoprotective, anti-cancer and oxidants, and protect of body's cells from inflammations.

Keywords: Annona fruit- Antioxidants- Kidney- Trichloroacetic acid- inflammations- Malignant hepatocellular tumors.

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Introduction

Liver cancer, look like every other cancer, is manifested by the uncontrolled division and re-division and thus over-proliferation of the abnormal cells **(Butt et al., 2021)**. Hepatocellular carcinomas is the fourth most common cause of death and seventh in terms of prevalence, as the number of Hepatocellular carcinomas represents about half a million annually worldwide **(Justino et al., 2021).** Giving laboratory animals TCA by dosed gavage 500mg/kg once a day for 5 days induces tumors through potential mechanisms such as DNA hypo methylation, peroxisome proliferation, oncogene activation, cell proliferation, and inhibition of intercellular communication **(Abdel-Hamid et al., 2011)**. Annona fruit contains phenolic acids (p-coumaric, quinic, Gallic, and ferulic), flavones and derivatives (apigenin, epicatechin, 2′-5-dimethoxyflavone, 3′, 7-dimethoxy3-hydroxyflavone, kaempferol-3-O-glucoside and 3-O-rutinoside, procyanidin B2, quercetin-3-O-glucoside, and rutin), acetogenins (annonacin) and aporphine alkaloids (romucosine stephagine, and xylopine) **(Carvalho et al., 2022)**. Annona fruit contained phenolic acids, flavonoids, alkaloids, tannins, terpenoids, acetogenins, sesquiterpenes, and diterpenes. The presence of these actives is responsible for the great pharmacological potential such as, antioxidant, antimicrobial, anticancer, anti-inflammatory, antiulcer cytotoxic, leishmanicidal and hypoglycemic activities **(Silva et al., 2017 and Rocha et al., 2021)**. Cancer is a disease that is characterized by abnormal growth of cells in the body because of malfunctioning of the cell cycle. Annona fruits have shown the potential to be effective anticancer agents. Acetogenins from annona fruits have been shown to be the most important chemo preventive agents **(Behl et al., 2022)**.

Aim of study

The aim of study is evaluation of the anti-liver cancer properties of annona fruit (Annona crassiflora M.) extracts in the laborator. Study of the effect of Annona extract on liver and kidney functions and anti-inflammatory activity in rats with liver cancer.

Material and Methods

1) Material

Plant, chemicals, diet and microbiological environments:

a) Plant: Annona fruit (*Annona crassiflora Mart*) was obtained from Local market, Mansoura, Egypt.

b) Chemicals: Ethanol alcohol and trichloroacetic acid (TCA) were brought from El-Gomhouria for trading chemicals and medical appliance, Mansoura, Egypt.

c) Experimental rats: Twenty- four healthy adult albino male rats (Sprague- Dawley strain.) were at the age of 2- 4 months.The weight of male rats was about 130± 10g and were purchased from the Agricultural Research Center, Giza, Egypt. All experimental animals in this study were managed according to the guidelines for the Care and Use of Laboratory Animals in Neuroscience and Behavioral Research and were approved by the Research Ethics Committee, Home Economics Department, nutrition and food science, Mansoura University, Egypt, under animal protocol code No (R/35).

2) Methods

a- Preparation of annona fruit extracts:

The fruits were selected free from scratches and microbial infections or any color changes in preparation for making the ethanolic extract. Annona fruit was washed with tap water to remove surface dirt. The pulp and peels were cut into thin slices **(Arruda *et al*., 2016)**.

b- Annona pulp powder:

Annona seeds, peels and pulps were oven-dried at 45 °C. The dried pulps, peels and seeds were ground separately into powder by domestic electrical mill and stored at 4 °C until further use (**Shehata *et al*., 2021).**

c- Extraction method:

The powders of seeds, peels and pulps were weighed and soaked them separately in a containers with 95% ethanol was added at ratio (1:2 v/v) **(Abd-Elrazek *et al*., 2021)**. The soaking was done for three days with

95% ethanol (4 L) at room temperature (25 °C). This process was repeated 3 times. After filtration, ethanol was removed by using a rotary evaporator in a water bath at 40 °C **(Justino *et al.*, 2019)**.

Chemical analysis:

HPLC was measurement according to **Bataglion *et al.*, (2015).**

Induction of liver cancer:

TCA was neutralized with NaOH to a final pH of 6.5 **(Herren-Freund *et al.*, 1987)**. Trichloroacetic acid (TCA) at dose 500mg/kg orally once a day for 5 days had been given as a carcinogen after 28 day from experimental period consecutive according to **Tao *et al.*, (2000).**

Experimental rats design:

The animals were housed in polypropylene cages under the standard laboratory condition (25 ± 2°C, humidity 60–70%, 12-h light/dark cycles). They were fed with standard commercial rat pellet diet and water was provided ad libitum. The rats were acclimatized to laboratory conditions for 7 days prior to the commencement of the experiment. After acclimatization period, the animals were divided into six groups (6 rats/ group). One of them healthy control group and five liver cancer groups (including one without protected and two groups protected with annona extracts). The experiment continued for 47 days. The protected liver cancer groups received annona extracts for 28 days. Then, TCA was given for 5 consecutive days at dose 500mg/kg orally **(Tao *et al.*, 2000).** After that, the extracts were given for 14 day. It was arranged as follows**:**

- **Group 1:** The animals fed on based diet as normal control group during the experiment period.
- **Group 2:** liver cancer group which the animals were subjected to chemo-induction of liver cancer through administration of trichloroacetic acid (TCA) as positive control group>
- **Group 3:** liver cancer group protected by extracts mixture (seed, peel and pulp) in the rate of (1:1:1) by dose 100mg/kg B.W. by oral stomach tube once daily (AME).

- **Group 4:** liver cancer group protected by extracts mixture (seed, peel and pulp) in the rate of (1:1:1) by dose 150 mg/kg by oral stomach tube once daily (AMEX).

Determination of some liver functions in serum:

ALT (alanine aminotransferase) and AST (aspartate aminotransferase) enzymes activity were measured accordance to the method of **Hafkenscheid and Dijt, (1979).** ALP (alkaline phosphatase activity) enzymes was measured accordance to the method of **Tietz *et al.*, (1983).** Serum total bilirubin was measured accordance to the method of **Doumas *et al.*, (1985).**Total protein was measured accordance to the method of **Schneditz *et al.*, (1989).** Serum albumin was determined accordance to the method of **Doumas *et al.*, (1972).** Serum globulin was determined accordance to the method of **Fernandez *et al.*, (1966).**

Determination of some kidney function in serum:

Serum creatinine was determined according to the method of **Houot (1985)**. Urea concentration in serum was determined by NED Dye method (colorimetric Fix Time test**) (Patton and Crouch, 1977).**

Determination of oxidation stress in serum:

Malondialdehyde (MDA) was measured by the method of **Stocks and Donnandy, (1971).** GPX: glutathione peroxides GSH-PX activity in plasma was measured by the method of **Tappel, (1978).** CAT: catalase in plasma was measured by the method of **Aebi, (1984).**

Determination of inflammation markers in liver tissues:

Alphafeto protein (AFP) level in liver tissues of experimental rats was estimated according to the method of **(Abelev, 1974; Uotila et al., (1981); Chan and Miao, (1986) and Mohamed et al., (2016)**. Cyclooxygenase (COX-2) level in liver tissue was determined according to **Kulmacz and Lands, (1983)**. Interlochen-6 (IL6) level in liver tissue was measured by the method described by **Lemay et al., (1990)**. Prostaglandin (PEG2) levels in liver tissue of experimental rats were detected according with **Kelly et al., (1986).**

Histopathological examination: For histological study, liver samples were fixed in 10% neutral buffered formalin, cleared in xylol, embedded in paraffin, samples were cut 4-5 μm thick and stained with hematoxylin and eosin (H&E) **(Bancroft et al., 1996)**.

Statistical analysis: The gained data were statistically analyzed by SPSS computer software according to **Artimage and Berry, (1987).** The calculation accrued by analysis of variance ANOVA & follow up LSD (SPSS) Computer program variation.

Results and Discussion

Chemical results of annona fruit extracts:

Data presented in **Table (1)** showed the HPLC conditions of phenols of annona extracts (seed and peel). These results showed that, seed, peel, and pulp extracts, the highest phenols are Gallic acid, Catechin, and Catechin but the lowest is Vanillin, Daidzein, and Cinnamic acid, respectively. On the other hand, the seed extract doesn't have Catechin, Methyl gallate, Ellagic acid, Ferulic acid, and Hesperetin. While the peel extract doesn't have Vanillin, Ferulic acid, Naringenin, and Querectin, Cinnamic acid, and Apigenin. The pulp extract doesn't have Pyro catechol, Ellagic acid, Apigenin, and Hesperetin. our results was agreed with those reported by **Roesler et al., (2007)** who cleared that ethanolic extracts of annona pulp, peel and seeds includes bioactive components as potent anti-oxidants such as caffeic acid, ferulic acid, caffeoyltartaric acid, caffeoyl glucose and quercetin. While, **Arruda et al., (2018)** found that the Catechin is the highest phenols in the extract of peel and pulp of annona fruit but the amount of the catechin in the peel extract more than the pulp. While the seed extract doesn't have catechin.

Table(1): Some phenolic compounds of annona extracts (seed, peel and pulp) :

Sample	Seed		Peel		Pulp	
Phenolic acids	Conc. (µg/ml)	Conc. (µg/g)	Conc. (µg/ml)	Conc. (µg/g)	Conc. (µg/ml)	Conc. (µg/g)
Gallic acid	3.52	70.49	7.81	156.15	4.76	95.17
Chlorogenic acid	1.77	35.48	11.58	231.66	5.53	110.61
Catechin	0.00	0.00	18.90	377.93	5.63	112.65
Methyl gallate	0.00	0.00	3.07	61.48	0.69	13.89
Coffeic acid	0.61	12.17	2.56	51.28	0.23	4.61
Syringic acid	0.43	8.63	0.62	12.35	0.10	2.03
Pyro catechol	0.76	15.28	0.87	17.41	0.00	0.00
Ellagic acid	0.00	0.00	0.48	9.55	0.00	0.00
Vanillin	0.07	1.37	0.00	0.00	0.15	2.91
Ferulic acid	0.00	0.00	0.00	0.00	0.09	1.89
Naringenin	1.56	31.23	0.00	0.00	0.40	7.91
Daidzein	2.39	47.83	0.30	5.91	0.57	11.37
Querectin	0.28	5.59	0.00	0.00	0.33	6.65
Cinnamic acid	0.38	7.53	0.00	0.00	0.06	1.27
Apigenin	0.13	2.59	0.00	0.00	0.00	0.00
Hesperetin	0.00	0.00	0.92	18.37	0.00	0.00

Biological results:

Data presented in **Table (2)** showed the mean values of Alanine transaminase (ALT), Aspartate transaminase (AST), alkaline phosphatase (ALP), Bilirubin (BiL), Globulin (GLb), total protein (TP), and Albumin (Alb) of normal control and liver cancer groups. The obtained results showed that, non-protected group of rats with liver cancer showed a significant raise in ALT, AST, ALP and BiL, but correspondingly a significant fall in TP, Alb and GLb compared with the normal control (-ve) group. Liver cancer group protected by AMEX showed a significant lower in ALT, AST, ALP and BiL but on the other hand showed a significant

higher in TP, GLb and Alb levels, compared to the positive group Followed by AME. Our results agreed also with **Jadon et al., (2007)** and **Rasool et al., (2010)** who stated that the estimation of enzymes in the serum is a useful marker of the extent and type of hepatocellular damage. High AST and ALT levels in serum has been attributed to the damaged structural integrity of the liver because these are cytoplasmic in location and are released into circulation after cellular damage. Reduced serum enzymes in TCA-induced liver cancer by gallic acid (phenol in seed, peel and pulp of annona extracts) may be due to the prevention of the leakage of intracellular enzymes by its membrane-stabilizing and antioxidant activity. While, **Zhang et al., (2014)** who pointed that Polyphenols, especially flavonoids, are compounds have hepatoprotective effects against liver damage caused by toxins and free radical.

Table (2): Effect of tested annona extracts on some liver functions parameters of control and liver cancer rat groups:

Variable / Groups		ALT (U/L)	AST (U/L)	ALP (U/L)	BiL (mg/dl)	TP (g/dl)	ALB (g/dl)	GLU (g/dl)
Non- protected Groups	Normal control	d 24.75 ±2.50	d 68.25 ±3.40	d 192.75 ±4.50	d 0.21 ±0.02	a 7.53 ±0.06	a 4.49 ±0.02	a 2.37 ±0.04
	Positive (+ve)	a 55.00 ±2.94	a 244.75 ±10.21	a 367.75 ±10.21	a 0.66 ±0.06	c 5.83 ±0.09	c 2.94 ±0.08	d 0.84 ±0.09
Liver cancer groups protected with	AME	b 35.75 ±2.50	b 108.75 ±13.72	b 219.25 ±8.06	b 0.26 ±0.03	b 7.08 ±0.19	b 4.13 ±0.13	c 1.91 ±0.18
	AMEX	bc 33.25 ±2.06	cd 98.00 ±7.35	bc 209.75 ±9.57	bc 0.24 ±0.02	ab 7.25 ±0.07	b 4.24 ±0.06	b 2.07 ±0.11

Values (mean± SD, n= 4). Means in within the same column sharing the different superscript are significantly different (P> 0.05). ALT: Alanine

transaminase, AST: Aspartate transaminase, ALP: Alkaline phosphatase, BiL: Bilirubin, GLU: Globulin, TP: Total protein, Alb: Albumin, AME: Mixture anonna extract at level 100 mg/ kg and AMEX: Mixture annona extract at level 150 mg/ kg.

Data presented in **Table (3)** showed the mean values of in creatinine and urea of experimental groups. The non-protected group of rats with liver cancer (+ve) showed a significant higher of creatinine and urea, compared to the normal control (-ve) group. Liver cancer groups protected by AMEX showed a significant lower in creatinine and urea levels, compared to the positive control followed by AME. Our results are consistent with those of **El Arem et al., (2014)** who confirmed that creatinine in the serum increased significantly when mice were given trichloroacetic acid at a dose of 500 g/L in drinking water, compared to normal rats. While, **Saha, (2011)** stated that resulted of oral administration of annona aqueous extract to diabetic rats for 30 days a major reduced urea and creatinine that near to control group levels.

Table (3): Effect of tested annona extracts on some kidney functions parameters of control and liver cancer rat groups:

Variable / Groups		Creatinine (mg/dl)	Urea (mg/dl)
Non-protected Groups	Normal control	d 0.42±0.03	d 20.63±0.79
	Positive (+ve)	a 1.19±0.02	a 49.23±3.04
Liver cancer groups protected with	AME	b 0.58 ±0.07	b 21.65±3.35
	AMEX	c 0.53±0.04	bc 21.13±2.05

Values (mean± SD, n= 4). Means in within the same column sharing the different superscript are significantly different (P> 0.05). AME: Mixture annona extract at level 100 mg/ kg and AMEX: Mixture annona extract at level 150 mg/ kg

Data presented in **Table (4)** showed the mean values of malondialdehyde (MDA), glutathione peroxidase (GPX) and catalase (CAT) antioxidant enzymes of normal control and liver cancer groups. The obtained results showed that, non-protected group of rats with liver cancer showed a significant raise in MDA, but correspondingly a significant fall in GPX and CAT compared with the normal control (-ve). Liver cancer group protected by AMEX showed a significant lower in MDA but on the other hand showed a significant higher in GPX and CAT levels, compared to the positive group followed by AME. Our results agreed with **Fouad et al., (2013)** who indicated that oral administration of TCA led to hepatocellular tumors in rats due to the carcinogenic effect of this chemical as a result of increased oxidative stress, lipid peroxidation and cellular proliferation. While, **Roesler, (2011)** and **Justino et al., (2017)** who reported that the hepatoprotective effect is mainly associated with the phenolic compounds in annona fruit that can modulate various biochemical parameters (such as scavenge reactive species, lipid peroxidation reduction, endogenous antioxidants production or regulation, defense system regulation and drug detoxification activation).

Table (4): Effect of experimental annona extracts on glutathione peroxidase GPX, catalase CAT and malondialdehyde MDA in plasma of control and liver cancer rat groups:

Groups \ Variable		MDA (nmol/ml)	GPX (mU/ml)	CAT (U/L)
Non-protected Groups	Normal control	d 7.73±0.49	a 127.23±2.82	a 2.83±0.05
	Positive (+ve)	a 34.10±1.31	c 52.20±4.53	c 0.91±0.07
Liver cancer groups protected with	AME	b 11.98±2.29	b 118.65±7.42	b 2.40±0.24
	AMEX	c 9.73±1.34	ab 125.63±7.45	b 2.58±0.13

Values (mean± SD, n= 4). Means in within the same column sharing the different superscript are significantly different (P> 0.05). MDA:

malondialdehyde, GPX: glutathione peroxidase, CAT: catalase, AME: Mixture annona extract at level 100 mg/ kg and AMEX: Mixture annona extract at level 150 mg/ kg

Data presented in **Table (5)** showed the mean values of alfa fetoprotein (AFP), cyclooxygenase-2 (COX2), interleukin 6, and prostaglandin (PGE2) of normal control and liver cancer groups. The non-protected liver cancer group showed significant higher in AFP, COX2, IL6 and PGE2, compared with normal control. Liver cancer group protected by AMEX and AME showed a significant lower in AFP, COX2, IL6 and PGE2 levels, compared to the positive group. Our results agreed with **Fouad et al., (2013)** who indicated that giving TCA for 5 days orally at a dose of 500 mg / kg led to an increase in the level of alpha-fetoprotein as a result of liver cancer. While, **Jagan et al., (2008)** who stated that high levels AFP are believed to be strongly suggestive of liver cancer because greater than 70% of liver cancer patients have high serum concentration of AFP because of the tumor secretion. However, Gallic acid in annona fruit significantly reduced the levels of AFP which revealed the anti-tumor effect of the compound against liver cancer. Add to that, micronutrients including vitamins C, and B9 in annona extracts are necessary dietary constituents for cancer prevention. This micronutrient contain a public functions like antioxidant and anti-inflammatory agents; however, they also contain specific functions such as regulating genes associated with carcinogen metabolism and carcinogenesis **(Fagbohun et al., 2023).**

Table (5): Effect of mixture annona extracts on some inflammation markers in liver tissues at the end of experimental period:

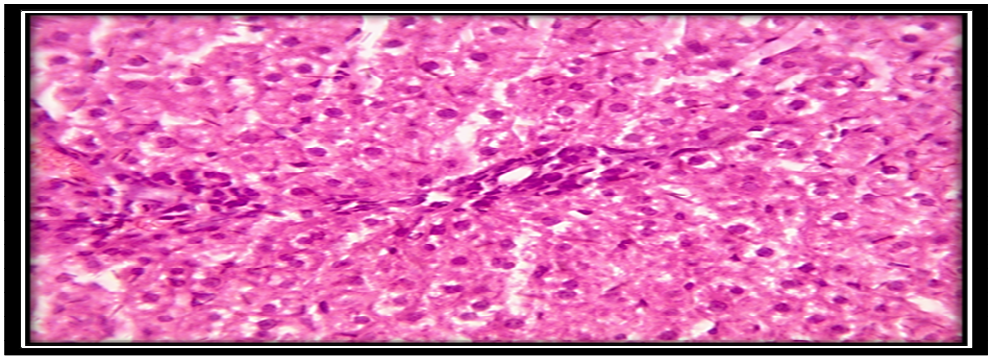
Groups \ Variable		AFP (ng/mg Protein)	COX2 (ng/mg protein)	IL-6 (Pg/mg protein)	PGE2 (Pg/ml)
Non-protected Groups	Normal control	d 1.93±0.09	d 1.27±0.03	d 26.27±0.74	d 44.35±1.59
	Positive (+ve)	a 4.42±0.120	a 3.61±0.03	a 49.97±1.07	a 91.50±3.60
Liver cancer groups protected with	AME	b 2.39±0.16	b 1.58±0.13	b 31.77±1.80	b 60.73±4.93
	AMEX	b 2.23±0.11	bc 1.42±0.05	bc 29.40±0.80	bc 57.38±4.30

Values (mean± SD, n= 4). Means in within the same column sharing the different superscript are significantly different (P> 0.05). AFP: Alphafeto protein, COX2: Cyclooxygenase, IL6: Interlochen-6, PEG2: Prostaglandin, AME: Mixture annona extract at level 100 mg/ kg and AMEX: Mixture annona extract at level 150 mg/ kg.

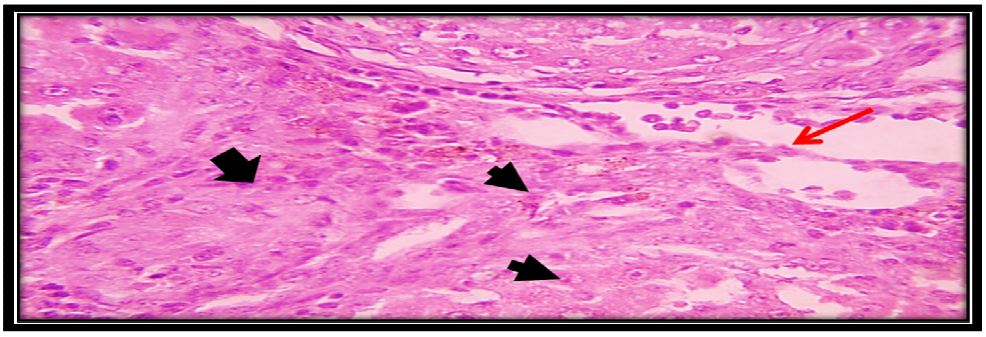
Histopathological results:

Microscopically, liver tissue sections of normal control group rats showed no fibrosis in portal areas (PA) (Pic.1). After TCA administration n positive control group (Pic.2) Liver tissue showed loss of normal architecture with oval- or irregular-shaped hepatocytes. Many transformed liver cells of foci were substantially enlarged, largely vesiculated and frequently binucleated, necroinflammatory and fibrotic lesions characterized by extended portal areas containing many congested blood vessels and dilated lymphatics proliferated bile ductules and mononuclear cells infiltration. Hepatic sections from protected group consumption AME (Pic.3) showed very mild fibrosis of portal area (PA), with few dilated blood vessels. While, protected group consumption AMEX (Pic.4) showed mild fibrosis of portal area (PA). Our results agree with **Abdel-Hamid and Morsy, (2010)** who reported that TCA induced dysplastic hepatocellular

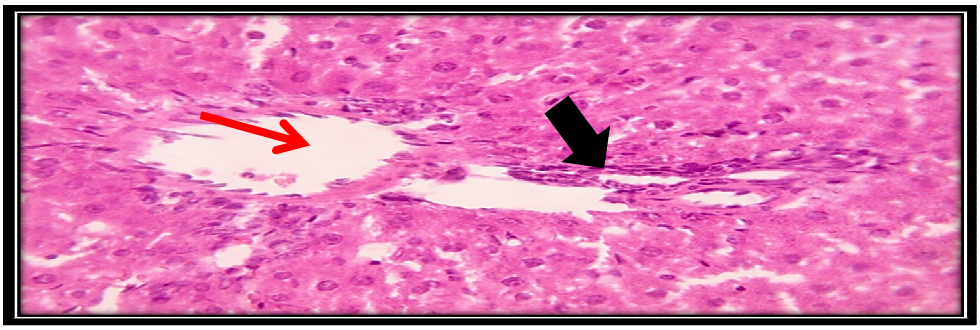
changes, per portal congestion, fatty change, multinucleolosis and increased nuclear size considered to be early signs of liver cancer. While, **Ruiz-Margáin et al., (2021)** who found that the polyphenols in fruits, can regulate the angiogenesis and metastasis in liver cancer through regulation of multiple intracellular signals and finally reducing the risk of liver cancer.



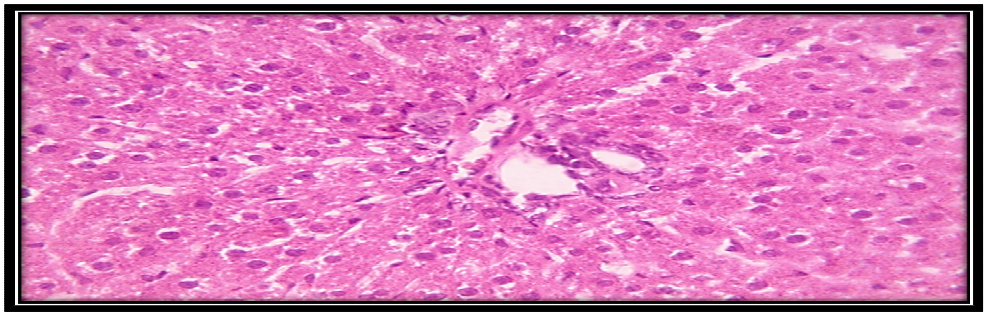
Picture (1): liver sections of rats from normal control group showed no fibrosis in portal areas (PA) (X: 400 bar 50)



Picture (2): liver sections of rats from positive control no-protected group showed marked necroinflammatory and fibrotic lesions characterized by extended portal areas (thin black arrow) containing many congested blood vessels (red arrow) and dilated lymphatics proliferated bile ductules, mononuclear cells infiltration, elongated anastomosing thick fibrous tissue deposition into hepatic parenchyma surrounded by many apoptotic (closed arrowheads) and necrotic (opened arrowheads) cells (X: 400 bar 50).



Picture (3): Hepatic sections from protected group consumption AME showing very mild fibrosis of portal area (PA), with few dilated blood vessels (red arrow) (X: 400 bar 50).



Picture (4): Hepatic sections from protected group consumption AMEX showing slight fibrosis of portal area (PA) (X: 400 bar 50).

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تأثير المستخلصات من فاكهة القشطة على سرطان الكبد الناجم عن حمض ثلاثي كلورو أسيتيك في الفئران

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الملخص العربي:

تم إجراء البحث الحالي لفحص التأثيرات الوقائية المحتملة للمستخلصات الإيثانولية لفاكهة القشطة ضد سرطان الكبد الناجم عن حمض ثلاثي كلورو أسيتيك. بعد الانتهاء من تحضير مستخلصات فاكهة القشطة، تم تقديرمحتوي الفينولات لكل مستخلص على حدة. استخدمت التجربة البيولوجية أربعة وعشرين فأرًا ألبينو. بعد فترة التكيف، تم تقسيم ذكور الفئران (١٣٠ ± ١٠ جرام) إلى اربع مجموعات (٦ فئران لكل مجموعة). تم اعتبار إحداهما كنترول سالبة وأخرى كنترول موجبة (مجموعة حمض ثلاثي كلورو أسيتيك). تم تقسيم المجموعات المتبقية إلى مجموعتين مكونة من خليط مستخلصات فاكهة القشطة بمستويات ١٠٠ و ١٥٠ ملجم/كجم. تم جمع عينات الدم لتحديد مستوي وظائف الكبد مثل إنزيم ناقل أمين الألانين إنزيم ناقل أمين الأسبارتات إنزيم الفوسفاتيز القلوي و الببيليروبين و الالبيومين و البروتين الكلي و الجلوبيولين و كذلك قياس بعض وظائف الكلي مثل اليوريا و الكرياتينين ودلالات التأكسد بالدم مثل الجلوتاثيون بيروكسيديز و الكتاليز و المانوالدهيد . بالاضافة لذلك تم تجميع عينات من انسجه الكبد لتحديد علامات الالتهابات مثل الانترلوكين٦ و الالفافيتوبروتين و البروستاجلاندين و الكوكس٢ و عمل التحاليل الهيستوباثولوجية عليها. وكانت نتائج الدراسة على النحو التالي: سجلت جميع المجموعات المحمية من سرطان الكبد والمتناوله لمستخلص لفاكهة القشطة تحسنا ملحوظا في وظائف الكبد ووظائف الكلى والإجهاد التأكسدي وعلامات الالتهاب والنتائج النسيجية عند مقارنتها مع مجموعةالكنترول الموجب ولذلك توصي هذه الدراسة بإدخال فاكهة القشطة في الوجبات الغذائية لمرضي سرطان الكبد لما لها من تأثيرات وقائية للكبد ومضادة للسرطان والاكسدة وتحمي خلايا الجسم من التهابات.

الكلمات المفتاحية: فاكهة القشطة – مضادات الاكسدة – الكلي - حمض ثلاثي كلورو أسيتيك – الالتهابات- أورام الكبد الخبيثة.

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