Middle East Journal of Applied Sciences, 4(4): 1100-1109, 2014
ISSN: 2077-4613

Nutraceutical Effects of Some Medical Fruits against Carbon Tetrachloride Induced Hepatotoxicity in Rats

Abd El-Ghany, M.A., Sedki, A.G. and Bakr A. E.

Department of Home Economics, Faculty of Specific Education, Mansoura University, Egypt

ABSTRACT

The aim of this study was to determine the chemical composition and antihepatotoxic activity of Hyphaene thebaica (HT, Doum), Physalis peruviana (PP, Harankash) and Zizyphus spina- christi (ZS, Nabag) using the Carbon tetrachloride induced hepatotoxicity in rats. Thirty male rats of Sprague Dawley strain weighted from 110± 14g, divided into normal group and five hepatotoxic rat groups (2 ml/kg b.w by CCl4 diluted with corn oil). Then, hepatotoxicity rats were randomly classified into control (+ve) group and treated groups with 10% powder of ZS, PP, HT and mixed fruits (MF) for 60 days. The chemical results showed that HT has the highest values of dry matter, ash, carbohydrate and polyphenols and the lowest values of protein and lipids while PP has the highest values of protein, lipids and flavonoids and the lowest values of carbohydrates but ZS has the highest value of tannins and the lowest values of ash, polyphenols and flavonoids. Also, results proved the presence of tannins, flavonoids, sterols, saponins, carbohydrates and alkaloids and absence of resins in all experimental fruits.In addition, feeding hepatotoxic rats on tested fruits in diets increased significantly weight gain, weight gain percent and FER compared to control +ve rat group. ZS, HT and MF showed normal liver function. The tested fruits groups showed normal values of serum antioxidant enzymes and hepatic superoxide dismutase and catalase. This is might be due to the polyphenols and flavonoids contents of these medical fruits which act as antioxidant hence protects hepatocytes from toxicity by CCl4. It can be recommended that increase consumption of HT, PP and ZS powder of their effective impact in reducing the side effects of hepatotoxic rats.

Key words: Hyphaene thebaica, Physalis peruviana, Zizyphus spinachristi, hepatotoxic rats.

Introduction

Liver plays a pivotal role in regulating various physiological processes. It is involved in several vital functions, such as carbohydrate, protein and fat metabolism, secretion of bile and storage of vitamins. Liver is responsible for the metabolism of drugs and toxic chemicals as it becomes the primary target organ for nearly all toxic chemicals. Most of hepatotoxic chemicals damage liver cells mainly by inducing lipid peroxidation and oxidative stress in liver. Hepatotoxicity is one of very common ailment resulting into serious complications ranging from severe metabolic disorders to even mortality (Patel *et al.,* 2008 and Ahsan *et al.,* 2009). Therefore, the maintenance of a healthy liver is vital to overall health and well being. In spite of the tremendous advances in modern medicine, there is no effective drug available that stimulates liver function, offer protection to the liver from damage or help to regenerate hepatic cells. There is urgent need, therefore, for safe, inexpensive effective drugs to replace/supplement those in current use for therapy of liver diseases (Adewusi and Afolayan 2010). So nowadays, there is a trend to make scientific studies on medicinal plants to find out antihepatotoxic natural products that are safe and inexpensive.

The genus Ziziphus belongs to the family Rhamnaceae. This genus comprises of about 100 species of deciduous or evergreen trees and shrubs distributed in the tropical and subtropical regions of the world. The fruits are applied on cuts and ulcers. They are also used to treat pulmonary ailments and fevers and to promote the healing of fresh wounds, for dysentery. The leaves are applied locally to sores, and the roots are used to cure and prevent skin diseases (Adzu *et al.,* 2003). In addition, Zizyphus spina-christi is known for its medicinal properties as liver protective agent, antioxidant, hypoglycemic, hypotensive, anti inflammatory, antimicrobial, antitumor and as an immune system stimulant (Said *et al.,* 2006). *Physalis peruviana* is a member of the *Solanaceae* botanical family and is excellent in fruit or mixed salads. They can also be used as filling for pies or turnovers. With a little sugar, to cut their tartness, they make a refreshing juice. Because of their appearance they also make a nice garnish for fruit trays. *Physalis peruviana* has traditionally been used as a medicinal folk remedy for a large number of ailments. Indeed, it acts as a febrifuge, a diuretic and has anti-inflammatory, antirheumatic properties as well as antihepatotoxic effect (Arun and Asha 2007 and Puente *et al.,* 2011). Doum palm fruit (Hyphaene thebaica) is a desert palm tree with edible oval fruit, originally native to the Nile valley. It is listed as one of the useful plants of the world. Its fibre and leaflets are used by people along the Nile to weave baskets. The trunks of the palm are used as part of construction, as well as for manufacture of various domestic utensils and the leaves are used to make mats, packing and writing paper. The oblong, yellow-

Corresponding Author: Abd El-Ghany Department of Home Economics, Faculty of Specific Education, Mansoura University, Egypt
E-mail: elghny61@yahoo.com

orange apple sized fruit has a red outer skin, a thick, spongy and rather sweet fibrous fruit pulp (mesocarp) that tastes like gingerbread and a large kernel. The fruit has a brown outer fibrous flesh which is normally chewed and spewed out. Doum palm fruit is also a source of potent antioxidants (Ellison and Ellison 2001and Hsu *et al.,* 2006 and Al-Amer and Rashwan 2012).

The objective of this study was to investigate the antihepatotoxic effect of three experimental fruits; Hyphaene thebaica (Doum), Physalis peruviana (Harankash) and Zizyphus spina-christi (Nabag) by studying the effect of the addition of their powder to the diets on hepatotoxicity-induced by CCl_4 in rats.

Materials and Methods

Materials:

Hyphaene thebaica (HT) and Physalis peruviana (PP) fruits were purchased from the local market of El-Mansoura , Cairo, Egypt whereas Zizyphus spina-christi (ZS) which was obtained from the garden of Mansoura University, El-Dakahlia Governorate. Carbon tetrachloride (CCl_4) was obtained from El-Gomhoria Company for chemicals, Egypt. Thirty male rats of Sprague Dawley strain were purchased from the Agricultural Research Center, Giza, Egypt and weighted 110± 7g. PP (Harankash) and ZS (Nabag) fruits were exposed to hot air oven at 60^{o}C then crushed into fine powder while edible part of HT was crushed into fine powder. The standard diet composition (g/kg) was diet 200 g casein, 497 g corn starch, 100 g sucrose, 20 g vitamin mixture, 100 g mineral mixture, 50 g corn oil, 30 g cellulose and 0.003 g methionine according to NRC (1995).

Methods:

Chemical study:

Gross Chemicals composition had been done on the experimental fruits according to AOAC (2005) and carbohydrate was determined by difference.In addition, phytochemical screening and estimation of polyphenols, flavonoids and tannins in these experimental fruits were estimated using HPLC method according to Tuzen and Ozdemir (2003) and Harborne (1967) and modified by Sedki (2010). Results are expressed as a percentage of dry weight, and were taken an arithmetic mean ±SD of three determinations.

Biological study:

This study was performed based on the guidelines for the use and care for laboratory animals. All of the rats were housed in stainless steel cages under standard conditions in a room in groups of five rats per cage at a temperature of 21-24°C and constant 12 h light/dark cycle. All of the experimental procedures were carried out between 08.00- 11.00 Am. Food and water was provided ad-libtum. After five days of adaptation, five rats served as normal group while the other rats (25 rats) were injected i.p with 2 ml/kg b.w by CCl_4 diluted with corn oil (1:1) to induce hepatotoxicity (Abd El-Ghany 2006). Then, hepatotoxic rats were randomly classified into non-treated which act as control (+ve) while the others hepatotoxic rat groups were ZS, PP, HT and mixed fruits (MF) treated rat groups respectively that fed on diets supplemented with 10% powder of one variety from the experimental fruits and 10% mixture of equal percent of these fruits under study for 60 days. Daily food intake (FI) and weekly body weight (BW) was recorded and Food efficiency ratio (FER) was calculated at the end of experiment according to Chapman *et al.,* (1959).

After 60 days, rats were anaesthetized by diethyl ether and sacrificed. Blood samples of each rat were withdrawn in test tubes and left for coagulation then centrifuged at 3000 rpm for 15minutes to obtain serum. Serum samples were kept at -20°C till analysis. Liver from each rat was removed and placed on ice bath.

Laboratory Analysis:

Serum alanine & aspartate aminotransferases (ALT&AST), alkaline phosphatase (ALP), total bilirubin (T.B), albumin , serum glutathione peroxidase (GPX), superoxide dismutase (SOD) and catalase (Cat) according to Reitman and Frankel (1957), Kind and King (1954), Jendrassik (1938), Bartholomev and Delany (1966), Beutler *et al.,*(1966), Dechatelet *et al.,*(1974) and Aebi,(1984), respectively.

1g portion of the liver was used to prepare homogenate of the liver (10%) in ice cold potassium chloride (KCl) solution (1.15% w/v), using Teflon homogenizer. The homogenate was centrifuge at 4000 rpm for 10 min to remove nuclear fraction. The supernatant was used for the estimation of liver GPX, SOD and Cat enzymes using test kits according to Weiss et a1., (1980), Beuchamp and Fridovich, (1971) and Luck (1965), respectively. The other parts of liver samples were immersed in 10 % neutral buffered formalin as fixative and then sent to Pathological Department of Veterinary Medicine, Cairo University for histopathological examination according to Carlton (1979).

Statistical analysis:

All the obtained data were statistically analyzed by SPSS computer software. The calculated occurred by analysis of variance ANOVA and follow up test LSD by Petrie and Watson (1999).

Results

It is clear that the chemical composition of moisture content of dried experimental fruits of HT, PP, ZS and MF were 6.74± 0.02, 9.89± 0.33, 7.88± 0.24 and 8.46± 0.10%; respectively. The highest value of moisture was observed in PP but the lowest value was in HT and vice versa of dry matter. The highest values of protein and lipids content were found in PP (12.44± 0.21 and7.32± 0.46 %, respectively), while the lowest values were observed in HT (5.22 ± 0.15 and 0.15± 0.03%, respectively). With respect to ash and carbohydrates, the highest content of ash and carbohydrates were observed in HT (7.22± 0.01 and87.41±2.17 %, respectively) but the lowest values were found in ZS and PP (5.28± 0.02 and 74.36±0.87%, respectively) as shown in table (1). From data in table (2), it is clear that all experimental fruits under study contain tannins, flavonoids, sterols, saponins, carbohydrates and alkaloids. On the other hand, they do not contain resins.

From data in table (3), it is clear that the highest polyphenols content was present in HT (581.04 ± 4.31mg/100g as pyrogallol), whereas the lowest one was in ZS (310.15± 2.32 mg/100g as pyrogallol). Concerning to the flavonoids content of dried experimental fruits under study, the highest flavonoids content was in PP (435.93 ± 0.61mg/100g as rutin) but the lowest value was found in ZS. With respect to tannins content in dried fruits under study, the highest content was in ZS (1712.86± 4.50) but the lowest tannins content was observed in PP (536.71± 3.11 mg/100g as tannic acid).

Table 1. Gross chemical composition of dry medicinal fruits

Variables / Fruits	Moisture %	Dry matter %	Chemical composition of dry matter (%)			
			Crude protein	Crude Lipids	Ash	Carbohydrates
HT	6.74± 0.02	93.26±1.80	5.22 ± 0.15	0.15± 0.03	7.22± 0.01	87.41±2.17
PP	9.89± 0.33	90.11±1.77	12.44± 0.21	7.32± 0.46	5.88± 0.04	74.36±0.87
ZS	7.88± 0.24	92.12±1.30	7.42± 0.11	1.13± 0.01	5.28± 0.02	86.17±2.11
MF	8.46± 0.10	91.54±1.22	8.36± 0.17	4.23± 0.05	6.20± 0.03	81.21±1.41

Table 2. phytochemical screening of dry fruits of the studied medicinal fruits.

	Tannins	Flavonoids	Sterols	Saponins	Cardenolides	Carbohydrates	Alkaloids	Resins
HT	+	+	+	+	+	+	+	-
PP	+	+	+	+	-	+	+	-
ZS	+	+	+	+	+	+	+	-
MF	+	+	+	+	+	+	+	-

- Negative *+ Positive*

Table 3. Polyphenols, flavonoids and tannins content of dry fruits of the studied medicinal fruits

	Polyphenols (mg/100g as pyrogallol)	Flavonoids (mg/100g as rutin)	Tannins (mg/100gas tannic acid)
HT	581.04± 4.31	171.06± 0.36	1563.69± 13.57
PP	440.15± 5.08	435.93± 0.61	536.71± 3.11
ZS	310.15± 2.32	135.63± 0.52	1712.86± 4.50
MF	444.83± 7.51	236.83± 0.12	1431.07± 4.71

It is clear that control (+ve) rats group which administered CCl_4 showed a significant decrease in final weight, weight gain, weight gain percent, food intake, and FER at ($P< 0.001$) compared with normal control group. ZS rat group showed a significant decrease in final weight ($P< 0.001$), weight gain and food intake ($P< 0.01$) while PP showed a significant decrease in weight gain final weight ($P< 0.001$) and food intake ($P< 0.01$) but HT showed a significant decrease in final weight ($P< 0.001$), weight gain ($P< 0.01$) and FER ($P< 0.05$) compared with normal control group. In comparing with control (+ve) rat group, PP and HT groups showed increase of final weight while HT and MF showed increase of food intake. In addition, feeding hepatotoxic rats on tested fruits in diets increased significantly weight gain, weight gain percent and FER. MF group showed improvement of nutritional values and appear within normal values as illustrated in table (4).

The control (+ve) rat group showed a significant increase in serum ALT, AST and ALP enzymes ($p< 0.001$) and T.B ($p< 0.01$) while PP showed a significant increase in serum ALT ($p< 0.05$) AST and T.B ($p< 0.01$) compared with normal group. In addition, feeding hepatotoxic rats on tested diets decreased significantly the above mentioned liver function parameters values in comparing with control (+ve) rat group. ZS, HT and MF showed normal liver function parameters as presented in table (5). Data from table (6) represented that the control (+ve) rat group which administered CCl_4 showed a significant decrease in serum and hepatic antioxidant enzymes as SOD, GPX($P<0.001$) and CAT ($P<0.001$ &0.05) compared with normal group. All treated rats with fruits under study showed non-significant difference in serum and hepatic antioxidant enzymes except hepatic GPX which decreased ($P<0.05$) as compared with normal group. Also, it is clear that values of these enzymes were significantly increased in the tested fruits groups in comparing with control (+ve) rat group.

Table 4. Nutritional indicators for hepatotoxic rats after feeding on diets supplemented with 10% powdered of each dried fruits under study.

Variables Groups	Initial body weight (g)	Final body. weight (g)	Body weight gain (g)	Body Weight gain (%)	Food intake (g /day)	(FER)
Normal	117.0± 1.82 [a]	192.8± 1.86 [a]	75.8± 2.22 [a]	64.92± 2.69 [a]	15.87 ± 0.20[a]	0.085± 0.002[a]
Control(+ve)	124.6±4.46 [a]	155.8±1.59[c***]	31.2 ±3.02[c***]	25.54±3.50 [c***]	14.22±0.12[b***]	0.039±0.004[c***]
ZS	116.8±1.77 [a]	178.6±0.51[c***]	61.8±1.36 [b**]	53.03±2.04 [a]	14.82±0.11 [b**]	0.074 ±0.002[a]
PP	110.2 ±2.54[a]	185.0±1.76[b***]	74.8± 3.57 [a]	68.27± 4.53 [a]	14.96± 0.14[c**]	0.089 ± 0.004[a]
HT	116.8±1.77 [a]	178.6±2.21[b***]	61.8±2.08 [b**]	53.00±2.23 [a]	15.36±0.13 [a]	0.072±0.002 [b*]
MF	112.2±2.69 [a]	187.0±1.41 [a]	74.8 ±1.63[a]	66.94±2.91 [a]	15.22 ±0.26[a]	0.088±0.002 [a]

*Each value represents the Mean ± SD .Significant with control (-ve) group * P<0.05 ** P<0.01 *** P<0.001*
Values with the same letters in column indicate non- significant difference (P>0.05) and vice versa

Table 5. Serum biochemical markers of liver functions for hepatotoxic rats after feeding on diets supplemented with 10% powdered of dried fruits under study.

Variables Groups	ALT(µ/L)	AST (µ/L)	ALP(µ/L)	Albumin(g/dl)	TB(mg/dl)
Normal	36.23±5.49 [b]	23.96 ±3.51b	137.3±6.00 [b]	3.23±0.30 [a]	0.88±0.18 [b]
Control(+ve)	60.31±3.43 [a***]	43.46±2.00 [a***]	224.5 ±2.71[a***]	2.98±0.20 [a]	1.55±0.01 [a**]
ZS	32.66±3.47 [b]	27.40±4.57 [b]	153.4±7.35 [b]	3.13±0.35 [a]	0.89±0.23 [b]
PP	21.9±1.551[c*]	12.52±0.16 [c**]	167.5±6.69 [b]	2.94±0.27 [a]	0.31±0.05[c**]
HT	28.00±4.32[b]	19.88±1.25 [b]	169.4±7.75 [b]	3.24±0.14 [a]	0.68±0.07 [b]
MF	33.14±2.81 [b]	19.8±4.001[b]	159.8±1.65 [b]	3.12±0.06 [a]	0.60 ±0.15[b]

*Each value represents the Mean ± SD .Significant with control (-ve) group * P<0.05 ** P<0.01 *** P<0.001*
Values with the same letters in column indicate non- significant difference (P>0.05) and vice versa

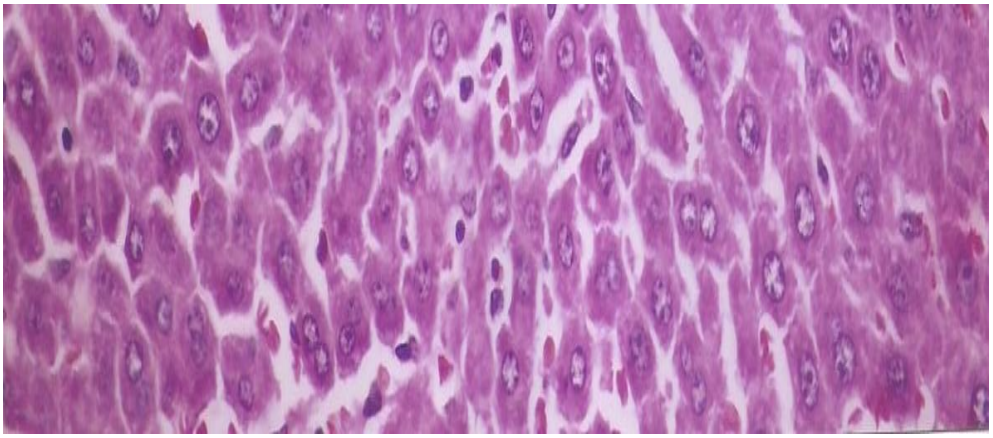
Table 6. Serum & hepatic antioxidant enzymes levels SOD, GPX, and Cat after feeding hepatotoxic rats on diets supplemented with 10% powdered of each dried fruits under study.

Variables Groups	Serum antioxidant enzymes(µ /ml)			Hepatic antioxidant enzymes(µ/mg protein)		
	SOD	GPX	CAT	SOD	GPX	CAT
Normal	154.4±1.74 [a]	29.57±2.09[ab]	317.3±10.45 [a]	2.93±0.07 [a]	7.30±0.40 [a]	23.28±1.76 [ab]
Control(+ve)	125.7±2.51[b**]	17.47±0.37[c***]	222.0±8.71 [b***]	0.72±0.06[b***]	3.51±0.20[c***]	19.49±0.66 [c*]
ZS	167.4±8.75 [a]	27.48±1.37[ab]	349.8 ±14.68 [a]	2.69±0.21 [a]	5.52±0.23[b*]	25.24±1.82 [ab]
PP	170.5 ±8.87 [a]	31.14±1.57 [a]	354.1±17.64 [a]	3.34±0.30 [a]	5.33±0.08[b*]	19.28±1.65 [a]
HT	164.1±7.84 [a]	25.11±2.63[ab]	358.1±16.54 [a]	3.23 ±0.26 [a]	5.18±1.08[b*]	27.14±0.91 [a]
MF	163.2±2.22 [a]	25.13±2.06[ab]	340.4 ±12.00[a]	2.73 ±0.38 [a]	5.79±0.18[b*]	30.44±2.05 [a]

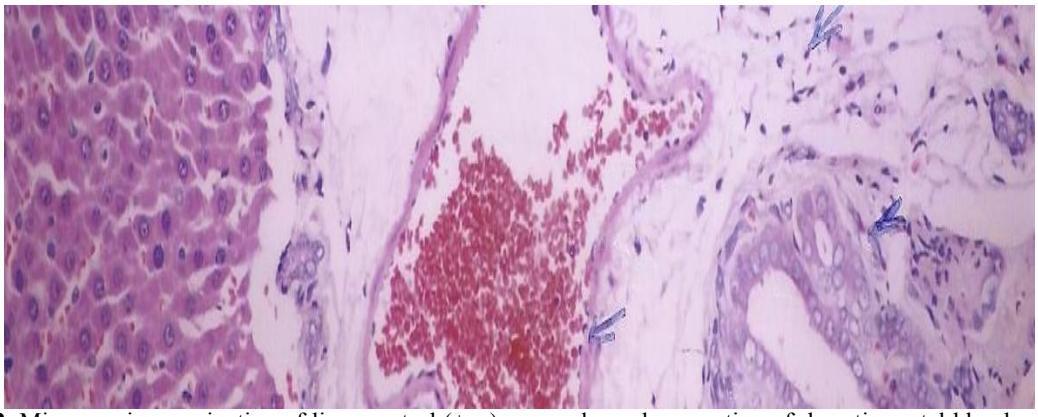
*Each value represents the Mean ± SD Significant with control (-ve) group * P<0.05 ** P<0.01 *** P<0.*
Values with the same letters in column indicate non- significant difference (P>0.05) and vice versa

Liver histopathological examination:

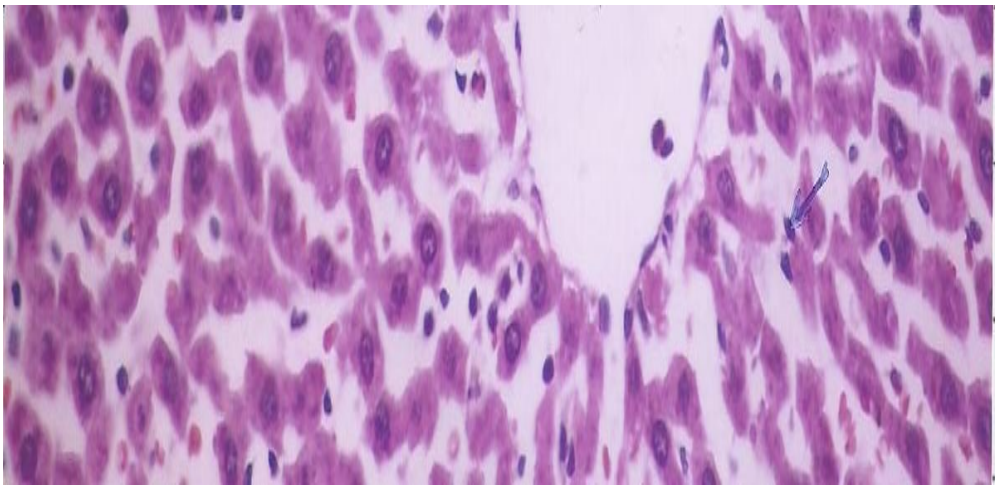
Microscopic examination of liver rat from the normal rat group revealed the normal histological structure of hepatic lobule (Pict 1) while liver from control (+ve) group showed congestion of hepatic portal blood vessel, portal edema and hyperplasia of epithelial liming bile duct (Pict 2). Microscopic examination of liver of hepatotoxic rats fed on diet supplemented with 10% powder of ZS showed kupffer cells activation (Pict 3). Examined sections of hepatotoxic rats groups fed on diet supplemented with 10% powder of PP showed no histopathological changes because it exhibits areas of normal liver architecture (Pict 4).Liver microscopic examination of hepatotoxic rats fed on diet supplemented with 10% powder of either HT or mixed of medical fruits showed a slight activation of kupffer cells (Pict 5&6).



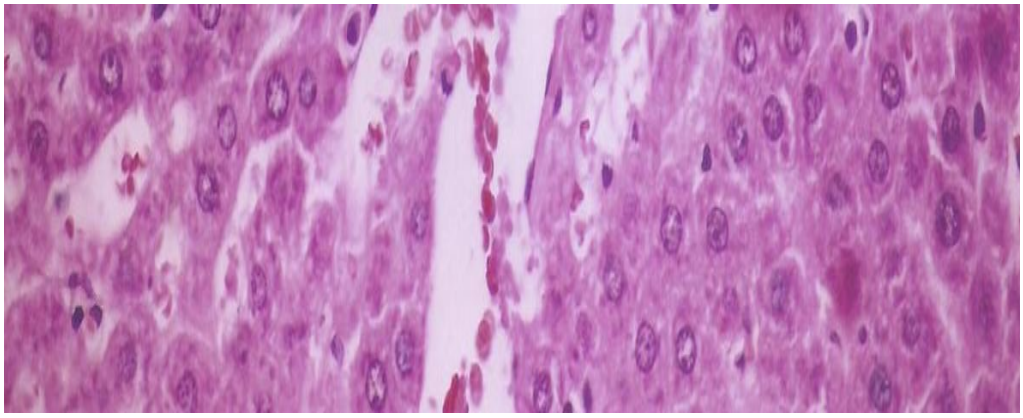
Pic. 1. Microscopic examination of liver from normal rat group showed the normal histological structure of hepatic tubule (H & E x 400)



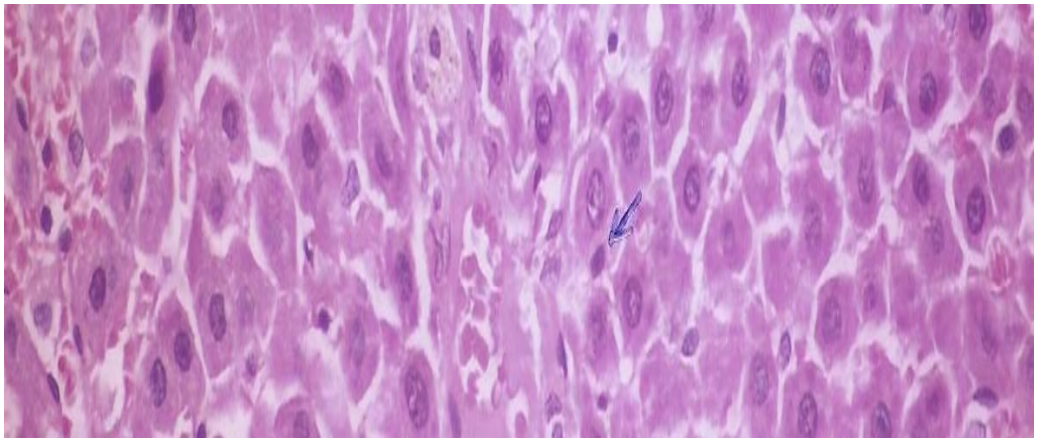
Pic.2. Microscopic examination of liver control (+ve) group showed congestion of hepatic portal blood vessel, portal oedema and hyperplasia of epithelial liming bile duct (H & E x 400)



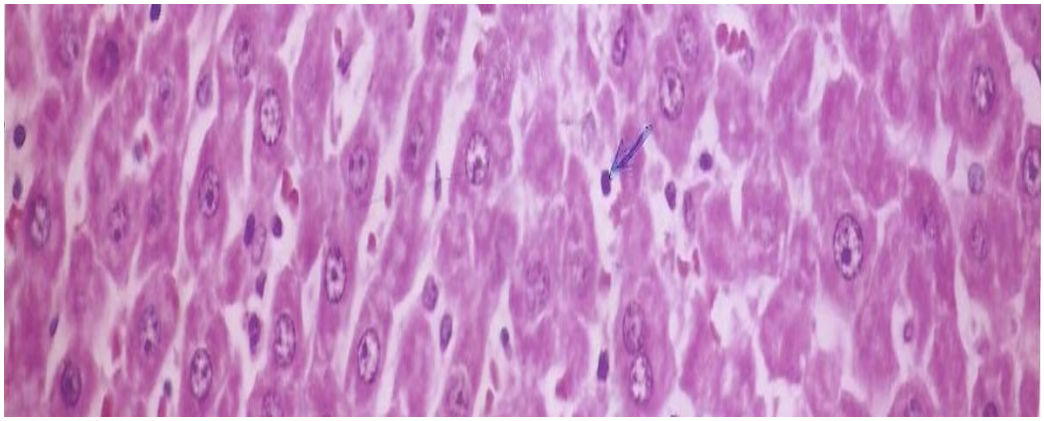
Pic. 3. Microscopic examination of liver from hepatotoxic rat fed on diet supplemented with 10% powder of ZS showed kupffer cells activation (H & E x 400)



Pic. 4. Microscopic examination of liver from hepatotoxic rat fed on diet supplemented with 10% powder of PP showed non histopathological changes (H & E x 400)



Pic.5. Microscopic examination of liver from hepatotoxic rats fed on diet supplemented with 10% powder of HT showed a slight activation of kupffer cells (H & E x 400)



Pic.6. Microscopic examination of liver from hepatotoxic rats fed on diet supplemented with 10% powder of mixed fruits showed a slight activation of kupffer cells (H & E x 400)

Discussion

Comparisons of the obtained results are difficult because of differences in the fruit origin and analytical techniques used in studies. However, data concerning the chemical composition were agreed with Leung *et al.,* (1968) who reported that flour made from the pericarp of *Hyphaene thebaica* contains per 100 g edible portion: moisture 10.7 g, energy 1239 kJ (296 kcal), protein 2.6 g, fat 0.4 g, carbohydrates (including fibre) 79.0 g, fibre 14.0 g, ash 7.3 g, Ca 68 mg, thiamine 0.05 mg, riboflavin 0.10 mg and niacin 3.4 mg. The kernel contains per 100 g edible portion: moisture 5.7–6.2 g, energy 1654 kJ (395 kcal), protein 2.4–5.0 g, fat 4.9–8.0 g, carbohydrates (including fibre) 80.6 g, fibre 6.5–11.0 g, ash 1.9–5.4 g, Ca 121–168 mg and P 170–281 mg. The obtained result of PP was agreed with the structure of physalin T from Physalis alkekengi var. franchetti (Kawai *et al.,* 2001). Our results of preliminary phytochemical screening of the fruit samples were reported by several researchers. The phytochemical screening of the crude extract of ZS plants showed alkaloid, tannins, saponins, glycosides, steroids, flavonoids and terpeniods while the fractions contains majorly alkaloids, tannins, saponins, glycosides (Dangoggo *et al.,* 2012). The extract of ZS found was shown to contain beutic acid and ceanothic acid, cyclopeptides, as well as saponin glycoside and flavonoids, lipids, protein, free sugar and mucilage (Adzu *et al.,* 2003).

The phytochemical investigation of the physalis peruviana revealed the presence of phenols, flavonoids, glycosides, sterols, saponins, tannins, and alkaloids. In addition, phenolic and flavonoid compounds. It is worth to notice that most of the phytochemicals found in crude PP have antioxidant property. The amounts of phenols and flavonoids determined in the present study were slightly different from those reported by Wu *et al.,* (2009) in which total flavonoids represent 226.19 ± 4.15 mg/g and total phenols represent 100.82 ± 6.25 mg/g.

Doum was reported to contain important substances including saponins, tannins, and flavonoids; hence the use of Doum, which is rich in flavonoids and saponins, in folk medicine is not surprising (Dosumu *et al.,* 2006). The quantitative phytochemical screening of *Hyphaene thebaica* revealed the presence of low level of

tannins, steroids and moderate level of saponins, carbohydrates, cardiac glycosides, flavonoids, Terpenes and Terpinoids (Mohammed *et al.,* 2012). Metabolite profiling and biological activity are reported from organic and aqueous extracts of the fruit from HT 17 compounds were simultaneously identified and quantified including 2 cinnamic acid derivatives, 5 flavonoids, 6 fatty acids, 2 sphingolipids, a lignan, and a stilbene. Hyphaene thebaica L. fruit organic extracts anti-inflammatory potential was assessed in vitro by cyclooxygenase-1 enzyme inhibition (Farag and Paré 2013).

In regarding to biological study results, data concerning the nutritional indicators showed that administration of CCl_4 resulted in a significant decrease in nutritional indicators values for hepatotoxic rats (control +ve) rats group at ($P<0.001$) when compared to normal rat groups This result agrees with that obtained by (Yossef *et al.,* 2011). The loss of body weight gain may be associated with food intake and malabsorption after intake of CCl_4. Also, feeding hepatotoxic rats on diet supplemented with fruits under study increased significantly these indicators as compared with control (+ve) rats group. the increase in body weight gain in rats following the administration of the examined fruits powder under study suggested that the plant affects body weight and hence enhances nutrient utilization in rats. ZS fruit has been useful as food and medicine as it contains vitamins needed by human body for healthy living (Dahiru and Obidoa 2008).The improvement of nutritional results of doum groups may be attributed to the energy available from consumption of the edible portions of the nut which is approximately 1300 Kcal/100 g. The kernels were also found to contain crude protein and lipids (Bonde *et al.,* 1990). The benefits associated with the consumption of PP are mainly due to their nutritional composition. It contains biologically active components that provide health benefits and reduce risk for certain diseases. Among its major components are its high amounts of polyunsaturated fatty acids, -carotene, vitamins A, B, and C and phytosterols, and the presence of essential minerals such as iron and vitamins such as E and K1 (Ramadan 2011).

It is well documented that the use of carbon tetrachloride is successfully induce hepatotoxicity in experimental animals due to oxidative damage by free radical generation. Administration of CCl_4 elevated the levels of AST, ALT, ALP and T.B in rats, indicating acute hepatocellular damage and biliary obstruction. SOD, GPX and CAT antioxidant enzymes are easily inactivated by excessive lipid peroxides resulting from CCl_4-induced liver damage, and thus, the levels of GPX and SOD in hepatic tissue are important indicators of liver injury (Yang *et al.,* 2011). One of the most striking results of the present study is the improvement of the liver functions markedly developed both by AST and ALT levels in response to examined fruits powder supplementation, with parallel reduction in the concentration of both albumin and total bilirubin levels in serums. Also, each of glutathione peroxidase, superoxide dismutase levels and catalase was increased. Explanation of the possible mechanism underlying the hepatoprotective properties of the doum is having five flavone glycosides were isolated and identified from doum fruits. Antioxidant property is claimed to be one of the mechanisms of hepatoprotective (Cook *et al.,* 1998 and Abd El-Ghany and Nanees, 2010). Whereas animal treated/fed with various preparations of PP showed significant lowering effect ($p<0.05$) in the elevated levels of serum markers like ALT, AST, ALP, creatinine and bilirubin indicating the protection against hepatic cell damage (Taj *et al.,*2014). PP has been proved to have antioxidant activities and anti-inflammatory activities. It is worth to know that the antioxidant activity of PP is not a property of a single photochemical compound, but the synergistic effect of different antioxidants exist which in turn could alleviate oxidative stress and improve directly or indirectly the biological and biochemical parameters and kidney histology in PP pretreated groups. Some of these compounds have a strong antioxidant property and prevent peroxidative damage to liver microsomes and hepatocytes. Physalis is one of the best natural sources of antioxidants. It contains a high amount of vitamin C or ascorbic acid, vitamin E, and vitamin A or beta carotene. These powerful antioxidants are essential to help keep us healthy, protect us against our environment and inhibit the grow of free radicals which cause diseases such as cancer. Physalis also has vitamin P, or bioflavonoids and B complex vitamins. Vitamin P is seldom talked about but is also very important as it helps our bodies to absorb vitamin C and strengthen our immune system. Physalis also contains B complex vitamins, pectin, a type of fiber and minerals as iron, potassium, phosphorus and the trace minerals magnesium and silicon. The antioxidant activity associated with PP is due to the high levels of polyphenols, good amounts of total phenolic and flavonoid (Wu *et al.,* 2005, Chang *et al.,* 2008 and Fang *et al.,* 2012). Moerover, results reported by (Amin and Ghoneim 2009) are simliar to the results of the current study which reported that , oral administration of ZS aqueous leaves extract ameliorated liver injury judged by reduced ALT and AST activities in serum. There are many published studies on hepatoprotective effects of other members of the Zizyphus family in which antioxidative and anti-inflammatory activities were introduced as the dominant mechanism of hepatoprotection (Kumar *et al .,*2009 Amin, A. and Ghoneim, D.M. (2009). The hepatoprotective activity of ethanol extract of Ziziphus mauritiana leaf against CCl4 - induced liver damage in rats and the antidiarrhoea activity of the methanol root extract were reported (Dahiru *et al.,* 2005 and Amin and Ghoneim, 2009). In addition, it retained control activities of endogenous antioxidant such as SOD and CAT in liver. The antioxidant activity of the aqueous extract of ZS leaf was also reported by Dahiru and Obidoa (2008).

The histological results reported in the current study confirmed the biochemical results and indicated that CCl_4 induced severe histological changes in hepatic tissue. Also, the consumption of the examined fruits could lower the morphological changes in liver because of high levels of antioxidants. These compounds could scavenge the free radicals of CCl_4 generated through Cytochrome P450 enzyme system, supplying a competitive substrate for unsaturated lipids in the membrane and /or accelerating the repair mechanism of damaged cell membrane thereby diminished the oxidative injuries in tissues (Nagata *et al.,* 1999).

From obtained results It can be recommend that increase consumption of HT, PP and ZS powder of their effective impact in reducing the side effects of hepatotoxic rats, which proved some chemical analyses of serum, blood and confirmed by the analysis of histopathological tissue of the liver, and nutritional status, and recommended research also need to enter the HT, PP and ZS powder within the food plan of liver disease diet and general beverages in quantities which achieved results on rats, which have been turned into quantities to humans, dose a 65 grams of powder daily to reduce and delay the complication of liver disease patients.

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