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Do diets supplemented with common herbs alleviate the symptoms of rich fructose diet in rats?

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The objective of this study was to determine whether the adverse effects of rich fructose diet can be modulated in the presence of common herbs specifically the effects on lipid profile, liver and kidney functions in male albino rats. The rats were divided into two main groups, the first main group (6 rats) fed on basal diet containing starch, while the second main group (66 rats) was divided into eleven subgroups (6 rats each) and fed on fructose-rich diet for 15 days and then supplemented with different herbs for 30 days. Feed intake was recorded during the experiment, rats were then sacrified and organ weight/body weight percentage were calculated recorded, liver and kidney functions and lipid profile were estimated. A significant reduction ($p<0.05$) of cholesterol has been noticed among rat groups that fed on fenugreek 2%, nutmeg 2%, and combined herbs 2% compared to positive control. Rat groups that were fed on nutmeg 2%, cardamom 2% and combined herbs 2%, showed a significant reduction of triacylglycerol ($p<0.05$). Liver and kidney functions were also improved. Microscopically examined liver and kidney of rats from ginger 2%, nutmeg 1%, cardamom 2% and combined herbs showed normal hepatocytes and fenugreek seeds 2%, cardamom 1%, nutmeg 1%, ginger 2% and combined herbs were revealed to normal renal cells.

Key words: rats, fructose, herbs, kidney and liver functions

INTRODUCTION

High-fructose diet (HFD) induces hypertriacylglycerolemia, hyperinsulinemia and hypertension that are common features in animal models of insulin resistance induced by HFD (Huang et al. 1997). The bulk of fructose metabolism occurs in the liver, and the presence of fructose stimulates glucose uptake by the liver (Daly et al. 1997). Ameliorating effects of herbs in improving lipid profile in rats fed a high fructose diet has been reviewed (Anitha et al. 2002). Beneficial effects of low quantities of fructose are in contrast to the impairments in hepatic glucose metabolism and insulin action that occur after exposure to diets enriched in sucrose or fructose (Bezerra et al. 2000) or when fructose was infused at relatively high rates (Dirlewanger et al. 2000).

Many antioxidants are found in spices and herbs and they may be effective in protecting against the effects of high fructose diets and peroxidative damage caused in living cells (Okezie 1999). The herbs and herb principles are also known to possess anticarcinogenic and anti-inflammatory properties (Srivastava and Mustafa 1989). These beneficial effects are mediated in part by inhibiting the formation of lipid peroxides and prostaglandin synthesis (Srivastava and Mustafa 1989). Spices also aid in digestion by intensifying the salivary flow and gastric juice secretion (Glatzel 1968).

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Cardamom (seeds) *Elettaria cardamomum*, fruit of cardamom is usually used as flavouring agent in Arabian coffee throughout the Arabian countries and as spices in many countries. They are medicinally used for treatment of flatulent indigestion and to stimulate the appetite in people with anorexia. The seeds of cardamom were also prescribed in Ayurvedic medicine for cough, cold, asthma, indigestion and bronchitis (Al-Zuhair et al. 1996). Eugenol, an active principle of cardamom (Sukumaran and Kuttan 1995) is also known for its antioxidant property due to its phenolic characteristics. Many spices and herbs are strong scavengers of reactive oxygen species (ROS) (Oya et al. 1997). Thymoquinone, the main constituent of the volatile oil from N. Sativa seed that is reported to inhibit eicosanoid generation in leukocyte, non-enzymatic peroxidation in ox brain phospholipids liposomes and membrane lipid peroxidation (Houghton et al. 1995).

Nutmeg (fruit) *Myristica fragrans* is one of the plants commonly found in Asian medicinal ingredients (Harborn and Baxter 1995). It contains many bioactive compounds including camphene, elemicin, eugenol, isoelemicin, isoeuglenol, methoxyeugenol, pinene, sabinene, safrol, myristic acid, myristicin, elimicin and lignans compounds (Morita et al. 2003). Nutmeg, which consists of dried kernels of the seeds of mystica fragrance (Myristicacae) contains not less than 5% v/w of volatile oils. It also contains 35% of solid fat, the chief fatty acid constituents are myristic acid (60%), palmatic, oleic, linoleic and lauric acids (Todd and Martindale 1967).

Fenugreek (seeds) *Trigonella foenum* graecum, is a leguminous plant native to many Asian, Middle Eastern, and Eu-

ropean countries (Chevallier 2000). The seeds and leaves of fenugreek are edible and are used as condiments and as Ayurvedic medicine in the Indian subcontinent to treat diabetes, high cholesterol, wounds, inflammation, and gastrointestinal ailments (Chevallier 2000). Fenugreek seeds have been successfully tested in laboratory animals and in humans with type I and type II diabetes as a hypoglycemic agent (Basch et al. 2003). The potential effect of fenugreek seeds has been examined to modulate several enzymes, including those associated with glucose and lipid metabolism (Raju et al. 2001). Among bioactive compounds identified in fenugreek seeds are protodioscin, trigoneoside, diosgenin, yamogenin, and others (Murakami et al. 2000).

Dry ginger, (*Zingiber officinale*), a traditional Chinese herbal remedy, has been used to treat a number of medical conditions, including headache, colds, and arthritis (Vutyavanich et al. 2001). Antiemetic actions of ginger have been reported in patients with nausea during pregnancy and in subjects with motion sickness (Vutyavanich et al. 2001). Its effectiveness in preventing postoperative nausea and vomiting is uncertain with some studies observing benefits and others showing no effect (Arfeen et al. 1995). The active ingredients responsible for the beneficial effects of ginger are uncertain, and the mechanisms responsible for reducing nausea and vomiting are unknown, although previous investigations have demonstrated inhibitory effects on prostaglandin and leukotriene synthesis (Kiuchi et al. 1992). In the present study, we examined the influence of different common herb ratio of the high-fructose diet on liver and kidney functions and lipid profile in male albino rats.

MATERIAL AND METHODS

Animals and Diets

Seventy two male albino rats (Sprague Dawley Strain) weighing (200 ± 5g) were obtained from Helwan farm (Egypt) and were kept in individual stainless steel cages under hygienic conditions. For one week all rats were fed on a basal diet for adaptation as *ad libitum* in the animal house of Nutrition and Food Science Department. The basal diet in the preliminary experiment consists of 20% casein (protein > 80%), soybean oil 5%, cellulose 5%, vitamin mixture 1%, salt mixture 3.5%, choline chloride 0.2% and the remainder is corn starch (Reeves et al. 1993). After a week of acclimatization, the rats were divided into two main groups, the first main group (6 rats) were fed on basal diet containing starch as the source of carbohydrate, while the second main group (66 rats) was fed with fructose-high diet for 15 days according to the method described by (Ramu et al. 2005), the composition of the control and fructose diets is given in the Table (1). Diet ingredients were purchased from El-Gomhoriya Company, Cairo Egypt. Fenugreek seeds *Trigonella foenum graecum*, dry ginger (rhizome) *Zingiber officinale*, cardamom seeds *Elettaria cardamomum* and nutmeg *Myristica fragrans* were purchased from local market, Cairo Egypt. The experiments were approved by the Faculty's Committee for Animal Experimentation.

Table 1. Composition of diets (g/100g)

Ingredients	Control diet	High fructose diet
	g/kg	g/kg
Corn starch	65.292	5.292
Fructose	--	60
Casein	20	20
Soybean oil	5	5
Cellulose	5	5
Salt mixture	3.5	3.5
Vitamin mixture	1	1
Choline chloride	0.2	0.2
Tert butylhydroquinone	0.008	0.008

Experimental Design

After this period, the second main group was divided into eleven subgroups (6 rats each). These groups were treated with a range of herbs for 30 day as follows: Subgroups (1&2) fed on HFD containing 1% and 2% fenugreek seeds (Fgs). Subgroups (3&4) fed on HFD containing 1% and 2% dry ginger (Gn). Subgroups (5&6) fed on HFD containing 1% and 2% cardamom seeds (Cm). Subgroups (7&8) fed on HFD containing 1% and 2% nutmeg (Nt). Subgroups (9&10) fed on HFD containing 1% and 2% combination herbs (Cmb) (Fgs, Gn, Cm, and Nt), respectively. Subgroups (11) fed on HFD only positive control group (PC).

Diets consumed and body weights were recorded every week, at the end of the experiment, the animals were fasted overnight before sacrificing. The rats were anaesthetized with ethyl ether after which blood samples were collected immediately from the retro orbital venous plexus in sterile tubes. Serum was collected after standing the tubes for half an hour at room temperature (20-22 °C). Centrifugation was carried out at 950 xg for 15 minutes (Sorvall RT7, Newtown, MA). Organs such as the kidneys and liver were removed in order to carry out histological examination.

Biochemical Studies

Serum total cholesterol and triacylglycerol concentrations were determined enzymatically using kits from Boehringer (Germany). Serum high-density lipoprotein (HDL) cholesterol was determined by a direct method (Unimate HDL Direct, Roche Diagnostics) that uses the combined action of polymers, polyanions, and detergents to solubilize cholesterol from HDL but not from VLDL-C, LDL-C, concentrations were calculated by the (Friedwald et al. 1972). Non-HDL-cholesterol concentration was calculated by subtracting HDL cholesterol from total cholesterol. The coefficients of variation (CVs) were 1.7% and 2.5%, and 2.6%, for total cholesterol, triacylglycerol, HDL-C, respectively. Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were determined by the ultraviolet spectrometry method, using Quickauto II. Serum alkaline phosphatase (ALP) was also measured (Bergmeyer and Brent 1974). These were analyzed using a Biochemical Autoanalyzer (AU5232; Olympus, Tokyo, Japan).

Serum uric acid concentration was determined by a carbonate phosphotungstate method and uric acid standard (Sigma, St. Louis, MO) (Henry et al. 1957). Serum urea nitrogen concentrations was determined by spectrophotometry using commercial colorimetric assay kits (Sigma, St. Louis, MO). The urea nitrogen assay was based on the breakdown of urea to ammonia by urease and the subsequent conversion of phenol to indophenol by sodium nitroprusside. Serum creatinine concentrations was determined using an enzymatic method (Roche Diagnostics, Mannheim, Germany) on a Hitachi 911 Autoanalyzer according to the manufacturer's procedures.

Histology

Specimen from the organs; liver and kidney were fixed in 10% neutral buffered formalin. Organ tissues were routinely processed for light microscopy, embedded in paraffin and stained with hematoxylin and eosin (H&E) according to (Bancroft and Gamble 2008). All tissues were coded and analyzed by the pathologist without knowledge of related characteristics or diet. Histological results have been graded by a scale from 0 to 4 according to severity of pathological changes in histological sections. 0 shows no histopathological results, 1 shows light degree of severity of pathological changes, 2 mild, 3 moderate and 4 severe histopathological changes.

Statistical analysis

The data obtained was analyzed statistically for standard deviation (±SD) and one way ANOVA test (Steel and Torrie 1980).

RESULTS

Table 2. Feed intake and ratio organ/body weight of rats

Parameter	Feed intake	Organ/body weight, %	
Groups	g/day	Liver	Kidney
NC	12.83±0.59^{ae}	2.46±0.17^{f}	0.44±0.04^{e}
PC	13.42±0.89^{ab}	3.88±0.13^{a}	0.69±0.07^{a}
Fgs1%	12.75±0.71^{bcdef}	3.36±0.22^{b}	0.57±0.07^{b}
Fgs 2 %	12.42±0.94^{cd}	3.88±0.27^{a}	0.59±0.04^{c}
Gn 1 %	13.00±0.95^{ad}	3.27±0.13^{bc}	0.51±0.04^{cd}
Gn 2 %	11.33±0.68^{e}	3.26±0.18^{d}	0.54±0.04^{de}
Cm 1%	13.75±0.79^{a}	3.15±0.08^{cd}	0.55±0.04^{bd}
Cm 2 %	13.83±0.75^{ad}	3.53±0.12^{b}c	0.59±0.05^{cd}
Nt 1 %	11.83±0.75^{f}	2.98±0.06^{e}	0.60±0.04^{b}
Nt 2%	11.58±0.69^{ce}	3.74±0.27^{ab}	0.56±0.05^{ce}
Cmb1%	13.01±1.05^{ac}	3.11±0.11^{de}	0.55±0.07^{bc}
Cmb 2%	14.08±0.69^{a}	3.33±0.17^{cd}	0.64±0.03^{b}

Values are expressed as mean ± SD. Significance at p<0.05.

Values which do not share the same letter in each column are significantly different.

NC: Negative control, PC: positive control, Fgs: fenugreek seed, Gn: ginger, Cm: cardamom, Nt: Nutmeg, Cmb: Combined herbs

Feed intake and Organ weight/body weight

Feed intake

Feed intake (g/day for each rat) did not differ significantly between the controls groups (fed on basal diet or HFD). The results indicated that, non-significant differences in food intake were observed in the groups fed on HFD containing Gn1%, Cm1%, Cm2%, Cmb1% and Cmb2%, as compared to the negative and positive control groups.

Organ weight/body weight percentage

Table 2 showed that, weights of liver and kidney changed by HFD. Statistical analysis showed a significant increase in liver and kidney weight/body weight % for the positive control group compared to the negative control group (NC). Adding herbs to the HFD at levels (1% and 2%), decreased liver and kidney weight/body weight% significantly (p<0.05), as compared to the PC group, except the liver of the group of rats fed on HFD containing Fgs 2% and Nt 2%. On the other hand, kidney weigh/body weight % of rats fed on HFD containing Gn2% or Nt 2% recorded non-significant difference, as compared to NC group.

Table 3. Serum levels of total lipids, triacylglycerol and cholesterol concentrations

Parameters	mg/dl		
Groups	Cholesterol	Triacylglycerol	Total lipids
NC	58.62±4.77^{h}	51.36±5.81^{j}	276.45±5.09^{h}
PC	111.70±3.46^{a}	181.14±5.10^{a}	405.93±7.28^{a}
Fgs1%	77.94±3.76^{ef}	165.12±6.22^{b}	308.37±6.51^{g}
Fgs 2 %	67.53±3.18^{g}	119.94±4.54^{e}	280.45±3.88^{h}
Gn 1 %	98.22±3.52^{b}	149.20±4.32^{c}	378.58±7.47^{b}
Gn 2 %	83.60±3.46^{cd}	127.66±5.27^{d}	335.89±6.04^{d}
Cm 1%	79.04±3.32^{de}	132.66±4.23^{d}	357.70±4.30^{c}
Cm 2 %	73.46±3.89^{f}	69.92±5.52^{h}	328.30±3.35^{e}
Nt 1 %	84.16±5.12^{c}	78.06±10.66^{g}	308.88±3.58^{g}
Nt 2%	67.10±3.12^{g}	62.16±4.35^{i}	290.85±5.84^{h}
Cmb1%	74.10±3.75^{f}	104.86±3.26^{f}	324.74±5.48^{ef}
Cmb 2%	67.49±3.34^{g}	76.22±2.81^{gh}	318.79±2.5^{8f}

Values are expressed as mean ± SD. Significance at p<0.05. Values which do not share the same letter in each column are significantly different.

Table 3 presents the effect of Fgs, Gn, Cm, Nt and Cmb with two levels on total cholesterol, triacylglycerol and total lipids of serum rats fed on HFD. The mean values of serum cholesterol, triacylglycerol and total lipids (mg/dl) increased significantly at p<0.05 in the positive control groups in comparison with the negative control group. All groups which received HFD containing 1% and 2% herbs showed a significant decrease p<0.05 in serum cholesterol, triacylglycerol and total lipids, in comparison to PC group. Generally herbs demonstrated a potential effect in lowering total lipids specifically in Fgs 2% and Nt 2% rat groups (p<0.05).

Table 4. Effect of common herbs on liver function

Parameters	IU/l		
Groups	AST	ALT	ALP
NC	38.00±2.12^{h}	24.40±1.14^{i}	265.73±6.32^{j}
PC	71.00±3.74^{a}	48.40±2.30^{a}	434.85±6.09^{a}
Fgs1%	52.20±2.17^{c}	40.00±1.87^{bc}	383.60±6.23^{d}
Fgs 2 %	43.40±4.22^{e}	33.20±2.28^{efh}	295.70±5.54^{g}
Gn 1 %	57.20±3.35^{b}	43.20±3.96b	417.40±3.65^{b}
Gn 2 %	47.80±2.28^{d}	31.80±3.42^{gh}	318.60±11.08^{e}
Cm 1%	43.20±2.78^{e}	38.00±3.16^{cd}	392.58±11.51^{c}
Cm 2 %	39.20±1.30^{fg}	33.20±2.39^{efg}	305.94±5.23^{f}
Nt 1 %	42.00±1.58^{eg}	35.60±1.52^{df}	301.00±5.20^{fg}
Nt 2%	39.80±1.48^{fgh}	31.80±2.49^{gh}	286.44±4.38^{h}
Cmb1%	42.20±1.30^{ef}	35.80±1.64^{de}	295.80±5.59^{g}
Cmb 2%	38.80±1.30^{h}	32.20±3.56^{gh}	278.00±2.12^{i}

Values are expressed as mean ± SD. Significance at p<0.05. Values which do not share the same letter in each column are significantly different

The data presented in Table 4 of AST, ALT and ALP (IU/l) for PC group showed a significant increase (p<0.05), as compared to the NC group. All rat groups fed on HFD containing (1 & 2% herbs) showed a significant reduction in the mean values of liver function (p<0.05), compared to PC group. Table (4) shows a significant reduction (p<0.05) of liver enzymes when rats were administered herbs in their diets specifically for AST in Cm 2%, Nt 1% and 2%, Cmb 1% and 2% rat groups. Significant reduction (p<0.05) of ALT has been noticed in Fgs 1%, Gn 2%, Nt 2% and Cmb 2%. Same results were found for ALP in Nt 2% and Cmb 2% rat groups.

Table 5. Effects of common herbs on kidney function

Parameters	mg/dl		
Groups	Uric acid	Urea nitrogen	Creatinine
NC	1.840±0.114^{h}	19.694±2.164^{g}	0.720±0.08^{f}
PC	4.460±0.167^{a}	46.340±3.037^{a}	1.900±0.123^{a}
Fgs1%	3.460±0.305^{b}	34.320±3.432^{c}	1.640±0.054^{b}
Fgs 2 %	2.640±0.1673^{f}	23.480±2.451^{f}	1.400±0.071^{c}
Gn 1 %	3.000±0.123^{cd}	40.400±3.274^{b}	1.420±0.084^{c}
Gn 2 %	2.340±0.123^{g}	31.560±2.499^{cd}	1.200±0.010^{d}
Cm 1%	3.120±0.130^{c}	31.840±1.950^{c}	1.440±0.089^{c}
Cm 2 %	2.960±0.152^{ce}	28.540±2.368^{de}	1.260±0.114^{d}
Nt 1 %	3.080±0.228^{c}	27.400±1.817^{e}	1.440±0.114^{c}
Nt 2%	2.300±0.187^{g}	22.000±2.549^{fg}	1.140±0.109^{d}
Cmb1%	2.800±0.158^{def}	27.520±2.013^{e}	1.160±0.107^{d}
Cmb 2%	2.180±0.217^{g}	23.600±1.812^{f}	0.940±0.116^{e}

Values are expressed as mean ± SD. Significance at p<0.05. Values which do not share the same letter in each column are significantly different

The results in Table 5 revealed that serum uric acid, urea nitrogen and creatinine increased significantly (p<0.05) in the PC group that were fed on HFD, as compared to NC group fed on basal diet. Addition of herbs with two levels (1 and 2%) to HFD, led to lower values of serum uric acid, urea nitrogen and creatinine than PC group. It is worth mentioning that the results of serum uric acid recorded for the groups fed on HFD containing Gn 2%, Nt 2% and Cmb 2%, groups showed significant decrease in this parameter, as compared to other tested groups. However, the group of rats fed on HFD containing Nt 2% achieved the best result in serum urea nitrogen, followed by Cmb 2% and Fgs 2%, respectively. Serum Creatinine level for the group which was received HFD containing Cmb 2% recorded significant decrease (p<0.05), as compared to other tested groups, followed by Gn 2%, Cm 2%, Nt 2% and Cmb 1%, respectively.

Histological results

Effect of fructose on rat organs

Histologically, livers of NC rats showed normal histological structure of hepatic lobule (Fig. 1, A). In contrast, livers of PC rats showed activation of kupffer cells and sinusoidal leucocytes (Fig. 1, B). Examined liver of rat from Fgs 1% and 2% revealed vacuolation of some hepatocytes and slight hydropic degeneration of some hepatocytes (Fig. 1). However, rat livers from Gn 2%, Nt 1%, Cm 2% and Cmb 1% and 2 % showed vacuolar normal hepatocytes (Fig. 6). Examined rat liver from group Gn 2% showed apparent normal hepatocytes.

Microscopically, kidneys of NC revealed normal histology of renal parenchyma (Fig. 2). Meanwhile, kidneys of rats from PC showed hyaline cast in the lumen of renal tubules (Fig. 2). Examined kidneys of rat from Fgs 2%, Cm 1%, Nt 1%, Gn 2% and Cmb 2% revealed normal histology of renal cells. On the other hand, kidneys of rat from group Gn 1% revealed vacuolation of epithelial lining and some renal tubules associated with presence of hyaline cast (Fig. 2).

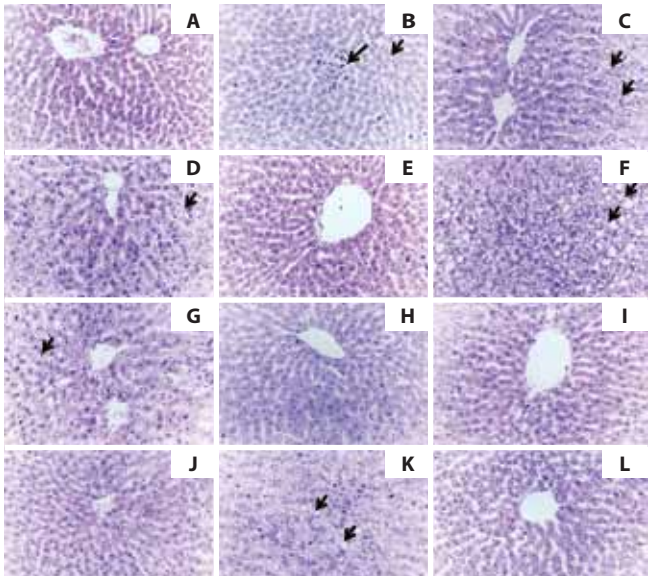

Figure 1. Liver of rats

(NC (A) showed normal histological structure of hepatic lobule (H and E X200) (-). Liver of rats from PC (B) showed activation of kupffer cells and sinusoidal leucocytes (++). Liver of rats from Fgs1% (C) showed vacuolation of some hepatocytes (+). Liver of rats from Fgs 2% (D) showed slight hydropic degeneration of some hepatocytes(+). Liver of rats from Cmb 2% (E) showed no histopathological changes. Liver of rats from Gn 1% (F) showed vacuolar degeneration of hepatocytes (++). Liver of rats from Cm 1% (G) showed hydropic degeneration of some hepatocytes (+). Liver of rats from Gn 2% (H) showed apparent normal hepatocytes (-). Liver of rats from Nt 1% (I) showed no histopathological changes (-). Liver of rats from Cm 2% (J) showed no histopathological changes. Liver of rats from Nt 2% (K) showed vacuolar degeneration of hepatocytes (++). Liver of rats from Cmb 1% (L) showed no histopathological changes.)

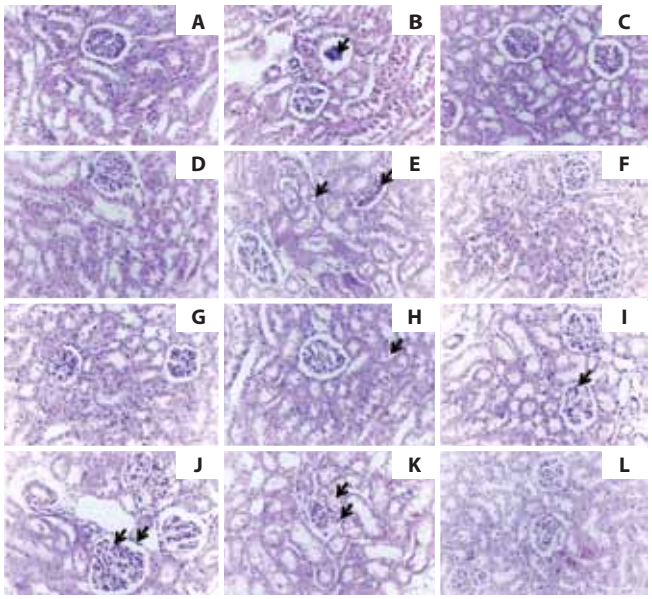

Figure 2. Kidney of rats

(NC (A) showed normal histolgy of renal parenchyma (H and E X200) (-). Kidney of rats from PC (B) showed atrophy of some glomerular tufts (+++). Kidney of rats from Fn 2% showed no histopathological changes (C). Kidney of rats from Crm 1% (D) showed apparent normal renal parenchyma (-). Kidney of rats from Gn 1% (E) showed vacuolation of epithelial lining and some renal tubules associated with presence of hyaline cast (++). Kidney of rats from Cmb 2% (F) showed no histopathological changes (-). Kidney of rats from Nt 1% (G) showed no histopathological changes (-). Kidney of rats from Cm 2% (H) showed vacuolation of epithelial lining of some renal tubules (+). Kidney of rats from Fgs 1% (I) showed vacuolation of the epithelial lining of renal tubules and endothelial lining of glomerular tufts (++). Kidney of rats from Nt 2% (J) showed hypertrophy and vacuolization of glomerular tufts (++). Kidney of rats from Cmb 1% (K) showed vacuolation of epithelial lining renal tubules and endothelial lining of glomerular tufts (++). Kidney of rats from Gn 2 % (L) showed apparantly normal renal parenchyma (-)).

DISCUSSION

The main objective of this study was to evaluate the potential efficacy of different common herbs that were used in different ratios with high-fructose diet to look at liver and kidney functions, and the lipid profile in male, albino rats. In the past, fructose was considered to be beneficial in the dietary management of diabetes mellitus and insulin resistance, because fructose ingestion results in smaller postprandial glycemic and insulin excursions than do glucose and complex carbohydrates (Glinsmann and Bowman 1993). However, diets high in fructose were found to induce insulin resistance in rodents (Zavaroni et al. 1980). Thorburn et al. (1989) fed rats a diet containing 35% of energy as fructose for 4 weeks and found reduced insulin sensitivity associated with impaired hepatic insulin action and whole-body glucose disposal. Many processed foods and drinks such as jams and soft drinks that contain fructose corn syrup will contribute to human total fructose intake however; most of the fruits and vegetables do not provide such an extremely large amount of fructose.

From biochemical studies, fructose is the component of sucrose that is considered to be responsible for some of the adverse effects of this disaccharide on blood triacylglycerol (Reiser 1985). Fructose consumption has been shown to induce hypertriacylglycerolemia. Because insulin resistance and reduced insulin binding have been reported in hypertriacylglycerolemic individuals (Bieger et al. 1984), this may be one mechanism by which fructose diets promote insulin resistance. There are numerous studies in which dietary fructose has been shown to induce hyperlipidemia in rodents (Okazaki et al. 1994). The results of the present study is in agreement with results of previous studies, however the studied herbs demonstrated a potential effect in lowering lipid profile significantly ($p<0.05$) in the presence of a high fructose diet in comparison to PC.

As noticed in our results, triacylglycerol was increased in high fructose diets especially without treatment with the studied herbs; this was in agreement with the results of (Bjorntorp 1994). As they found an increased supply of non-esterified fatty acids in the liver, also leads to an increase in the production of VLDL and triacylglycerol (Arner 2001).

It has been reported that dietary fructose possesses hyperlipidemic properties (Hallfrisch 1990) and does not stimulate lipoprotein lipase (Bar-On and Stein 1968) consequently, the rate of removal of triacylglycerol from circulation when fructose is fed might be slower than when starch is fed, leading to higher blood triacylglycerol levels. A greater rate of conversion of acetate to fatty acids has been reported in fructose-fed rats compared to glucose-fed rats (Baker et al. 1952). Some spices especially fenugreek seeds (Madar et al. 1988) have been found to have a hypolipidemic effect by enhancing faecal excretion of bile acid and cholesterol, which could explain in part the hypocholesterolemic properties of fenugreek seeds (Valette et al. 1984). In this aspect there is a confirmation of the current results with cited literature.

Many studies have reported that fructose administration can have profound effects on plasma and tissue lipids levels. (Thorburn et al. 1989) described an increase in total liver lipids in rats when glucose was isocalorically substituted by either sucrose or fructose. This effect was attributed to the induction of various lipogenic enzymes in liver by fructose. Fructose feeding may lead to hypertriacylglycerolemia by increasing the formation of glycerol-3-phosphate, a precursor of lipid synthesis. Hypertriacylglycerolmia may also arise due to defect in removal of VLDL from plasma or increased secretion of VLDL in the liver. Lipoprotein lipase is an important enzyme responsible for the hydrolysis of triacylglycerol (TAG) from chylomicrons and LDL. Plasma lipoprotein lipase activity was reported to be lowered in high fructose-fed rats (Anitha Nandhini et al. 2002). The elevated TAG concentration may be associated with impaired insulin action. Bieger et al. (1984) have shown that an increase in blood TAG concentration can reduce the number of insulin receptors thereby reducing insulin sensitivity.

Activity of hepatic enzymes regulating lipogenesis and gluconeogenesis is increased with diets having fructose in place of starch (Fields et al. 1985). In addition, redox changes occur after the consumption of fructose (Bellomo et al. 1987) which may be necessary for hepatic fatty acid synthase gene transcription (Wilson et al. 1997). Our results are in agreement

with previous studies which indicated the values of AST, ALT and ALP (IU/l) for PC control showed a significant increase ($p<0.05$) as compared to NC group. Generally, supplementing fructose rich diets with herbs, (1 and 2% herbs) showed significant reduction in the mean values of AST, ALT and ALP at ($p<0.05$), compared with the positive control group. Little data is known about the effect of the studied herbs in this study on kidney function, although our results indicate an improvement of kidney function, increasing the consumption of spices could serve as an effective support therapy in the prevention and management of kidney function.

Nutmeg contains 25–30% mixed oils and 5–15% volatile oils such as camphene, elemicin, eugenol, isoelemicin, isoeugenol, methoxyeugenol, pinene, sabinene, safrol, and also chemical substances such as dihydroguaiaretic acid, elimicin, myristic acid, myristicin and lignan compounds (Janssen et al. 1990). Additionally the histological examination in this study indicates that the liver of rat from group nutmeg 1% showing no histopathological changes. Kidney of rat from group nutmeg 1% (G) showing no histopathological changes.

A study found that ethanol extract of nutmeg was administered orally to rabbits with experimentally induced hyperlipidemia and it was observed that levels of lipoprotein lipids were significantly lowered. Also, there was decrease in total cholesterol: HDL and LDL: HDL ratio (Grover et al. 2002). Hepatoprotective effect of essential oils of nutmeg was observed in rats with experimentally produced liver damage. Myristicin from the volatile oil was found to be responsible for the hepatoprotective effect.

Fenugreek *Trigonella foenum graecum* is reported to have a cholesterol-reducing effect (Sharma 1984). Fenugreek has also shown an overall stimulatory effect on the specific as well as non-specific immune functions in mice (Bin-Hafeez et al. 2003). Additionally, the histological examination in this study indicates that the kidney of rats from group fungreek seeds (Fgs) 2% showed no histopathological changes compared to PC.

Generally, some of the constituents might be having mitogenic effects, which in turn lead to stimulatory effects on immuno-competent cells. Some of these constituents also possess antioxidant properties and they may induce the immuno-stimulant effects. Both the pro-oxidant and antioxidant effects of flavonoids have previously been identified (Shen et al. 2004). In this study, the combined herbs (Cmb) at a ratio of 2% led to an improvement of the histological features in liver and kidney. Similarly, liver and kidney histology were improved when 2% of ginger was added to the diet. The effect of added cardamom (2%) excelled the results of added cardamom (1%) in high fructose diet in terms of biochemical and histological changes.

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