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Differential Effects of High Fat, High Sucrose and High Starch Diets on Some Aspects of Carbohydrate and Lipid Metabolism and the Hepatic Oxidative Status in Adult Male Albino Rats

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Keywords

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Abstract

Background & objectives: It is well-established that diet composition can have a direct impact on normal physiological functions, as well as on pathological conditions such as obesity, diabetes, and cardiovascular disease. Therefore, this study was designed to investigate the effect of 4 weeks' different feeding programs comparing body weight, food intake, lipid profiles, serum glucose, insulin and leptin. In addition, we evaluated the oxidative state and the histological appearance of the liver. ***Methods:*** Twenty four male albino rats were fed with high fat diet (HFD), high sucrose diet (HSD), and high starch diet (HTD) for a period of 4 weeks compared with a control diet (CD) group of equal caloric values. ***Results:*** Rats fed the different experimental diets showed dyslipidemia, hyperleptinemia, hyperglycemia, hyperinsulinemia and alteration of oxidative markers and histological changes in the hepatic tissues (steatosis, micro and macrovacuolation, inflammatory cell infiltration and focal necrosis in different zones). HSD showed the severest changes while HTC the least. HSD decreased the final daily food intake, body weight (BW) and body mass index (BMI), while HFD increased at first then decreased finally daily food intake in spite of increased final BW and BMI. HTC decreased final BW and BMI in spite of increased food intake. ***Conclusion*** Improper selection of diet macronutrients is more serious than excess caloric intake especially for obese or those with hepatic or other organ challenges. High fat diet has deleterious metabolic effects. The type of carbohydrate is also a determinant factor; complex carbohydrates (starch) being less hazardous than simple ones (sucrose).

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INTRODUCTION

Diets with adequate energy (30% originating from fat) are sufficient to promote normal growth and normal sexual maturation; conversely, diets that exceed this amount may result in excessive weight gain. Dietary fat plays a major role in human nutrition and serves many essential functions, while excessive caloric intake has been proposed as a causative factor in the development of metabolic syndrome. In this regard, the quantity as well as the quality (primarily) of dietary fat consumed strongly predicts the prevalence and possibility of insulin resistance, type 2 diabetes and atherosclerosis.[1]

Carbohydrates play an important role in human nutrition by providing cellular energy requirements to cells in the body, particularly the brain. Carbohydrates enter the body as starches or other compound sugars that must undergo stepwise enzymatic degradation to be absorbed. In the gut lumen, starch that is made up of long chains of glucose is first degraded by pancreatic amylase into smaller sugars, maltose, maltotriose, and dextrins, which are subsequently degraded into glucose by enterocyte membrane-bound-glucosidases. Similarly, sucrose that is composed of 50% glucose, and 50% fructose, linked together, is degraded to fructose and glucose by sucrase.[2]

A few years ago, there was a belief that the high fat ingestion was one of the factors that mostly contribute to obesity. However, today it´s known that reducing the amount of ingested fat does not necessarily result in a decrease in the prevalence of obesity since such a measure is, in most cases, associated with an increase in the consumption of carbohydrates. The mechanism is regulated by the interaction of several metabolic factors such as glucose, cytokines, and hormones as leptin which indicate the amount of fat and metabolic status (triglyceride synthesis) of adipocytes, ghrelin and insulin.[3]

Experimental evidence has shown that fructose which is a monosaccharide present in small amounts in fruits and honey can induce metabolic syndrome in animals, whereas this is not observed in controls fed equal amounts of glucose. Studies in humans have also shown that high doses of fructose can result in insulin resistance, postprandial hypertriglyceridemia, intra-abdominal fat accumulation, and elevated blood pressure.[4] If fructose is a mediator of metabolic syndrome, a key question is whether sucrose that is found in substantial amounts in sugar cane and beets is different from their individual components, fructose and glucose, in its metabolic effects or not?

Most experiments in nutrition research have analyzed the differential effects of high-fat diets on metabolic control, but few studies have focused on carbohydrates. To achieve this goal groups of rats fed a high-fat, a high-sucrose and a high-starch diets were used to study the effect on weight gain, metabolic control, insulin resistance, oxidative status and histological appearance of liver in comparison with rats fed a normal standard diet.

MATERIALS AND METHODS

Animals:

Twenty four adult male albino (Sprague Dawely strain) rats, of average weight 150-170 gm, about 4 months old were used in the present study. Rats were purchased from the National Research

Center, Cairo, Egypt. Rats were housed in stainless steel mesh cages offering individual housing. Each rat had a tag number. They were left freely wandering in their cages for two weeks with normal hour's dark: light cycle for acclimatization before starting the experiment. All experimental protocols were approved by the animal care committee of Minia University and coincide with international guide for caring and use of laboratory animals.[5]

The rats were randomly classified into the following four equal groups (6 rats in each) taking in consideration that at the onset of the experiment, the mean body weight of the rats of the different groups wasn't statistically significant:

1- Control diet (CD) group: in which rats were fed a commercially available CD for 4 weeks.[6]

2- High fat diet (HFD) group: in which rats were fed HFD for 4 weeks.[7]

3- High sucrose diet (HSD) group: in which rats were fed HSD for 4 weeks.[8]

4- High starch diet (HTD) group: in which rats were fed HTD for 4 weeks.[8]

Table (1): Diet compositions:

Components (g/kg of diet)	**HFD**	**HSD**	**HTD**
Casein	164	200	200
Butter oil	190.0	0	0
Soybean oil	10.0	50	50
Sucrose	89.9	650	0
Cornstarch	303.1	0	500
Maltodextrin	115	0	150
Cellulose	58.6	50	50
Vitamin Mixture	11.7	10	10
Mineral mixture	41.0	35	35
Choline bitartrate	2.9	2	2
Caloric value, kcal/g	4.1	4.1	4.1

HFD: High fat diet[7], HSD: High sucrose diet, HTD: high starch diet[8]

Diet protocol:

Control diet was according to the formula of ***Santure et al.***[6] that contained (Fat 5.1% [corn oil 5.1%], carbohydrates 64.4% [corn starch 36.3% and sucrose 28.1%], proteins 20.1% [casein 20% and DL-Methionine 1%], fiber 4.6%, salt mixture 4.8%, and vitamin mixture 1%) and provided 4.04 kcal/g of diet, while the HFD, HSD and HTD formulae were prepared as described in previous studies [7,8], respectively and the details of the diets are presented in *table (1).*

CD was purchased from El-Gomhoria Company, Cairo, Egypt, while high fat, sucrose and starch diets were prepared manually and preserved at 4°C until used. The daily food intake was measured for each group. Individual body weight of rats in each group was assessed once a week.

Body mass index (BMI):

Body length (nose-to-anus length in centimeter) was determined in all rats. The measurements were done in anaesthetized rats with light ether. Using a ruler to measure body length, this is considered to

be the distance between the bottoms of the lower incisors to the anus from ventral surface. Rats were weighed in gram using electronic balance (FY 2000). All rats were weighed and their nose to tail length was measured and BMI was calculated weekly. The body weight and length were used to determine BMI according to the following formula:-

Body mass index (BMI) = body weight (g)/length^2 (cm^2).

As considered by ***Novelli et al.***,[9] a significant increase in BMI in comparison to a control is a marker of obesity and also obesity is usually taken as any significant increase in body weight or energy content relative to control animals. This was also according to ***Li et al.***[10]

Sample collection:

At the end of the 4-weeks' dietary period, rats were allowed to fast overnight then, anesthetized with intraperitoneal pentobarbital sodium (60 mg/Kg body weight) and all rats were killed by decapitation immediately. Blood samples were obtained from the jugular vein and were rapidly centrifuged. Sera were separated and stored in aliquots at -80°C till used for estimation of lipid profile including; total cholesterol (TC), triglycerides (TGs), low density lipoprotein

Table (2): Body weight changes during 4 week treatment in the experimental groups:

Body weight (g)	CD	HFD	HSD	HTD
initial	165.4 ± 4.4	166.00 ± 3.7	169 ± 5	164.2 ± 3.7
After 1 week	184.8 ± 4.7	187.4± 4.1	159.8 ± 5.7^{ab}	154.8 ±4.6 ^{ab}
After 2 weeks	207.4 ± 5.7	227.6 ± 6^{a}	149.6 ± 5.6^{ab}	146.3 ± 3.4 ^{ab}
After 3 weeks	213.4 ± 6.8	235.2± 6.3^{a}	145.9± 5.2 ^{ab}	148 ± 6.2 ^{ab}
After 4 weeks	224.8 ± 2.8	239 ± 3.7^{a}	138.2± 4.4 ^{ab}	134.9± 7.2 ^{ab}

Data are expressed as mean ± S.E.M. of 6 rats in each group.a: Significant from control diet group (CD), b: Significant from high fat diet group (HFD), c: Significant from high sucrose diet group (HSD), $P< 0.05$.

Table (3): Changes in daily food intake during 4 week treatment in the experimental groups:

Food intake (g)	CD	HFD	HSD	HTD
1st week	15.5 ± 1.3	19.5± 1.5^{a}	16.7 ± 1.2	29.4 ±1.7^{abc}
2nd week	13.1 ±1.2	19.3 ± 1.3^{a}	16.6± 0.99^{a}	20.4± 0.9^{a}
3rd week	14.1± 0.2	15.5± 0.8	5.3± 0.99 ^{ab}	22.6 ± 1.2 ^{abc}
4th week	14.3± 0.23	13 ± 0.3 ^{a}	4.9 ± 0.3 ^{ab}	16.6± 0.6 ^{bc}

Data are expressed as mean ± S.E.M. of 6 rats in each group.a: Significant from control diet group (CD), b: Significant from high fat diet group (HFD), c: Significant from high sucrose diet group (HSD), $P< 0.05$.

(LDL), and high density lipoprotein (HDL) by enzymatic colorimetric methods using commercial kits (Biodiagnostic, Egypt). Serum insulin was measured by Glory Science Insulin Enzyme-Linked Immunosorbent assay (ELISA), serum glucose by enzymatic colorimetric method using commercial kits (Biodiagnostic, Egypt) and serum leptin by CUSABIO Rat Leptin Enzyme-Linked Immunosorbent assay (ELISA).

Preparation of tissue homogenates:

Specimens from liver were weighed and homogenized separately in potassium phosphate buffer 10 mM pH (7.4). The ratio of tissue weight to homogenization buffer was 1:10. The homogenates were centrifuged at 5000 rpm for 10 min at 4°C. The resulting supernatant was used for determination of malondialdehyde (MDA) according to the method of ***Ohkawa et al.***[11]

Histological Examination:

Specimens were fixed in 10% neutral-buffered formalin, dehydrated, cleared, and embedded in paraffin wax. Tissue sections of 5-6μm thickness were obtained and deparaffinized. Sections were stained with hematoxylin and eosin.[12]

Statistical analysis:

Data were represented as means ± standard error of the mean (SEM). Statistical analysis was performed using Graph pad Prism 5 software and significant difference between groups was done by one-way ANOVA followed by Tukey-Kramar post hoc test for multiple comparisons with a value of $P \leq 0.05$ considered statistically significant.

Results:

Effects of experimental diets on the body weight, BMI and food intake:

By the end of the 4 weeks, HFD fed rats showed a significant higher body weight as compared to the CD group, while HSD and HTD significantly lowered the final body weight as compared to CD and HFD groups *(table 2)*. As regard the daily food intake, feeding HFD showed a significant higher amount of food intake in the first and second weeks and a lower amount in the fourth week as compared with CD group. On the other hand, HSD significantly lowered the food intake in the third and fourth weeks as compared to HFD and CD groups, while, HTD showed significantly higher food intake as compared to all groups *(table 3)*.

As shown in *table (4*), there was a significant increase in the final body weight as compared with its initial value in CD group but without any significant change in BMI and final food intake. In addition, HFD group showed a significant increase in the final body weight and BMI as compared with its initial values inspite of the significant decrease in the final food intake. On the other hand, there was a significant decrease in the final body weight, BMI and food intake as compared with its initial values in HSD and HTD groups.

Effects of experimental diets on serum lipid profiles:

As shown in *table (5)*, feeding of HFD showed significant higher levels of TC, TG, and LDL with lower level of HDL as compared with the CD group. In addition, rats fed HSD showed significant higher levels of TC, TG and LDL with lower level of HDL as compared with HFD group

Table (4): Comparison between initial and final body weight, BMI and food intake in the different experimental groups:

Parameters / Groups	Body weight		BMI		Food intake	
	Initial	Final	Initial	Final	Initial	Final
CD	165.4 ± 4.4	224.8 ± 2.8 [a]	0.56±0.01	0.59±0.01	15.5 ± 1.3	14.3± 0.23
HFD	166.00 ± 3.7	239 ± 3.7 [a]	0.5±0.009	0.65±0.01 [a]	19.5± 1.5	13 ± 0.3 [a]
HSD	169 ± 5	138.2± 4.4 [a]	0.56±0.02	0.49±0.01 [a]	16.7 ± 1.2	4.9 ± 0.3 [a]
HTD	164.2 ± 3.7	134.9± 7.2 [a]	0.5±0.009	0.42±0.009 [a]	29.4 ±1.7	16.6± 0.6 [a]

Data are expressed as mean ± S.E.M. of 6 rats in each group.a: Significant from its initial value, *P*< 0.05.CD: control diet group, HFD: high fat diet group, HSD: high sucrose diet group, HTD: high starch diet group, BMI: Body mass index.

Table (5): Effects of experimental diets on serum lipids:

Parameters	CD	HFD	HSD	HTD
TC (mg/dl)	59.4 ± 1.2	79.7 ± 2.5 [a]	89.3± 2 [ab]	68.6 ± 3.5 [abc]
TGs (mg/dl)	31.5 ± 1.7	60.8± 3.4 [a]	74.8 ± 3.2 [ab]	39.4± 2.7 [abc]
HDL-c (mg/dl)	28.2 ± 1.9	18.7 ± 0.8 [a]	16.1± 0.1 [ab]	23.5± 0.8 [abc]
LDL-c (mg/dl)	24.9 ± 1.8	48.6 ± 3 [a]	60.4 ± 2.7 [ab]	37.1± 2.4 [abc]

Data are expressed as mean ± S.E.M. of 6 rats in each group.a: Significant from control diet group (CD), b: Significant from high fat diet group (HFD), c: Significant from high sucrose diet group (HSD), *P*< 0.05. TC: Total choloesterol; TGs: Triglycerides; HDL: High density lipoprotein; LDL: Low density lipoprotein.

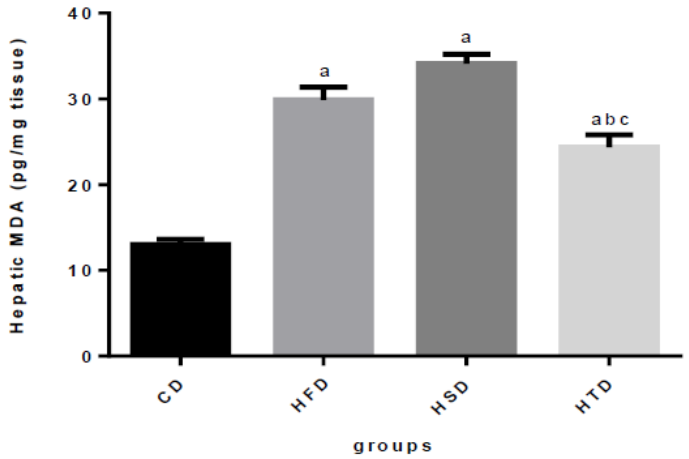

Fig. (1): Hepatic MDA level in different experimental groups. a: Significant from control diet group (CD), b: Significant from high fat diet group (HFD), c: Significant from high sucrose diet group (HSD), *P*< 0.05.

Table (6): Effects of experimental diets on glycemic control parameters (glucose, insulin) and leptin:

Parameters	CD	HFD	HSD	HTD
Serum glucose (mg/dl)	55.9 ±3.4	82.9± 5 ^{a}	112.3 ± 3.2 ^{ab}	100.9 ± 1.1 ^{abc}
Serum insulin (mIU/l)	2.8 ± 0.1	4 ± 0.2^{a}	6.4± 0.4 ^{ab}	5.1 ± 0.2 ^{abc}
Serum leptin (ng/ml)	4.9 ± 0.3	7.8± 0.4^{a}	6.5± 0.3^{ab}	5.8 ± 0.2 ^{ab}

Data are expressed as mean ± S.E.M. of 6 rats in each group. a: Significant from control diet group (CD), b: Significant from high fat diet group (HFD), c: Significant from high sucrose diet group (HSD), $P< 0.05$.

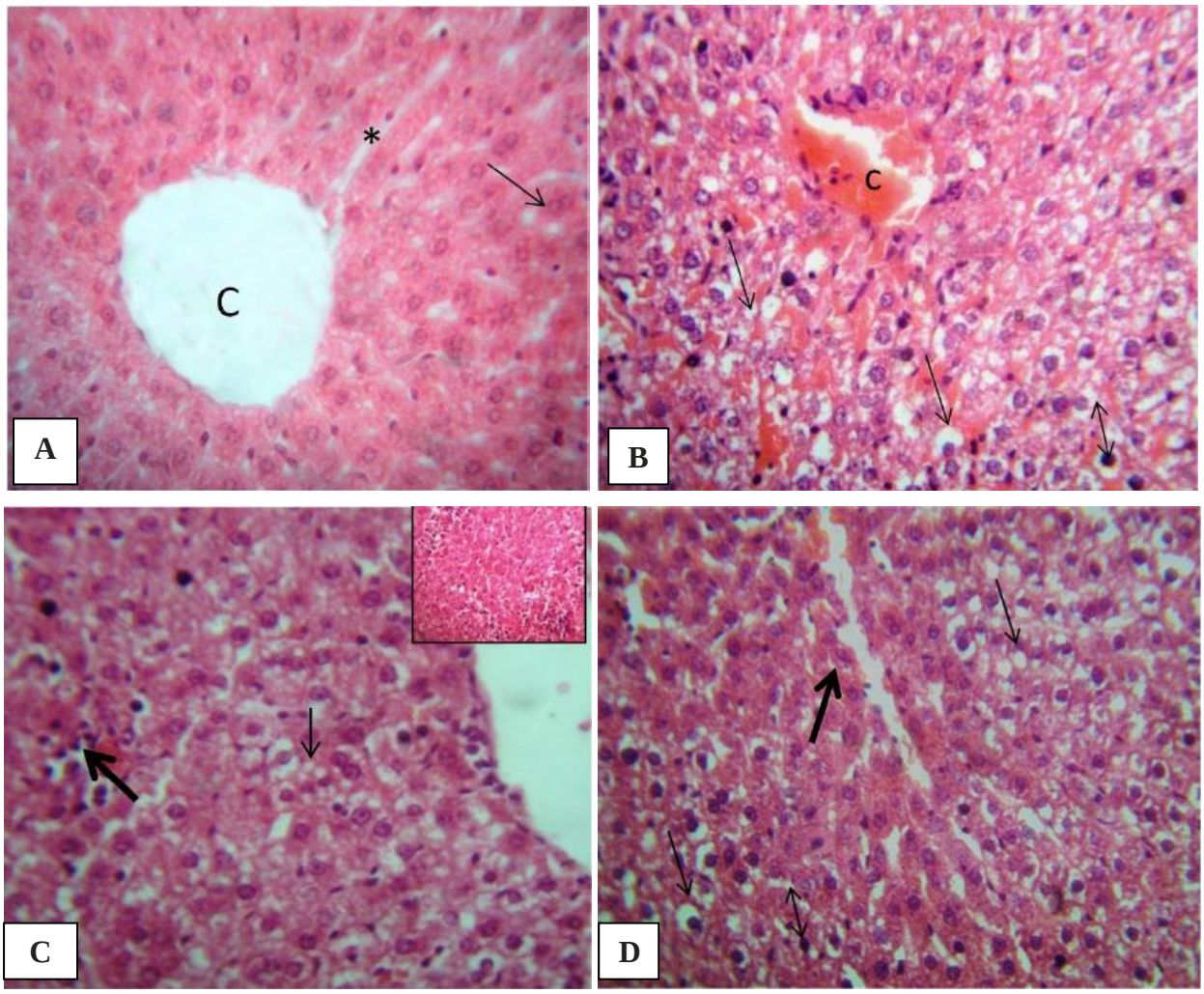

Fig. (2): A photomicrograph of liver sections of the A) control group showing normal architecture of hepatic lobule in which hepatocytes are radiating from central vein (c). Hepatocytes with acidophilic granular cytoplasm and central vesicular nuclei. Some of these cells are binucleated (arrow). Hepatocytes are separated by blood sinusoids (*), B) HFD group showing disorganized hepatocytes with cytoplasmic vacuolations, micro and macrovesicular steatosis and ballooning (arrows) affecting both periportal and pericentral areas. Some hepatocytes have pyknotic nuclei (double headed arrow). Notice congestion of the central vein (c) and hepatic sinusoids. Inset showing most of the hepatocytes around portal area (P) with empty cytoplasm and dark nuclei and inflammatory cell infiltrate, C) HSD group showing loss of normal architecture and scattered necroinflammatory foci (thick arrows). Hepatocytes around the central vein showing micro and macrovesicular steatosis (thin arrow). Some hepatocytes have pyknotic nuclei. Inset showing many necroinflammatory foci and D) HTD group showing most of the hepatocytes with cytoplasmic vacuolations, micro and macrovesicular steatosis and ballooning (arrows). Hepatocytes around central vein appeared less affected (thick arrow) than that at the periphery. Some hepatocytes have pyknotic nuclei (double headed arrow). H&E X 400

while HTD significantly lowered the lipid profile levels (TC, TG, and LDL) as compared with HFD group but still significantly higher than CD group. HDL, however, showed the reverse.

Effects of experimental diets on the serum level of glucose, insulin and leptin:

In *table (6),* feeding HFD, HSD, and HTD caused significant higher serum glucose and insulin levels than the CD group. Highest levels were obtained with HSD than HTD and the least rise was in the HFD group, however, the differences between all groups were statistically significant.

As regard leptin, HFD feeding showed a significant higher serum level of leptin as compared with CD, HSD and HTD groups and in the last two groups, the leptin levels were still significantly higher than that of the CD group.

Effects of experimental diets on the hepatic level of MDA:

Our results showed that feeding HFD, HSD, and HTD caused significant higher levels of hepatic MDA than the CD group. Highest levels were obtained with HSD than HFD and the least rise was in the HTD group, however, the differences among all groups were statistically significant *(fig. 1).*

Effects of experimental diets on the histological findings in the hepatic tissue:

Examination of liver in control group revealed normal preserved hepatic architecture (Fig.2A). On the other hand, the hepatic tissue of HFD group showed less severe picture compared with HSD in the form of disorganized hepatocytes with severe micro and macrovesicular steatosis affecting periportal and pericentral areas, hepatocyte ballooning, vacuolations and less amount of inflammatory cell infiltrate *(fig.2B).* Hepatic tissue of HSD group showed severe damage which involved loss of normal architecture and scattered necroinflammatory foci with micro and macrovesicular steatosis especially around the central vein as shown in *fig. 2C.* As regard HTD group, the histological picture showed cytoplasmic vacuolations, micro and macrovesicular steatosis and ballooning affecting periportal more than pericentral areas with no inflammatory cell making it a less damaged picture compared with HSD and HFD *(Fig.2D).*

Discussion:

Diets rich in sucrose, dextrose, fructose, and fat promote important changes in carbohydrate metabolism resulting in insulin resistance and type 2 diabetes, weight gain and adiposity, dyslipidemia, as well as arterial hypertension.[13] The differential effects of HFD *vs.* simple carbohydrates have been previously studied; however, only few studies focused on the differential effects of complex carbohydrates on the metabolic control. Therefore, in the present study, the effects of simple carbohydrates as sucrose, complex carbohydrates as starch, and HFD on energy balance, metabolic control and insulin resistance in a group of adult male albino rats were analyzed in comparison with rats fed a normal standard diet.

In the present study, the result clearly demonstrated that the final body weight of the CD group significantly increased as compared

with its initial body weight, in spite of the fact that BMI and food intake weren't changed. This could be explained by a natural body growth with no excess fat deposition since the BMI did not significantly change. This agrees with the results reported by ***Ble-Castillo et al.***[14]

In the present study, the rats that consumed the HFD showed a significant higher amount of food intake with correlated increase in body weight in the first and second weeks as compared with CD group as reported by ***Paula Pinto et al.*** [15] This could be explained by the fact that HFDs are characterized by a high palatability that is often considered to increase the energy intake and also promote hyperphagia in the first weeks of study.

Various mechanisms have been suggested for the reduction in the satiety signaling accompanying HFD consumption; including: (1) attenuated enterogastric inhibition of gastric emptying and secretion of satiety hormones (cholecystokinin, peptide YY "PYY" and glucagon-like peptide-1); (2) inhibition of fatty acid oxidation, so that HFDs lower the rate of oxidation of fatty acids, hence they may increase the food intake [16] and at the same time, it increased fat synthesis and deposition in the adipose tissue causing increase in body weight as reported by ***Amin et al.***[17]

In the final week of the present study, the result clearly demonstrated that the body weight of HFD group still significantly increased as compared with its initial body weight and with the CD group in spite of the decrease in the final food intake, taking into consideration that high caloric value of diet was excluded by the equal caloric balance of all diets. This could be attributed to the increase in the leptin level as reported in our study and others[18] which reduces food intake by inhibiting Neuropeptide Y/Agouti related peptide (NPY/AgRP) neurons and increases signaling by anorexigenic Proopiomelanocortin and Cocaine- and Amphetamine-Regulated Transcript (POMC/CART) neurons in the arcuate nucleus region of the hypothalamus. [19] However, leptin failed to decrease body weight as leptin alone couldn't fight adiposity in the presence of continuous HFD consumption but only decreases food intake and prevents further gain in body weight. HFD has been found to stimulate both hyperplasia and hypertrophy of adipocytes irrespective of the amount ingested.[16]

Moreover, with the increase in adipose tissue weight, not only serum leptin levels tend to increase, but also the ability of insulin to stimulate glucose transport and metabolism in adipocytes and skeletal muscle is impaired resulting in peripheral insulin resistance and hyperglycemia[20] as observed in our study with HFD group when compared with CD group. On the other hand, Insulin synergistically acts with leptin to inhibit NPY/AgRP neurons in the hypothalamus to decrease food intake. The significant decreased food intake at the end of the study in the HFD group in spite of the increased serum leptin and insulin levels indicated that the central mechanism for insulin is still working in spite of the development of peripheral insulin resistance marked by the associated hyperglycemia. In addition, the high blood glucose level may also induce satiety peripherally through either direct vagal stimulation or the release of insulin, incretin peptides (Glucagon

like peptide-1 and Glucose- dependent insulinotropic polypeptide), or both.[21]

The increased blood glucose level with HFD, beside its satiating effect, was converted to fat by *de novo* hepatic lipogenesis (insulin independent). Insulin resistance also initiates the characteristic triad of high triglyceride level, low HDL cholesterol level and high small dense LDL level caused by the increased release of free fatty acids from insulin-resistant fat cells. The increased flux of free fatty acids (FFA) into the liver in the presence of adequate glycogen stores promotes triglyceride production, which in turn stimulates the secretion of apolipoprotein B (ApoB) and VLDL cholesterol. These results agree with our result and other previous studies.[22,23] Additionally, the increase in the bioavailability of FFA could eventually increase lipid peroxidation [24] as expressed by the increased hepatic tissue levels of MDA.

The effect of sucrose diet on the body weight is still controversial. Some investigators reported an increase in body weight of rats consuming sucrose diet, in particular in liquid form,[25] others showed no change in total body weight when compared with control.[8] This study clearly demonstrated that HSD feeding was associated with a significant decrease in the final food intake which induced a marked progressive loss of weight as compared with CD and HFD groups. Now the question is "Which of the sucrose components, glucose or fructose, is responsible for its higher satiating effect and the body weight reduction?"

Sucrose consists of 50:50 glucose and fructose that undergo different metabolic pathways after its rapid digestion and absorption from the small intestine. The higher serum glucose response with the sucrose-rich diet can be explained by the large amount of available glucose from the higher sucrose of this diet with consequent increased insulin secretion and higher insulin resistance.[26] Both of them play an important role in the mechanisms that explain the higher satiating effect of HSD. Firstly, glucose acts peripherally as stated above. Secondly, insulin stimulates leptin release [27] as shown in our study, and both act centrally on satiety centers leading to more suppression of food intake.

On the other hand, the fructose portion of sucrose is rapidly and efficiently removed completely by first pass hepatic extraction. As a consequence, most fructose in portal blood is rapidly converted into triose-phosphate in hepatocytes. This leads to 1) a high consumption rate of hepatic ATP for the initial phosphorylation of fructose, which can lead, when fructose intake is high, to transient ATP depletion, formation of AMP and degradation of adenosine to uric acid; 2) an overflow of triose-phosphates, which are secondarily converted into glucose, glycogen, lactate, pyruvate and fatty acids. These particular substrates will promote the over-production of TG, as well as the development of dyslipidemic state and hepatic steatosis [28] as shown in our study and others.[29] At the same time, fructose inhibits hepatic lipid oxidation, thus favoring fatty acid reesterification and VLDL-triglyceride (TG) synthesis and decreases its clearance.[30]

From the above mentioned data, both components of sucrose were responsible for the higher satiating effect of HSD with the correlated decrease in the body weight by direct effect of

glucose and indirect effect of fructose by rising blood glucose level. In addition, oxidative degradation of both components with the alteration in the lipid composition also led to the production of free radicals elevating MDA level.[31] Consequently, the previous results of severe state of dyslipidemia and hyperglycemia of HSD feeding explained the more elevation of hepatic MDA level in HSD group as compared with HFD group.

In the present study, HTD showed less severe alterations of glucose and lipid metabolism due to delayed digestion and absorption of starch. This led to lowered increase of serum glucose and insulin levels as a consequence, less suppression of food intake, less dyslipidemic effect, and less elevation in the hepatic MDA level as observed in our study compared with other groups and in accordance with ***Koo et al.*** [32] ***and Chun et al.***[8] Furthermore, delayed digestion and absorption of starch allows it to be readily and efficiently oxidized with minimal storage,[33] so these features also help in the unexpected weight loss shown in our study. Additionally, the decrease in body weight with HTD may be due to the decrease in the final food intake compared with its initial value or the increase of the energy expenditure caused by the elevating serum level of leptin [27] as observed in our study.

In the present study and others,[34] it was found that the metabolic changes of HSD feeding were significantly increased as compared with metabolic changes induced by other diets. Hence, the next question is "Why did the dyslipidemic effect of HSD feeding become more severe than that of the other diets?" The reason was probably due to the large hepatic synthesis of triose phosphates by the fructose component of sucrose, the most potent lipogenic nutrient in our diet.[28]

The concept of metabolic zonation has been known for long. Although it is complicated to assess 'zone specific' metabolism, it is of importance to consider the concept when studying hepatic metabolism. Regarding glucose and fatty acid metabolism, periportal hepatocytes are more involved in gluconeogenesis and F.A oxidation, while pericentral hepatocytes are more engaged in glycolysis, lipogenesis, lipid peroxidation and oxidative stress.[35]

According to the concept of metabolic zonation, sucrose rich diet will primarily result in periportal zonation of microvesicular steatosis, since fructose is taken up mainly by periportal hepatocytes thenthe periportal accumulation of FFA metabolites may cause insulin resistance in these hepatocytes, while pericentral hepatocytes may take up less FFAs and therefore remain relatively insulin sensitive. This will explain selective accumulation of TGs in pericentral hepatocytes in HSD.[35] In addition, the histological picture of HSD showed necroinflammatory foci from enhanced lipid peroxidation and oxidative stress. These foci are known to occur at lower oxygen tensions and account for the predominant pericentral hepatocyte damage. These results are also in accordance with previous result of ***Mosrey et al.***[36]

On the other hand, the histological examination of HFD feeding showed disorganized hepatocytes with cytoplasmic vacuolations, severe micro and macrovesicular steatosisand inflammatory cell infiltrate affecting periportal and pericentral zones as reported by

Kumar et al. [20] This could be explained due to the zonal distribution of enzymes involved in glucose and fatty acid metabolism between periportal and pericentral hepatocytes. Histological examination of HTD feeding showed less severe steatosis but without signs of inflammation, which was more localized in the periportal zones as the oxidative stress caused more enzymes damage in the central zone so most of the effects of lipid accumulation appear in the periportal zone.

The histological finding of HFD and HTD are considered the first degree of steatohepatitis that is characterized by the accumulation of intrahepatic lipid due to the disrupting metabolic pathways and the increasing vulnerability to cell damage, while HSD feeding triggers the second degree of steatohepatitis that is caused by the increased oxidative stress which led to death of hepatocytes, inflammation and ultimately, fibrosis as reported by ***Schultz et al.*** [37]

In conclusion and according to our results, after 4-week administration, simple and complex carbohydrates significantly decreased the final body weight compared with HFD in spite of similar caloric value. Unexpectedly, the intake of HSD resulted in severe dyslipidemia, insulin resistance (IR), hepatic steatosis, excessive generation of reactive oxygen species (ROS), malfunctioning of the liver and depletion of the hepatocyte population more than HFD and HTD groups. Therefore, not only fat composition is important because its deleterious effect on glycemic and lipidic control, but also the type of carbohydrate is a determinant on the metabolic control; complex carbohydrates being less hazardous than simple ones. This should be considered in selecting macronutrients of a proper healthy diet regimen especially for obese or those with hepatic challenge. Future studies are required to study the effects of different diets with other influencing factors such as age, sex, genetic predisposition or physical activity.

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الملخص العربى

مقارنة الأثار الناتجةمن تناول وجبات غذائية عالية الدهون وعالية السكروز وعالية النشا على بعض جوانب التمثيل الغذائي للكربوهيدرات والدهون والحالة التأكسدية للكبد في ذكور الجرذان البيضاء

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الخلفيات والأهداف: اصبح من الراسخ بأن مكونات النظام الغذائي يمكن أن يكون لها تأثير مباشر على الوظائف الفسيولوجية العادية، فضلا عن الحالات المرضية مثل البدانة ، والسكري، وأمراض القلب والأوعية الدموية. لذلك، تم تصميم هذه الدراسة لمعرفة تأثير 4 أسابيع من برامج غذائية مختلفة على وزن الجسم، وكمية الطعام اليومية، ومستوى الدهون والجلوكوز في الدم والأنسولين والليبتينومع تقييم الحالة التأكسديةوالفحص المجهريللكبد . **الطرق:** حيث تم أجراء البحث على عدد أربعة وعشرين من ذكور الجرذان البيضاء قسموا الي أربعة مجموعات متساوية على النحو التالى: مجموعة ضابطة خضعت لوجبة غذائية طبيعية وثلاث مجموعات خصعوا لثلاث أنواع من الواجبات عالية الدهون، وعالية السكروز، وعالية النشويات مع مراعاة تساوي قيمة السعرات الحراريةالمكونة للوجبات الغذائية.**النتائج:** أظهرت نتائج الدراسة وجود أختلافات دالة أحصائيا فى أختلال أيض الدهون مع حدوث زيادة فى مستوىالليبتين، وسكر الدم، والأنسولين وأختلال فى نظام الأكسدة ومضادات الأكسدة وحدوث تغيرات نسيجية فى الكبد (تنكس دهني، وفجوات صغيرة وكبيرة، والخلايا الالتهابية ونخر بؤري في مناطق مختلفة). وحدثت أشد التغيرات مع المجموعة التى تناولت وجبة غذائية عالية السكروز وأدنى التغيرات كانت لدي المجموعة عالية النشويات. كما أحدثت الوجبة الغذائية عالية السكروز انخفاض ذات دالة احصائيا في الاستهلاك الغذائي اليومي النهائي، ووزن الجسم ومؤشر كتلة الجسم النهائي، في حين ان الوجبة الغذائية عالية الدهون أحدثت زيادة فى الاستهلاك الغذائي اليومي في البداية ثمانخفض فى نهاية الدراسة على الرغم من زيادة وزن الجسم ومؤشر كتلة الجسم النهائي. وأحدثت الوجبة الغذائية عالية النشويات انخفض في وزن الجسم ومؤشر كتلة الجسم النهائي على الرغم من زيادة تناول الطعام**الاستنتاج:** الأختيار الغير مناسب من مغذيات النظام الغذائي هو أكثر خطورة من السعرات الحرارية الزائدة خصيصا للبدناء أو الذين يعانون من تحديات الجهاز الكبديأو غيرها . فالنظام الغذائي عالي الدهون له آثار ضارة على عمليات الأيضوأيضا نوع الكربوهيدرات عامل حاسم فالكربوهيدرات المعقدة (النشا) ظهرات أقل خطورة من تلك البسيطة (السكروز).ولذلك توصى الدراسة بالأهتمام بمكونات الوجبة الغذائية بجانب المحتوى الحراري لها.

الكلمات الدالة:

وجبة غذائية عالية الدهون، وجبة غذائية عالية السكروز، وجبة غذائية عالية النشوياتأختلال أيض الدهون، تنكس دهني.