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DIETARY THERAPY SUPPORTS HOMEOSTATIC ROLE OF HEPATIC CELLS AGAINEST PATHOLOGIC DISEASES

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ABSTRACT

Special interests have been directed to the liver longevity either under the effect of cholesterolemia (HC) or aflatoxin (AF). Dietary rich protein antioxidant (RPAO) was evaluated in this concept. Thirty male albino aged rats of 300g±8 average weight have been fed on high fat diet, no contaminated and AF contaminated diets with or without RPAO. The RPAO intervention was biologically examined in terms of liver blood enzymes activity, lipoprotein level and organ tissues histopathology. Liver function has been elevated more times, especially with AF contamination more than with HC. Moreover, AF found to causes a lot of liver pathological disorders. Mycotoxins, in fact, generate a massive stream of oxidative stress that initiate liver carcinoma throughout several tissues deterioration much faster than HC. However, dietary intervention stigmatically reduces the liver toxification of oxidative stress either frequently predisposed by HC or AF. Seemingly, RPAO mechanism centered on prevention against excessive oxidative damage or/and at an up-regulation biological tool. This proper gene expression is a possible role function for RPAO food products. Although RPAO is rich in containing n–3 FAs, provitamin A (PVA), VC, VE and polyphenols, its biological perfect effectiveness concerning liver function should be tested under nutratargeting of nanotechnology concept. It suggests that the oxidant defense mechanisms in this antioxidant nutrients function are sometimes independent of one another despite fighting in different areas and are said to have maximum benefit when used in combination.

INTRODUCTION

Oxidative stress can be a causative agent for several pathologic and pathogenic diseases. Mycotoxins and cholesterolemia as well, generate a sort of oxidative stress that frequently initiates liver carcinoma. However, whole-body sterol (cholesterol and xenosterol) balance is delicately regulated by the gastrointestinal tract and liver. Liver controls sterol absorption and excretion in contribution to the cholesterol pool by whole-body cholesterol synthesis (*Kidambi and Patel 2008*). Beyond cholesterol, prevention and treatment, fatty liver and liver necroses are a major consequence in these cases.

Another liver main risk factor is micotoxins. According to the USDA scientific letters, aflatoxins are potent hepatotoxic and carcinogenic metabolites produced by the some fungi. Unfortunately, their metabolites interact hepatitis B virus. It causes a lot of liver pathological disorders (*Mahmoud, 2006*). In human cellular studies, *Di Maso, et al (2007)* stated that hepatic cells APE1/Ref-1 are normally localized in the nucleus and regulate the cellular response to oxidative stress. This subcellular localization and its correlation were investigated in 47 consecutive patients undergoing hepatocellular carcinoma (HCC) resection. APE1/Ref-1 expression was determined by immunohistochemistry in HCC and surrounding liver cirrhosis (SLC) and compared with normal liver tissue where cytoplasmic

expression of APE1/Ref-1 was significantly higher in HCC than in SLC. Patients with poorly differentiated HCC showed a cytoplasmic expression three times higher than those with well-differentiated HCC. It is associated with a lower degree of differentiation and a shorter survival time. However, one of considered liver anticarcinogenesis is Maharishi Amrit Kalash (MAK). It is a formulation composed of two herbal mixtures, MAK-4 and MAK-5. That herbs are said to have maximum benefit when used in combination and evaluated for cancer inhibiting effects both in vitro and in vivo. The results show that a MAK-supplemented diet inhibits liver carcinogenesis in urethane-treated mice. The prevention of excessive oxidative damage and the up-regulation of connexin expression are two of the possible effects of these products *(Factor, et al, 2000).* As a matter of fact, the previous experiments have shown that chronic activation of mitogenic signaling induced by over-expression of c-myc and transforming growth factor (TGF) in mouse liver induces a state of oxidative stress. Here, increased reactive oxygen species (ROS) generation might be responsible for the extensive chromosomal damage and acceleration of hepatocarcinogenesis characteristic for TGF? In this study vitamin E (VE), a potent free radical scavenging antioxidant, was able to protect liver tissue against oxidative stress and suppress tumorigenic potential of c-myc oncogene. Dietary supplementation with VE, starting from weaning, decreased ROS generation coincident with a marked inhibition of hepatocytes proliferation while increasing the chromosomal as well as mtDNA stability in the liver. Similarly, dietary VE reduced liver dysplasia and increased viability of hepatocytes. At 6 month of age, VE treatment decreased the incidence of adenomas by 65% and prevented malignant conversion. These results indicate that ROS generated by over-expression of c-myc and TGF in the liver are the primary carcinogenic agents in this animal model. Furthermore, the data demonstrated that dietary supplementation of VE can effectively inhibit liver cancer development *(Factor, et al, 2000)*. Some bean's properties as antimutagenic effects of their natural phenolic compounds, e.g., black beans (Phaseolus vulgaris L.) protective agent against DNA damage have mentioned *(Azevedo et al, 2003).* Another health aspect is assigned for beans due to the presence of special substances are isoflavounes that found in some beans and taking for prevention of cancer, cardiovascular diseases, gynecological problems and possible immune dysfunction. However, epidemiological studies, for instance, strongly suggest an inverse relationship between dietary selenium (Se), found in soy and sunflower, and cancer. Despite evidence linking Se deficiency to hepatocellular carcinoma and liver necrosis, the underlying mechanisms for Se cancer protection in the liver remain to be determined (*Stemm et al 2008*). Legume proteins are also good source for what so called bioactive proteins. *Stave (1999)* used the cell signaling detection technique as well as regulators of cell cycle as molecular targets in evaluating the new or modified proteins in novel foods derived from genetic modified food (GMO). This is used as prostate cancer prevention in some reasonable dietary agents. There are also a number of plant substances of great health aspects. Yet, greater role is manifested to antioxidants (AO), *Regina, et al (2003)* stated that dietary components may prevent mutation-related diseases in humans. This study has been designed to detect the biological and medical effect of consuming AO in rats. It is unknown whether diets with a high dietary total antioxidant capacity (TAC) can modify oxidative stress, low-grade inflammation, or liver dysfunction, all of which are risk factors

for type 2 diabetes and cardiovascular disease. This was studied in a crossover intervention, 33 healthy adults received the HT and LT diets for 2 wk each. Dietary TAC, α-tocopherol, and ascorbic acid were significantly higher during the HT diet. Plasma α-tocopherol rose during the HT and decreased during the LT diet without changes in markers of oxidative stress except plasma malondialdehyde, which decreased unexpectedly during the LT diet. Plasma high-sensitivity C-reactive protein, alanine aminotransferase, gamma-glutamyltranspeptidase, and alkaline phosphatase concentrations decreased during the HT compared with the LT diet. Selecting foods according to their TAC markedly affects antioxidant intake and modulates hepatic contribution to systemic inflammation without affecting traditional markers of antioxidant status *(Valtueña et al, 2008).*

Does dietary antioxidants formula, rich protein AO (RPAO), support liver homeostatic role against both cholesterolemia and some hepatic carcinoma? RPAO, in accordingly, has been biologically examined, as a unique mixture of protein AO supplement, in protecting liver against these pathological diseases.

MATERIALS AND METHODES

The antioxidant (AO) rich protein (RPAO) preparation is a modified soy protein process conducted by *Ahmed et al (1999),* meanwhile, the combination of these prepared food materials was done according to *Ahmed et al (2005).* This was employed in the biological evaluation against both cholesterolemia and aflatoxin in two distinct animal trails.

Animals: Thirty male western strains albino rats of 300-g ±10 average weight were individually housed in well-aerated cages at the Ophthalmology Research Institute, Giza Egypt. After two weeks of adaptation period and feeding on basal diet, rats were divided into five groups (5x6 grouped animals). The first group, called negative control (NC) was exactly the standard diet *(Bowman et al, (1990),* and salt and vitamins mixtures have followed that of *AOAC (1984)*. NC continued fed on basal diet along the rest 5 week of the experimental period. The second group, called positive cholesterol control (PCC), was as NC providing with 1% pure cholesterol. Similarly, groups 3 fed diet of group 2 + RPAO, the plant high protein and antioxidants semi modified food, at 10% level of the basal diet. The G4 is the basal diet contaminated with 0.01 mg aflatoxin/kg diet; meanwhile, G5 was similar to G4 +10% of RPAO. The amounts of aflatoxin were tested according to *Roberts and Patterson (1975).* The biological effect of these food formulations listed in Table 1 has been conducted. Blood samples were collected from rat eye plexuses by a fine heparinized capillary glass tubes. These samples were placed into a dry clean glass tube until blood samples were collected at room temperature for 60 min. The serum of the collected samples was separated by centrifugation and kept in a cool condition until the liver function was determined. At the end of biological experiment, rats were anesthesiated and liver was separated and kept for histological examination. Blood analytical techniques: in lipoproteins measurements, total cholesterol was determined according to the method of *Allain et al (1974).* Determination of high density lipoprotein (HDL) was carried out according to the methods described by *Havel et al (1955),*

meanwhile, low density lipoprotein (LDL) method was described by *Hatch and Lees (1968).*

Table 1: The experimental dietary system.

Group #	*Diet # and ؛*	*Description*
1	*1-NC*	*Negative Control (Casein Basal diet without Cho)*
2	*1-PC*	*Positive Control (Casein Basal diet + 1% Cho)*
3	*1-RPAO*	*Se and VE + 1% cholesterol + VC and carotene (RPAO)*
4	*2-PC*	*Positive Control (Casein Basal diet + 0.001% diet afatoxin)*
5	*2-RPAO*	*Se and VE 0.01% diet afatoxin + VC and carotene (RPAO)*

Where= RPAO is re-extrusion of 20% sunflower with soy extrudates + 30% extractable Parsley curly (p) low thermal processing W/V, Cho = cholesterol challenge.

The determination of liver function: ALP, GPT and GOT were determined according to the method described by *Reithman and Frankel (1957).*

Histopathological examination of liver: livers were collected and post-mortem examination was done as soon as possible. Fixation was performed in 10% of natural formalin, dehydrated, cleared, and ended paraffin then sectioned at (4-6 mm), stained with Harris hematoxylin and casein for histopathological examination *(Frankel and Reichman (1963).* Data has been calculated as the mean of six animal sample tests.

RESULTS AND DISCUSSION

Dietary therapy includes several nutrients and agent who should evaluated for health promotion. Among the factors influence LDL/HDL ratio is antioxidants (AO). Table 2 records this ratio under the effect of some natural AO. The LDL, which is the most crucial health factor and may correlated with liver expectancy and considered to be an integral response to its level in blood *(Colin et al, 2008)*, was 4 times more than that of normal (NC) with cholesterol challenge. This may due to a lack in total cholesterol distribution upon higher dietary level of fats and fortunately almost cured in presence of RPAO. However, whole-body sterol balance is delicately regulated by the gastrointestinal tract and liver assuming a supporting role for AO here or their or in both together. Liver, in particular, controls sterol absorption and excretion in contribution to the cholesterol pool by whole-body cholesterol synthesis.

Table 2: Effect of AO in diet as RPAO on some lipoprotein in aged rats.

Diet #	LDL	NC%	HDL	NC%	HDL/LDL	Rank #
1-NC	33.46	100.00	27.36	100.00	81.8	1
2-PC	184.85	544.11	46.75	168.00	25.5	6
3-RPAO	51.98	150.00	51.31	182.14	98.1	1

Mean of six measurements.

Enormous studies have been made to establish specific transporters mediate the entry and exit of sterols and how it regulates selective sterol access to the body pools

(*Kidambi and Patel 2008*). As seen, a greater health role is manifested to RPAO in preventing cholesrolemia. This role can be discussed in different ways: the presence of needed cured nutritional element, its level, form, shape, bioavailability or its powerful nutratargeting effectiveness. According to *Biesalski and Tinz (2008*), this sort of processed soy protein can play a role in some particular AO distributions.
However, enzyme diagnosis is frequently used in liver function assessment. In general, hypercholesterolemia strongly associate some of these enzymes elevation especially both GPT and GOT. Eventually, Table 3 shows also that RPOA intervention was similar to the biological role govern HDL/LDL ratio and its ranking number as mentioned before.

Table 3: Effect of RPAO on liver function in rats with cholesterolemia.

Diet #	*GPT U/L*	*% GPT*	*GOT U/L*	*% GOT*	*ALP U/L*	*% ALP*	*Ranking #*
1-NC	16.40	100	40.08	100	3.21	100	1
2-PC	55.40	338	121.40	303	5.39	168	7
3-RPAO	15.41	94	44.50	111	3.33	104	2

Mean of six measurements.

This liver tolerance stimulated by RPAO administration included a low GPT diffusion that may comparable to the NC could be specifically enhanced by soy protein in this formula. Actually, *Lin, et al. (2005)* found that rats fed on soy protein diets had lower GOT and GPT levels than rats fed on casein under high-cholesterol diets. However, USFA play a specific role *(Jacobson, 2008),* but protein might have a link with AO role respected among all other protective factors. In connection, 0.5% pinitol supplementation protected the rats from the hepatotoxicity induced by GalN. At least part of its effect being attributable to attenuation of the oxidative stress and inflammatory process promoted by GalN (*Zhou et al, 2008*).
As a fact, the ranking numbers that established in Table 4 for the histopathological examination of these livers is actually data quit similar to that of former Tables, assuming a sort of connection between the liver histopathology, its function and the real viability of a particular feeding element. These findings indicate that dietary cholesterol is a risk factor for the progression to hepatic inflammation (*Wouters et al, 2008*). In addition, medical substances in soy may, therefore, be hypocholesterolemic agent, but has no enough ability to protect hepatic cells. Taking this in concern, a 2.0 ppm Se diet reduced the mean focal volume, indicating a possible protective effect by inhibiting progression of preneoplastic lesions into larger foci. Cell proliferation was not inhibited by Se in the liver and associated reduction in glutathione peroxidase activity (*Stemm et al 2008*). It seems that the effectiveness of Se, or Se plus VE, alone is also not enough in case of hypercholesterolemia. Nevertheless, Se functions through selenoproteins and vitamin E reacts with oxidizing molecules in membranes, a single nutrient may not work alone.

Table4. Histopathological examination of liver under the cholesterol experimental condition.

Histopathological parameters	NC	PC	RPAO
hepatocellular vacuolations		+	
Dilatation of hepatic sinusoids associated with atrophy of some hepatocytes		+	
Histopathological parameters		2+	
Hepatocyte hydropic degeneration		+	
Atrophy of hepatocyte		3+	+
Focal hepatic necrosis		+	
Molecular cell infiltration		+	
Hepatocytes vacuolation		3+	
Vacuolar degeneration sinusoids		3+	
Ranking #	1	6	1

Mean of six measurements. 3 to 7 are the AOs used in this study, respectively.

A summary of TC and RPAO contradicted role on cholesterolemia is appeared in Table 5 that concluded the overall biological evaluation of RPAO intervention. RPOA contains more natural reactive carotenoides, VC, Se, VE and polyphenols. Although carotene food ingredient is promoting mechanisms of liver protection against oxidative stress (OS) induced by cholesterolemia, protection mechanisms seems to be is not a matter of nutrints amount but definitely a matter of nutrints forms and antagonism. A synergistic effect of this AO/protein combination has made its ranking number closest to NC.

Table5: The overall ranking # in biological evaluation of liver under the experiment condition.

Group	*Lipoproteins*	*Liver function*	*Liver histology*	*Matching rate*
NC	*1*	*1*	*1*	*3*
PC	*6*	*6*	*7*	*19*
RPAO	*1*	*2*	*2*	*5*

In this concern, vitamin C, for instance, fulfills both antioxidative functions and metabolic ones as it helps in the formation of collagen structures. Approximately 40% of the body's ascorbate is stored in skeletal muscle and relatively have abundant cellular concentration, i.e., tenfold higher than the plasma level (*Biesalski and Tinz 2008*). It is a matter of enhancing the efficiency of a particular body nutrient storage. Mycotoxins, on the other side, also generate a sort of oxidative stress that initiates liver carcinoma. Liver carcinogenesis can spotlight some more information to what released before. The biological evaluation of rats consumed contaminated food with or without RPAO is tabulated in Tables from 6 to 8. A greater reverse shift in the activity of liver enzymes gave the worst ranking number to contamination*. ***Bradfiled, et al, (1985)* **noticed similar effects of mouse hepatic xenobiotic-metabolizing enzymes when animal commonly consumed contaminated vegetables. However, along with the liver three enzymes, as seen in Table 6, the RPAO intervention was found to be an acceptable prevention agent in correcting the complication of contamination effect.**

Table 6: Aflatoxin contaminant food effect on liver diagnostic enzymes.

Group	ALP U/L		GOT U/L		GPT U/L		Ranking #
NC	3.21	100	40.08	100	16.40	100	1
Aflatoxin	7.81	244.5	88.22	219.9	63.96	390.1	3
AO intervention	5.47	171	45.07	112.4	25.76	157.1	1

Mean of 6 rats.

Similar rank number to that of liver function is obtained for liver histopathology. Table 7 showed severe reverse effect of treated liver comparing the control.

Table 7: Effect of feeding rats on aflatoxin contaminants and AO on liver histopathology.

Group	NC	AF	RPAO
Dilatation and congestion of hepatoportal	-	3+	-
Kupffer cells activation	-	3+	-
Hepatocytes necrosis	-	4+	+
Hepatocytes active nuclai	-	4+	+
Epithelial vasicular lining bile duct	-	+	-
Portal infiltration	-	+	-
Lucocytic cells	-	+	-
Hepatocytes cytomegaly nuclai	-	+	-
Hepatocytes karyomegaly nuclai	-	-	-
Congestion of central vein	-	-	-
Granular degeneration of hepatocytes	-	-	-
Vacuolar degeneration of hepatocytes	-	-	-
Ranking number	1	4	2

Aflatoxin in diet. Main of 6 rats

Table 8: The total ranking number used in biological evaluation for the *effect of aflatoxin and RPAO.*

Group	Liver function	liver histology	*Matching rate*
NC	1	1	*2*
Aflatoxin	3	4	*7*
RPAO	1	2	*3*

This pathological disorders included dilatation and congestion of hepatoportal vessels, kupffer cells activation, hepatocytes necrosis, hepatocytes active nuclei, epithelial vascular lining bile duct, portal infiltration, lucocytic cells and hepatocytes cytomegaly nuclei as well as hepatocytes karyomegaly nuclai, congestion of central vein, granular degeneration of hepatocytes and vacuolar degeneration of hepatocytes, meanwhile cholesterolemia reverse response on hepatic cell was hepatocellular vacuolations, dilatation of hepatic sinusoids associated with atrophy of some hepatocytes, hepatocyte hydropic degeneration, atrophy of hepatocyte, focal hepatic necrosis, molecular cell infiltration, hepatocytes vacuolation, vacuolar degeneration sinusoids, and vacuolar degeneration sinusoids. However change in preneoplastic response to aflatoxin B1 in rats fed green beans, beets or squash reflect a reverse nutritional and health effect. All three vegetable contaminated diets, as compared to the basal semi-purified diets, enhanced both aflatoxin-B1-induced emergencies of hepatic cell foci of hepatic-glutamyl

transpeptidase (*Boyd et al, 1983).* Moreover, complication such as dilatation and congestion of hepatoportal vessels, Kupffer cells activation, hepatocytes necrosis, hepatocytes active nuclei, epithelial vascular lining bile duct, portal infiltration, lucocytic cells and hepatocytes cytomegaly nuclei were occurred *(Mahmoud, 2006). Likewise cholesterolemia,* mycotoxins generate a tough stream of oxidative stress that primary enough, even much more than *cholesterolemia,* to initiate liver carcinoma. *Di Maso, et al (2007)* noticed that dietary vitamin E (VE) protect liver tissue against oxidative stress and suppress tumorigenic potential of c-myc oncogene*.* RPAO has two different sources for VE. In contrary to what proposed for beans, RPAO has been shown to strongly protect liver and tissues as performed for liver histopathology examination. A high rate of correlation between liver function and organ pathology is noticed as shown in Tables 6 and 7. This is summarized in Table 8. Yet, how far AO metabolically acts regarding the cholesterolemia and cancer? They may control specific enzymes, or moreover do some up regulatory role all related OS. In this regard, three wheat antioxidant fractions were investigated for their potential effects on oxygen diffusion-concentration products in liposomes prepared with egg yolk phosphatidylcholine. Wheat antioxidants significantly down-regulated the mRNA of HMG-CoA reductase, the key enzyme for cholesterol biosynthesis, and up-regulated the mRNA of cholesterol 7alpha-hydroxylase (CYP7A1), the key enzyme for cholesterol metabolism, in primary rat hepatocytes. These data indicated the potential of wheat antioxidants in reducing the risk of atherosclerosis through multimechanisms (*Cheng et al, 2008*).

Finally, the mutagenic or antimutagenic effects of some natural rich in containing medical substances or phenolic compounds or natural antioxidants is an effective sort of dietary therapy. Dietary therapy seems to have the potential of homeostatic role besides its positive effect on organ longevity if used for long enough. It suggests that the oxidant defense mechanisms in these antioxidant nutrients function are sometimes independent of one another despite fighting in different areas *(Burk et al. 2008). The present data might relay on VE needed a parallel VC and caroteniods supplementation to perform their action as AO system. It is a matter of dietary powerful to enhances the targeting of potential nutrient and medical elements to a level of prevention of excessive oxidative damage and the up-regulation of connexin expression are two of the possible effects of these products*; a result suggests that the expression of some gene may be directly regulated by some RPAO fragments or at the transcriptional level (*Lee et al, 2008).* A substantial requirement for the development of carriers, such as protein fragment proposed here, for nutritargeting as specific carriers, which allow the selected nutrients to bypass the main barriers encountered when, for example, circumventing the enterable route in the targeting process. This role will be studied more in subsequent investigation.

REFERANCES

Ahmed A I S; M A H Saleh and N T Saleh (1999) Chemical characteristic of processed soybean. Arab conf. Food Sci March (1999) Cairo 520-30.

Ahmed, A. I. S.; G M Habbib A. A. Hammad And F El-Deeb (2005). Effect of Natural Plant Protein Digest on Hyperlipemia And Hyperglycemia In Some Animal Models". Egy J Biomed Sci, 17, 85-94.

Allian, CC; Poon, LS.and Chan, CS (1974). Enzymatic determination of total serum cholesterol. Clin. Chem; 20:470-475.

AOAC (1984) American Official Methods of Analysis, 14th ed 1984.

Aoki, H et al (2002) Soy protein reduces oxidative stress in rats, J Nutr, 132, 2258-62.

Azevedo ،L; C Gomes, P.C. Stringheta, A.M.M.C. Gontijo, C.R. Padovani, L.R. Ribeiro and D.M.F. Salvadori (2003) Black bean (Phaseolus volgaris L.) as a protective agent against DNA damage in mice. Food and Chemicals Toxicology, Volume 41, Issue 12, 1671-1676.

Beraza N, Malato Y, Vander Borght S, Liedtke C, Wasmuth HE, Dreano M, de Vos R, Roskams T, Trautwein C. (2008) Pharmacological IKK2 inhibition blocks liver steatosis and initiation of non-alcoholic steatohepatitis. Gut. 2008 May;57(5):655-63. Comment in: Gut. 2008 May;57(5):570-2.

Biesalski H K, and Tinz J (2008). Nutritargeting. Adv Food Nutr Res. ; 54:179-217.

Bowman, TA; M Gonewardene and CE Taylor (1990) VA deficiency decrease NKC activity. J Nutr, 120,1264-73.

Boyd, J.N; N. Misslbeak and G.S. Stoewsand, (1983) Change in preneoplastic response to aflatoxin B1 in rats fed green beans, beets or squash. Food and Chemical Toxicology, 21, 1, 37-40.

Bradfiled, et al, (1985) Bradfiled, C.A.; Y. Chang and L.F. Bjeldanes (1985) Effects of commonly consumed vegetables on hepatic xenobiotic-metabolizing enzymes in the mouse. Food and Chemical Toxicology, Volume 23, Issue 10, 345-351.

Burk RF, Hill KE, Nakayama A, Mostert V, Levander XA, Motley AK, Johnson DA, Johnson JA, Freeman ML, Austin LM. (2008). Selenium deficiency activates mouse liver Nrf2-ARE but vitamin E deficiency does not. Free Radic Biol Med. 2008 Apr 15;44(8):1617-23. Epub 2008 Jan 31.

Cheng Z, Zhou H, Luther M, Yin JJ, Yu LColin S, Bourguignon E, Boullay AB, Tousaint JJ, Huet S, Caira F, Staels B, Lestavel S, Lobaccaro JM, Delerive P (2008). Intestine-specific regulation of PPAR{alpha} gene transcription by Liver X Receptors Endocrinology. 2008 Jun 19.

Colin S, Bourguignon E, Boullay AB, Tousaint JJ, Huet S, Caira F, Staels B, Lestavel S, Lobaccaro JM, Delerive P (2008). Intestine-specific regulation of PPAR {alpha} gene transcription by Liver X. Receptors Endocrinology. 2008.

Di Maso, V Claudio Avellini, Lory Saveria Croc, Natalia Rosso, Franco Quadrifoglio, Laura Cesaratto, Erika Codarin, Giorgio Bedogni, Carlo Alberto Beltrami, Gianluca Tell, and Claudio Tiribelli (2007) Subcellular Localization of APE1/Ref-1 in Human Hepatocellular Carcinoma: Possible Prognostic Significance. BMol Med. 2007 Jan?Feb; 13(1-2): 89–96.

Factor,VM; Danuta Laskowska, Michael Rugaard Jensen, Joseph T. Woitach, Nicholas C. Popescu, and Snorri S. Thorgeirsson. (2000) Vitamin E reduces chromosomal damage and inhibits hepatic tumor formation in a transgenic mouse model. Proc Natl Acad Sci U S A. 2000 February 29; 97(5): 2196–2201.

Frankel, S. and Reitman, S. (1963) Clinical laboratory methods" The c.v. Mosbye Company, 1102.USA.

Hatch, F.T. and Lees, R.S. (1968) Practical methods for plasma lipoprotein analysis Adv. Lipid Res., 6:1- 68.

Havel, RJ; Eder, H.A. and Bragdon, J.H.(1955)The distribution and chemical composition of ultracentrifugally separated lipoproteins in human serum" J. Clin. Invest. 34 : 1345-1353.

Ibrahim, EM & AIS Ahmed (1990). Economical nonpolluting yeast production. Ag. Res. Rev. 68 (2) 379-87.
Kidambi S, Patel SB (2008). Cholesterol and non-cholesterol sterol transporters. Xenobiotica. 2008 Jul;38(7):1119-39.

Lin C Y; Tsai C Y. and Lin SH. (2005). Effects of soy components on blood and liver lipids in rats fed high-cholesterol diets. World J. Gastroenterol. ; 11(35):5549-52 (ISSN: 1007-9327).

Mahmoud, Neven M M (2006). biological evaluation for specific fungal aflatoxin contamination in some beans of rat's diet. Bul. High Inst. Pub. Health, 30, 3, 691-700.

Regina, R L and Daisy Maria Favero Salvadori (2003). Dietary components may prevent mutation-related diseases in humans. Mutation Research/Reviews in mutation Rasearch, Volume 544, Issues 2-3, Novamber 2003, pages 195-201

Reithman, S. And Frankel, S.(1957) A colormetric method for the determination of serum glutamic oxalacetic and glutamic pyrovic transaminase" Am. J. Clin. Path. 28,56.

Reitman, S. and Frankel S. (1954). Determination of glutamate pyruvate transferase. Am. J. Clin. Path., 28(7).56

Roberts, B.A. and Patterson D.S. (1975). Detection of twelve mycotoxins in mixed animal fecel stuffs using a movel membrane clean up. J.A.ssoc of Anal. Chem., 58:1178-1.

Stave, J W (1999) Detection of new or modified proteins in novel foods derived from GMO – future needs. Food Control, volume 10, Issue 6, December 1999, Pages 367-374.

Stemm DN, Tharappel JC, Lehmler HJ, Srinivasan C, Morris JS, Spate VL, Robertson LW, Spear BT, Glauert HP.(2008). Effect of dietary selenium on the promotion of hepatocarcinogenesis by 3,3', 4,4'-tetrachlorobiphenyl and 2,2', 4,4', 5,5'-hexachlorobiphenyl. Exp Biol Med. ;233(3):366-76.

Valtueña, V; Nicoletta Pellegrini, Laura Franzini, Marta A Bianchi, Diego Ardigò, Daniele Del Rio, PierMarco Piatti, Francesca Scazzina, Ivana Zavaroni and Furio Brighenti (2008). Food selection based on total antioxidant capacity can modify antioxidant intake, systemic inflammation, and liver function without altering markers of oxidative stress. American Journal of Clinical Nutrition, Vol. 87, No. 5, 1290-1297,

Jacobson, T A, 2008. Role of n–3 fatty acids in the treatment of hypertriglyceridemia and cardiovascular disease. American Journal of Clinical Nutrition, Vol. 87, No. 6, 1981S-1990S,

Wouters K, van Gorp PJ, Bieghs V, Gijbels MJ, Duimel H, Lütjohann D, Kerksiek A, van Kruchten R, Maeda N, Staels B, van Bilsen M, Shiri-Sverdlov R, Hofker MH (2008). Dietary cholesterol, rather than liver steatosis, leads to hepatic inflammation in hyperlipidemic mouse models of nonalcoholic steatohepatitis. Hepatology. 2008 Aug;48(2):474-86.

Yu, SY; WG Li and YJ Zhu (1989). Chemoprevention of human hepatitis with Se. Biol Trace Element Res. 20,15-20.

Zhou Y, Park CM, Cho CW, Song YS (2008). Effects of wheat antioxidants on oxygen diffusion-concentration products in liposomes and mRNA levels of HMG-CoA reductase and cholesterol 7alpha-hydroxylase in primary rat hepatocytes. J Agric Food Chem. 2008 Jul 9;56 (13):5033-42.

الملخص العربي

دور مضادات الاكسدة في الغذاء فى ثبات التوازن البيولوجي و حماية خلايا الكبد من مضاعفات ارتفاع كوليسترول الدم و بعض انواع السرطان فى الفئران

فضل السيد الديب* وسيد احمد فرحات و امل عبد الباقي و مها محمود

قسم الأغذية الخاصة والتغذية – معهد بحوث تكنولوجيا الأغذية- مركز البحوث الزراعية بالجيزة و*كلية التربية النوعية جامعة المنصورة.

هل لمضادات الاكسدةالمصنعة بطرق تكنولوجبة خاصة كغذاء مكمل دور فى حماية خلايا الكبد من مضاعفات ارتفاع كوليسترول الدم و بعض انواع السرطان ؟
تم دراسة هذة العلاقة فى الفئران عن طريق اضافة مضادات الاكسدة الطبيعية فى غذاء ذو تراكيب بروتينية خاصة للفئران لفترة كافية و متابعة بعض مكونات الدم و الكشف المجهري علي خلايا الاكبد. ومن الواضح ان الغذاء ومشتقاتة ذات الدور البيلوجي تلعب دورا هاما فى ضبط التوازن الهرمونى وان للاخير دورا هاما فى ضبط ليبيدات الدم و التوازن البيولوجي ومن ثمة الحفاظ علي صحة الاعضاء الهامة بالجسم. وترتكز اهمية هذا البحث فى الاشارة الى الادوار المتميزة لبعض مضاضات الاكسدة مع اهمية وجود العناصر الاخرى كا لبروتين للوصول الى التأثير البيولوجى الامثل على كوليسترول الدم و من ثمة الامراض الباثولوجية الاخرى مما يترتب علية علي وجة الخصوص من امراض الكبد. ومن الملاحظ ان اضافة مستخلص البقدونس الي التوليفة الغذائية من البروتين النباتي الخاص زاد من تأثيرها البيولوجي حيث يتميز الاخير علي ما يبدو بدورة في وصول تلك المغذيات الي الانسجة ذات الشأن. وقد يفسر ذلك الدور بالخاصية الايجابية للبروتين في تأثيرة علي مضاعفة دور مضادات الاكسدة وارتبط هذا الدور الغذائي المضاد للاختلال التأكسدى و التغيرات الميتابوليزمية التى ارتبطت بصحة انسجة الكبد كأرتفاع نسبة الليبوبروتين عالي الكثافة و انخفاض انزيمات الكبد. ان العلاقة الواضحة و الظاهرة خلال التقييم البيولوجى لفعل بعص السموم مثل التلوث بالافلاتوكسين فى غذاء الفئران تتشابة مع ما ثبت فى هذا من ارتباط صحة الكبد بخلل ليبوبروتينات الدم وان اختلف عن كثافة التغيير الحادث للكبد فيما يخص المسح الهيستولوجى الناتج من لتلوث الغذائي بالافلاتوكسين و المحدث لتغييرات دراماتكية لانزيمات الكبد بالاضافة الى تلك التغييرات المحسوسة فى الفحص الهستولوجى من التأثير الجائر علي الكبد. ومن النتائج المبشرة تحسن كل المظاهر البيولوجية و المرضية التى تولدت من تلوث الغذاء بالافلاتوكسين حتى مع استمرار وجودة فى الغذاء عند توافر بعص مضدات الاكسدة بالتركيبة سابقة الذكر حيث ظهر هذا جليا فى حماية كبد الفئران. و على ضوْ المفاهيم الخاصة بالنانو تكنولوجي فأن هذا التحسن الهوميوستازى السريع يؤكد طبيعة عمل هذه المشتقات على إعادة التوازن الهرموني إلى مستويات تنظيم بيولوجيه أعلي فى التأثير الإيجابي علي الكبد في مقاومة الشوارد الحرة ايا كن مصدرها.