

Structural and laboratory changes in the liver of female albino rats in cases of experimental high fat diet and curative role of some medicinal plants.

Ezz-Eldin E. Abdalla, Gamal S. Elgharabawi and Moustafa E. Elsayy
Histology Departments, Faculty of Medicine (Domiatta and Cairo)
Al-Azhar University

Abstract

High fat diets as well as hyperlipidemia represent an important clinical and social problem. It is referred to increased concentration of lipids (Triglycerides, Cholesterol and Fatty acids) in the blood. Such increase may lead to metabolic risks affecting blood vessels and paranchymatous organ mainly the liver.

Material and methods: Forty five adult female albino rats were used and divided into 9 equal groups. The **first group** was considered as a control group. The **second group** was of high fat diet (25% fat and 2% cholesterol) for 3 weeks. **Groups 3,4 and 5** were similar to the second group but received three medicinal plants respectively Oat ,Fennel and Triphala. The **sixth group** was also of high fat diet but for 6 weeks. **Groups 7, 8 and 9** were treated with same medicinal plants as groups 3, 4 and 5.

Two main parameters were performed; the first was microscopic study of the liver tissue while the second was laboratory evaluation of liver functions.

Results: The hepatic tissue greatly affected by the induction of high fat diet in the form of variable grades of fatty infiltration and vascular congestion either after 3 or 6 weeks of induction. Fibrous content and PAS +ve material were also affected. Structural changes were confirmed by laboratory data.

Conclusions: Medicinal plants and regulation of diet quality plays a good role in limiting the risk of fatty liver and atherosclerosis.

Keywords: High fat diet, Medicinal plants, Albino rat, Structural and Laboratory findings.

Introduction

High fat diet and hyperlipidemia represent an important social and clinical problem. This is referred to increased concentration of lipids (Triglycerides, Cholesterol or both) in blood. Such increase may lead to serious metabolic disorder as diabetes mellitus **Mori et al 2010**. Increased lipid level in the blood may be of genetic factor **Hansen et al 2009**. **Reihner et al 1990** and **Haines 2001**, Stated three forms of lipids , the first one was fatty acids which is simple lipids , the second form was sterols mainly cholesterol which may be of external source as from material syntheses in liver and other tissues .

Cholesterol plays an important role in the control of metabolic pathways such as bile acids metabolisms and steroid hormones and vitamins syntheses, finally the third form of lipid is triglycerides which represent the main source of energy in most mammalian.

Bernard 2008, reported that the primary lipid abnormality is hyperlipidemia which may lead to the initiation and progression of atherosclerotic syndrome **Harrison et al., 2003**.

Many medicinal plants can be used as hyperlipidemic lowering agents in Egypt as Oat, Fennel and Triphala.

Oat (*Avena sativa*), contain high concentration of proteins, lipids, vitamins,

antioxidants and minerals **Panfili et al., 2003.**

Fennel (*Foeniculum vulgare*), has an antioxidant activity and has lipid lowering effect. **Liu et al., 2004.**

Triphala (*Terminalia chebula*, *Terminalia bellerica* and *Embolica officinalis*) have capacity to reduce blood lipid and inhibit hepatic cholesterol biosyntheses and increasing local bile acid excretion. **Khanna et al., 1996.**

Fatty liver, also known as hepatic steatosis or nonalcoholic steatohepatitis (NASH), which is characterized by the accumulation of fat droplets within the cytoplasm of hepatocytes **Pessayre et al., 2001.**

Two essentially different metabolic processes can underlie the development of fatty liver. First, hepatic triglycerides (TGs) may accumulate because of an inadequate capacity of the liver to secrete TGs in VLDL. This has been reported in human subjects with hypobetalipoproteinemia **Schonfeld et al., 2003.** Second, TG synthesis in the liver may be accelerated to such an extent that mechanisms for fat oxidation and secretion are no longer sufficient to prevent intrahepatic TG accumulation. In this latter case, fatty liver can be associated with increased rates of VLDL secretion **Den et al., 2004.**

An example is fatty liver in human subjects with familial combined hyperlipidemia (FCHL) **Den et al., 2004,** as well as type 2 diabetes mellitus and the metabolic syndrome **Lewis et al., 2002.**

Fatty liver is a benign condition, but it can potentially progress into NASH, with the risk of progression into end-stage liver disease, i.e., cirrhosis or hepatocellular carcinoma **Caldwell et al., 1999** and **Lee 1989.**

The only way to confirm the diagnosis of fatty liver disease with certainty and to assess its severity is by liver histology. Autopsy results and hepatic histology from living-related liver donors consistently show the prevalence of significant steatosis is 20-40%.

Liver biopsy finding of macrovesicular fat (single large vacuole) in the cytoplasm of hepatocytes displacing the nucleus peripherally is the hallmark of hepatic steatosis caused by alcohol, diabetes, and obesity .

Lee 1995 In contradistinction, microvesicular steatosis is characterized by multiple small fatty inclusion bodies with a predominantly central nucleus and is associated with abnormalities of mitochondrial fatty acid oxidation, such as in acute fatty liver of pregnancy and Reye's syndrome. **Burt et al ,1998.**

In nonalcoholic steatohepatitis, additional histological features are seen, including Mallory's bodies, cytoplasmic balloon degeneration, perisinusoidal (zone III) fibrosis, and neutrophilic infiltrate **Lee 1995.**

However, many atypical findings may be found, such as the presence of lymphocytic infiltration and periportal fibrosis. It is not clear if these are different clinical entities that have been grouped as nonalcoholic steatohepatitis. The histological appearance of nonalcoholic steatohepatitis is identical to that of alcoholic liver disease, and the distinction between the two conditions has traditionally been made on the basis of the amount of alcohol intake **Lee 1995.**

Material and Methods

In this study 45 adult female albino rats (*Rattus Albinus*) were used and divided into 9 equal experimental groups each of 5 rats. The rats used weighting 150gm.

The first group was considered as a control group.

The second group was subjected to induction of high fat diet by administration of 25% fat and 2% cholesterol for 3 weeks. Rats received no doses of medicinal plants.

The next 3 groups (Third, Fourth and fifth groups) were treated by Oat, Fennel and Triphala respectively

The sixth group was of high fat diet by administration of 25% fat and 2% cholesterol for 6 weeks. Rats received no

doses of medicinal plants.

The next 3 groups (Seventh, Eighth and Ninth groups) were treated by Oat, Fennel and Triphala respectively.

Medicinal plants used and their dosage: **Oat (*Avena sativa*)** was added to diet in a dose of (200gm/ kg). **Fennel (*Foeniculum vulgare*)** was added to diet in a dose of (10mg /100gm B.Wt). **Triphala (*Terminalia chebula*)** was added to diet in a dose of (25mg /100gm B.Wt).

All of the estimated doses were taken to rats by oral way.

Parameters of the study:

A) Microscopic study: Liver sections from each group were prepared and stained by Hx & E , Mallory trichrome stain and Periodic acid & Schiff stain **Drury and Wallington ,1980 and Pearse ,1977.**

B) Laboratory tests: Collection of rat `s serum was taken for estimating the following parameters:

- 1- AST activity (Aspartate transaminase).
- 2- ALT (Alanine transaminase).
- 3- GGT (Glutamyl transferase).
- 4- Serum total hepatic lipids.

C) Statistically evaluation:

The Obtained results were statistically evaluated and analyzed using SPSS system.

Results

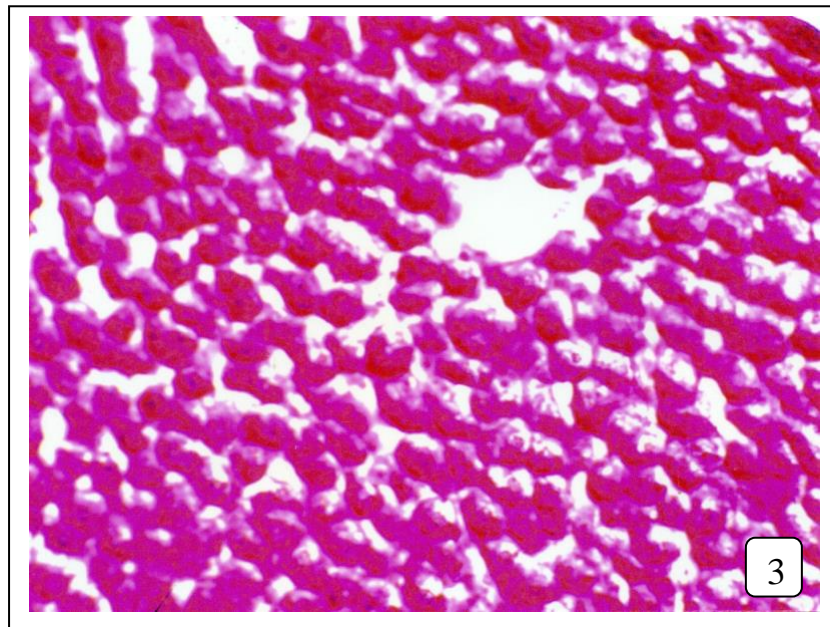
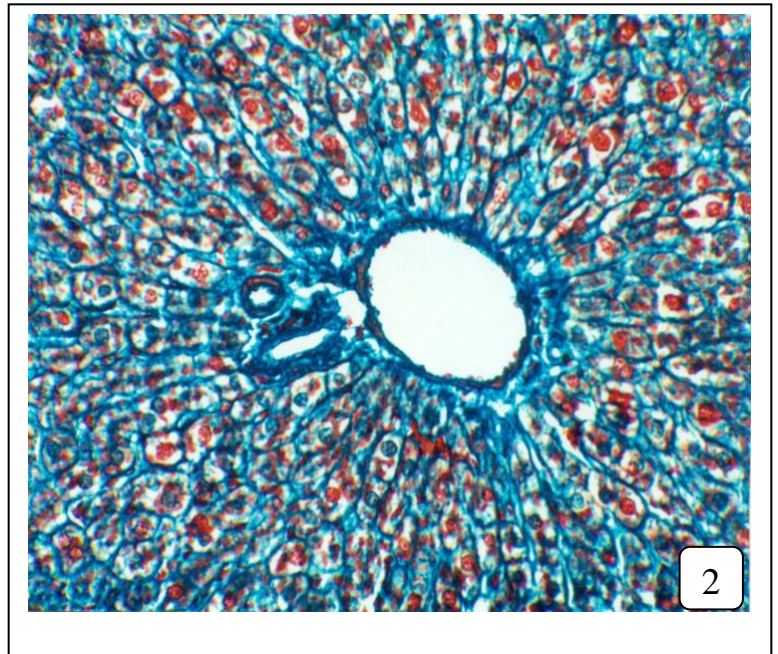
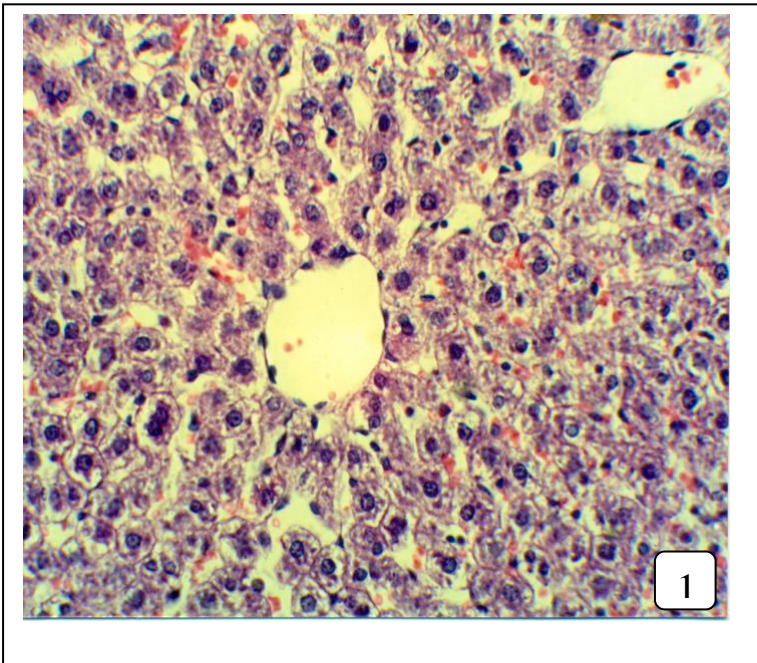
A) Microscopic changes:

I- Control liver (Figs 1,2,3):

Section in control liver stained by Hx& E stain shows normal hepatocytes arranged in radiating cords from the central vein to the periphery of the hepatic lobule. The cords are separated by hepatic sinusoids. Hepatocytes contain single sometimes double nuclei in the cell center .Region of portal tract shows the normal tract contents of hepatic artery, portal vein and bile duct.

The distribution of collagenous bundles were demonstrated in (fig 2) by Mallory stain technique, fine bundle collection seen surrounding the central vein and around hepatic cell cords, fibers are seen more dense at the region of portal tract.

Hepatic cellular content of Mucopolysacharride were seen after PAS stain .It was seen filling the hepatocytes cytoplasm as acidophilic dense granules (fig 3).



(Fig 1) Photomicrograph of control liver showing normal cellular arrangement
(Hx. & E stain x200)

(Fig 2) Photomicrograph of control liver showing normal distribution of collagen fibers
(Mallory trichrome stain x200)

(Fig 3) Photomicrograph of control liver showing normal content of PAS +ve material
(PAS stain x200)

II- Changes in hyperlipidemic group for 3 weeks (central & treated):

(Figs 5,6,7,8)

Induction of hyperlipidemia by high fat diet for 3 weeks greatly affected hepatic structure in the form of marked fatty infiltration as multiple fat droplets of variable sizes. Hepatic nuclei were shifted to the periphery of the cells .Fatty changes was of multivesicular hepatic changes (fig 4)

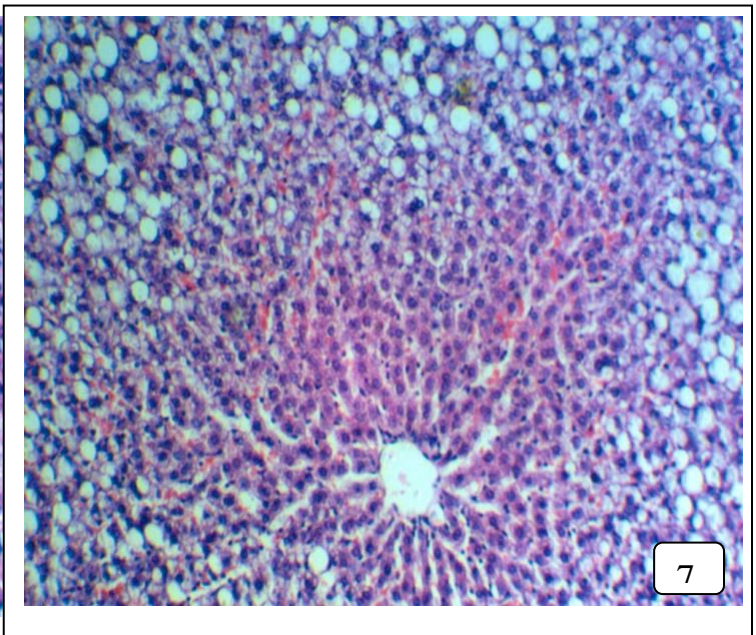
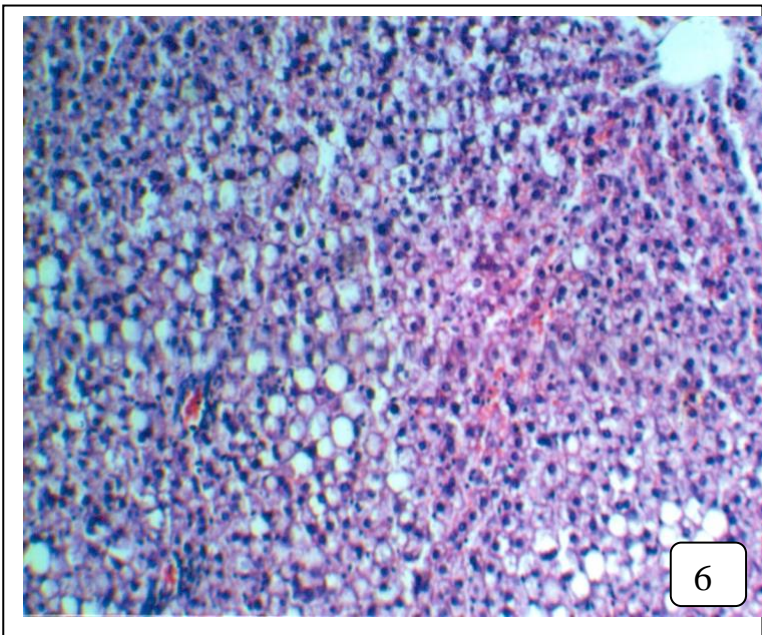
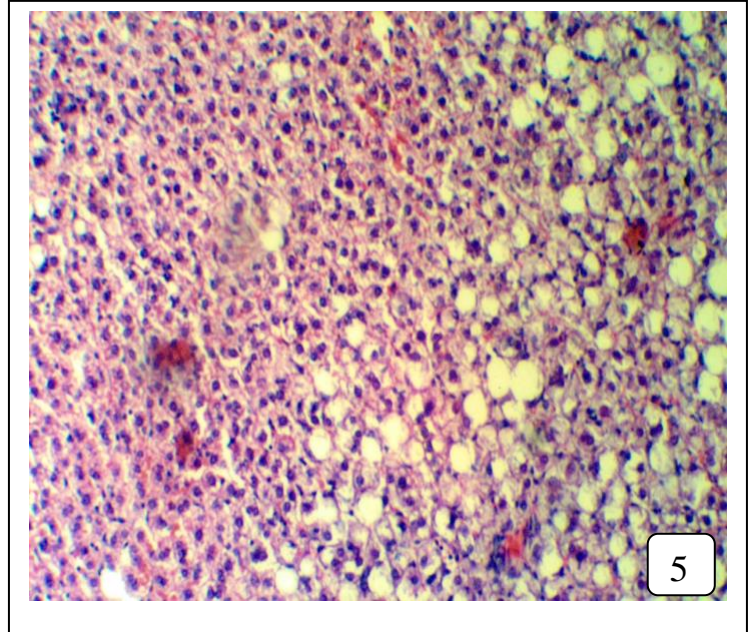
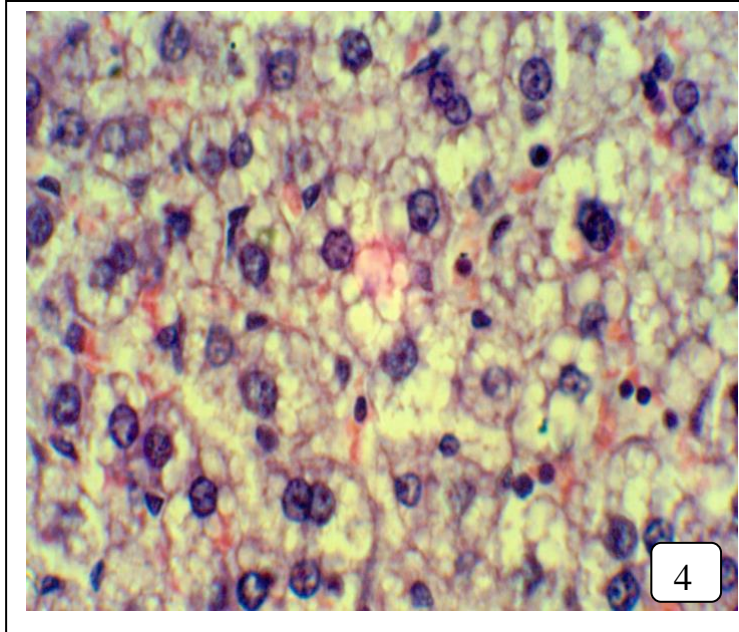
The role of medication by medicinal plants used in this study was variable from one plant to other. The value of Oat (fig 5) was moderate but fatty infiltration was of macrovesicular infiltration and good areas of hepatic cells were observed to be normal.

Medication by Fennel (fig 6) shows better changes than Oat. The numbers of affected hepatic cells were little in comparison to the control. The fatty infiltration was of macrovesicular type.

The role of Triphala (fig 7) was more in central hepatic lobule as fatty infiltration at in the periphery of the lobule, infiltration was of macrovesicular type.

Changes in the distributions of collagenous fibers in the different groups after induction of hyperlipidemia shows marked reduction in the collagen content in both control hyperlipidemic group and in different types of medicinal plants (fig 8, 9, 10, 11)

Mucopolysacharride contents in cases of control hyperlipidemia (fig 12) moderately decreased in the hepatocytes. Cases treated with the three used medicinal plants showed mild restoration of it `s contents especially cases treated by Fennel and Triphala (fig 13, 14, 15)

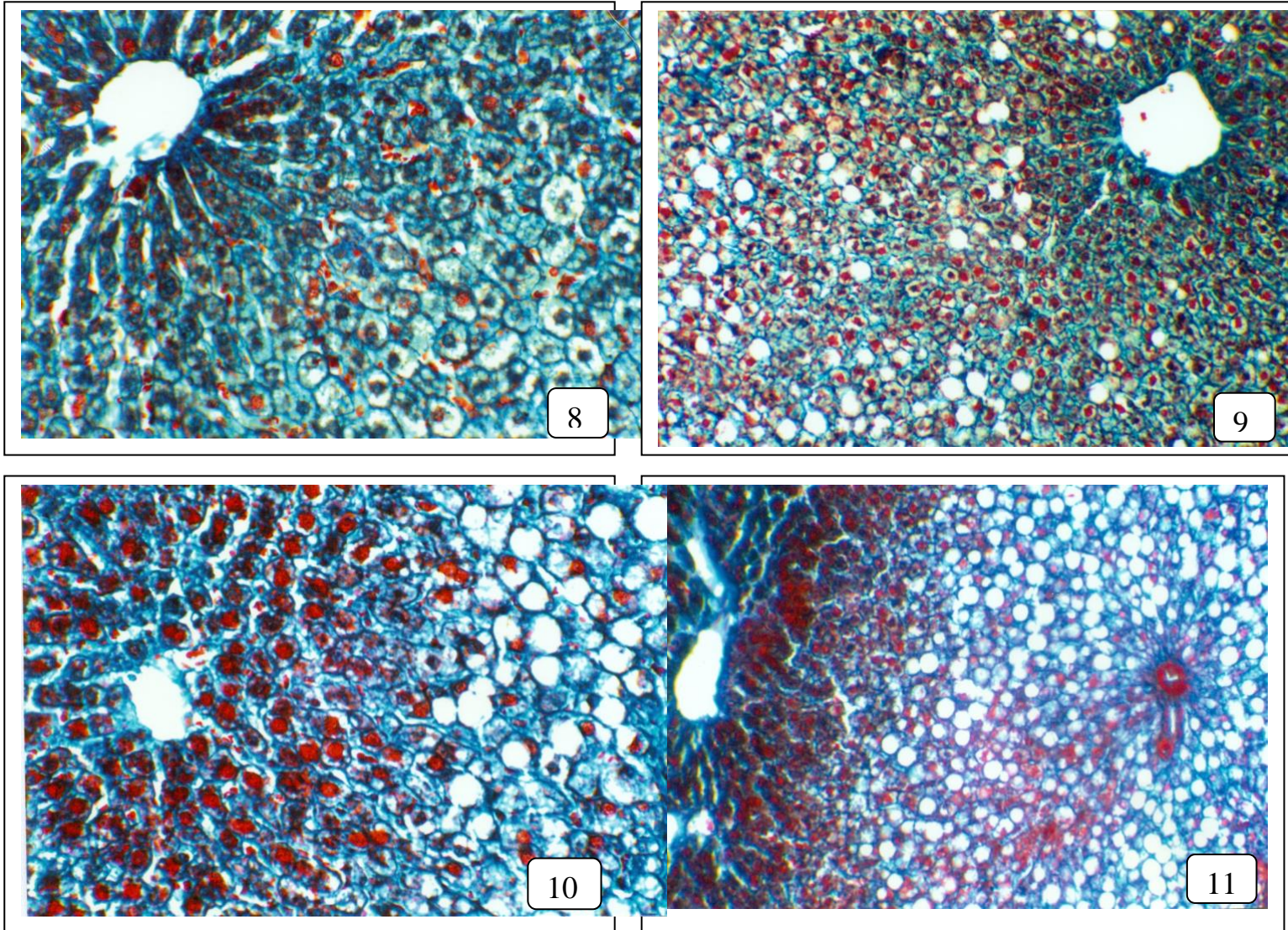


(Fig 4) Photomicrograph of hyperlipidemia for 3 weeks showing multivesicular fatty changes (Hx. & E stain x300)

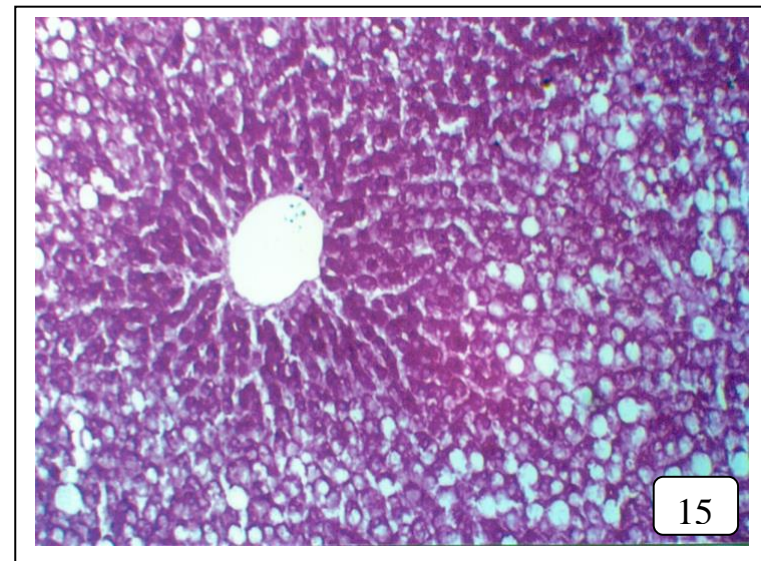
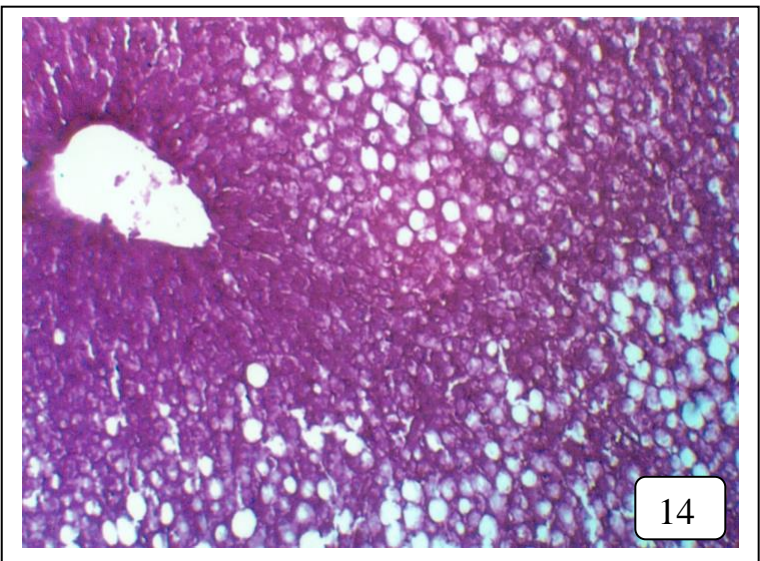
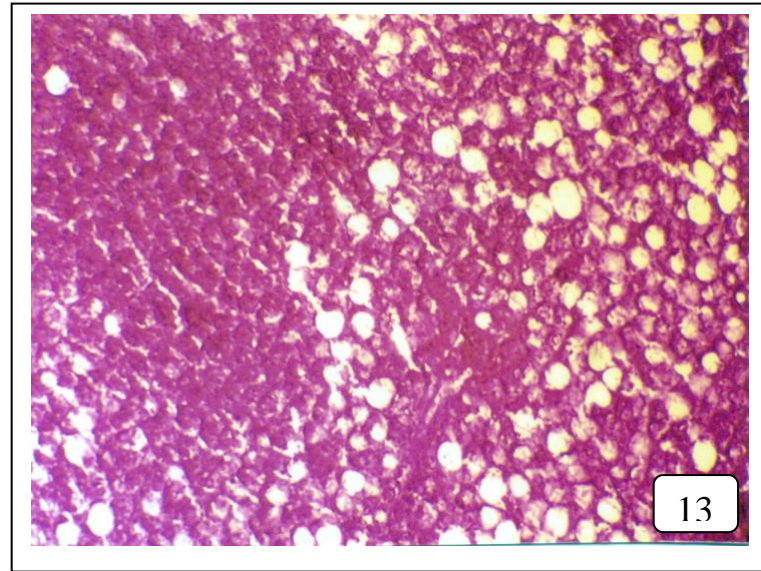
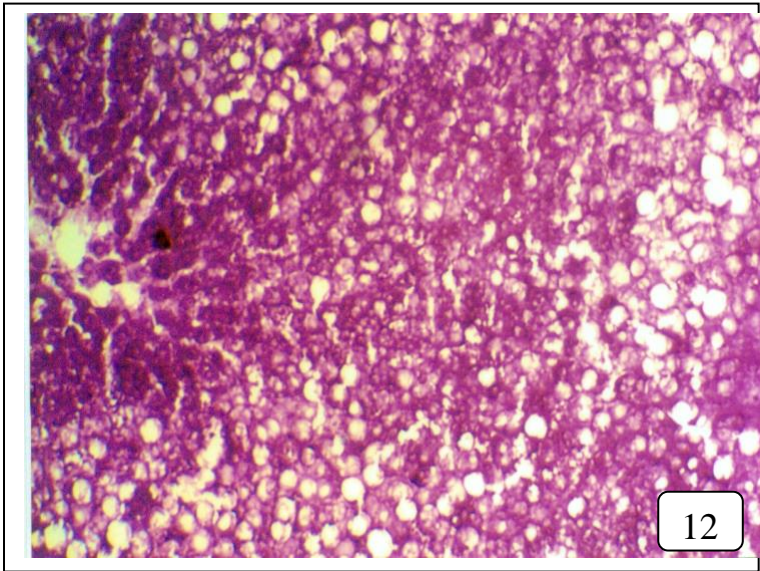
(Fig 5) Photomicrograph of hyperlipidemic rats treated by Oat for showing macrovesicular fatty changes and gradual appearance of healthy hepatic cells (Hx. & E stain x200)

(Fig 6) Photomicrograph of hyperlipidemic rats treated by Fennel for showing more areas of healthy hepatocytes with macrovesicular changes (Hx. & E stain x200)

(Fig 7) Photomicrograph of hyperlipidemic rats treated by Triphala showing more healthy cells with macrovesicular changes (Hx. & E stain x200)



(Fig 8) Photomicrograph of hyperlipidemia for 3 weeks showing decreased collagen fiber distributions (Mallory trichrome stain x200)
(Fig 9) Photomicrograph of hyperlipidemia for 3 weeks treated by Oat, decreased collagen content is noticed (Mallory trichrome stain x200)
(Fig 10) Photomicrograph of hyperlipidemia for 3 weeks treated by Fennel, decreased collagen content is noticed (Mallory trichrome stain x200)
(Fig 11) Photomicrograph of hyperlipidemia for 3 weeks treated by Triphala, decreased collagen content is noticed (Mallory trichrome stain x200)



(Fig 12) Photomicrograph of hyperlipidemia for 3 weeks showing decreased of PAS +ve content in hepatocytes (PAS stain x200)

(Fig 13) Photomicrograph of hyperlipidemia groups treated by Oat showing no changes of PAS positive content in comparison by control group (PAS stain x200)

(Fig 14) Photomicrograph of hyperlipidemia groups treated by Fennel shows mild restoration of PAS +ve content (PAS stain x200)

(Fig 15) Photomicrograph of hyperlipidemia groups treated by Triphala shows mild restoration of PAS +ve content (PAS stain x200)

III- Changes in hyperlipidemic groups for 6 weeks (control and treated)

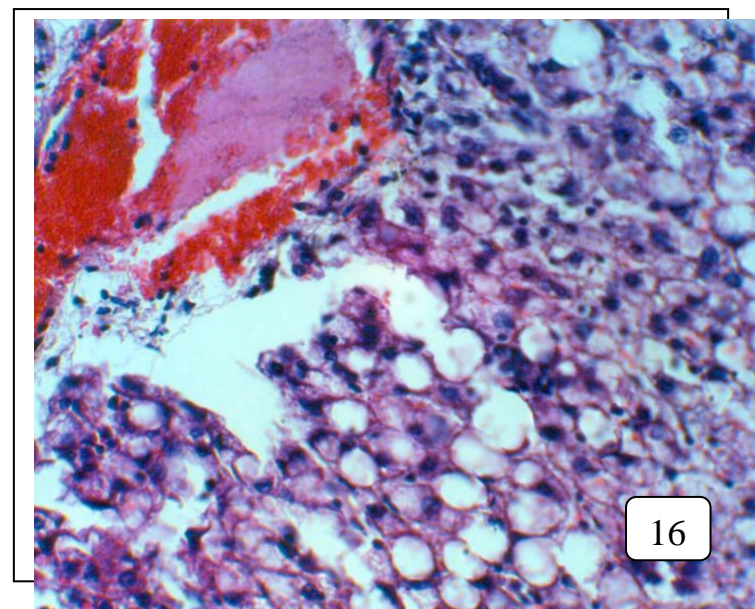
Induction of hyperlipidemia for 6 weeks greatly affect the hepatic structure (fig 16) the main changes were in the form of macrovesicular fatty changes inside the hepatocytes. Vascular dilatation and congestion were also noticed beside marked cellular infiltration.

The use of medicinal plants were of variable effects. Oat (fig 17) shows good regenerative effect on hepatic structure. Both Fennel and Triphala (fig 18, 19) shows mild regenerative effect on hepatic structure

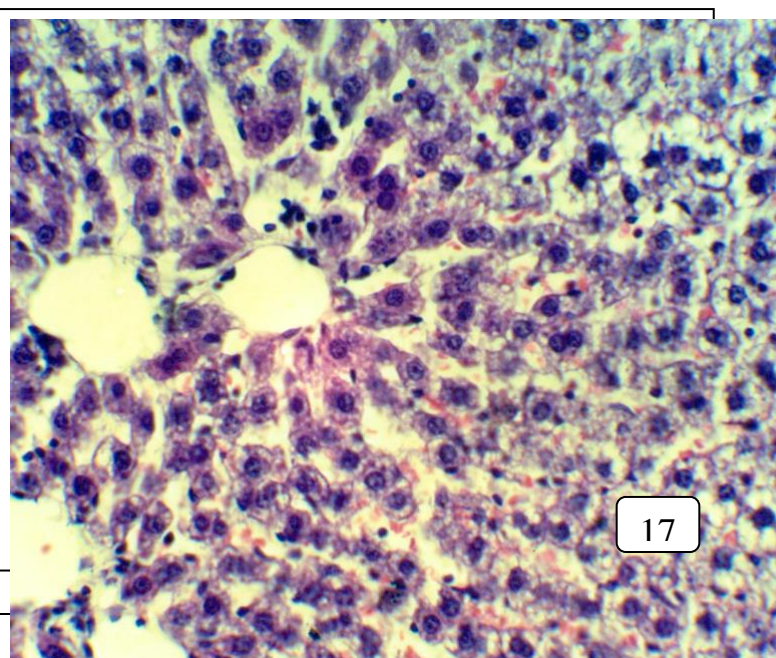
Hyperlipidemia for 6 weeks greatly reduced the fibrous collagen in the liver (fig 20) The use of medicinal plants were of variable effects. Oat (fig 21) shows good restoration of fibrous elements. While both Fennel and Triphala (fig 22, 23) shows mild restoration of fibrous elements of collageous fibers in liver sections

Induction of hyperlipidemia for 6 weeks doesn't induce any changes in the content of PAS +ve material in the liver tissue (fig 24)

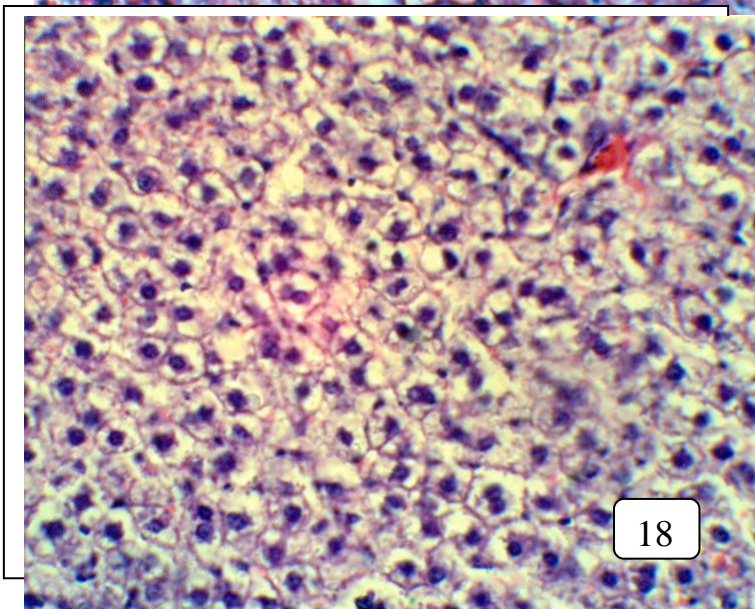
After use of medicinal plants Oat (fig 25), Fennel (26) and Triphala (27) shows no changes.



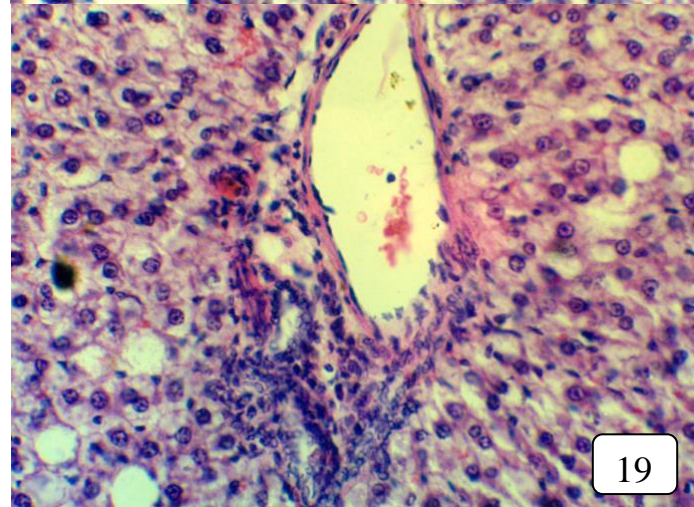
16



17

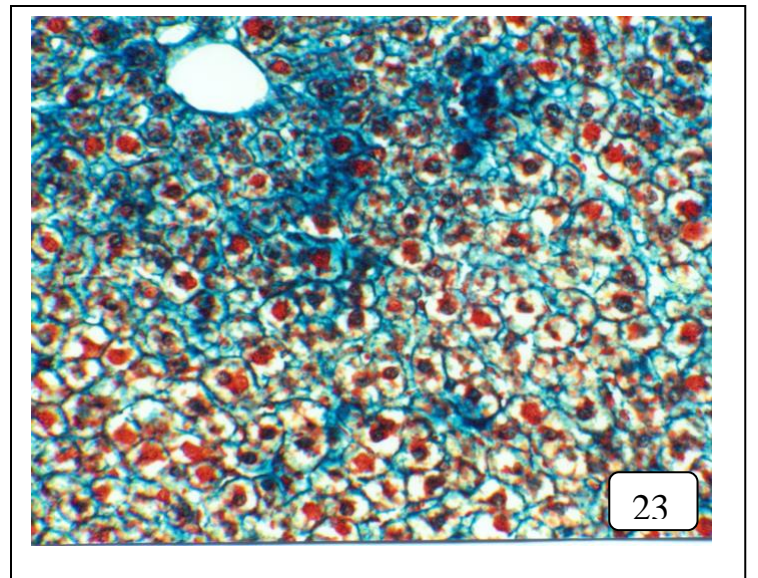
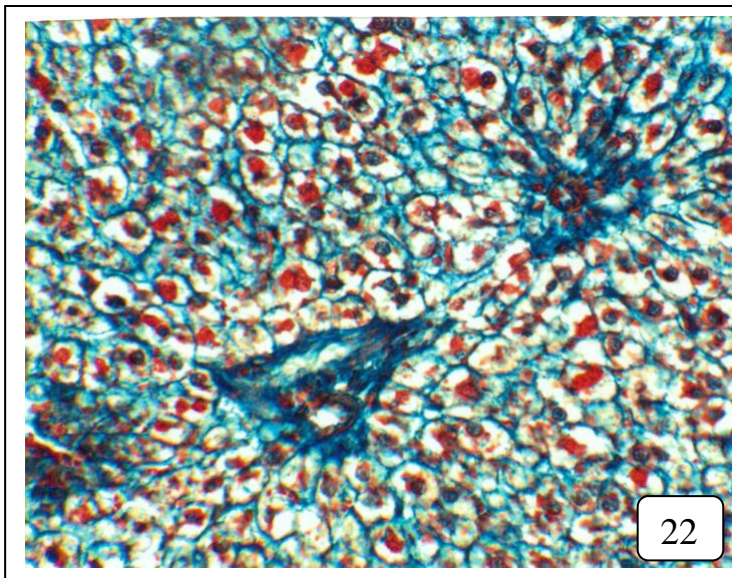
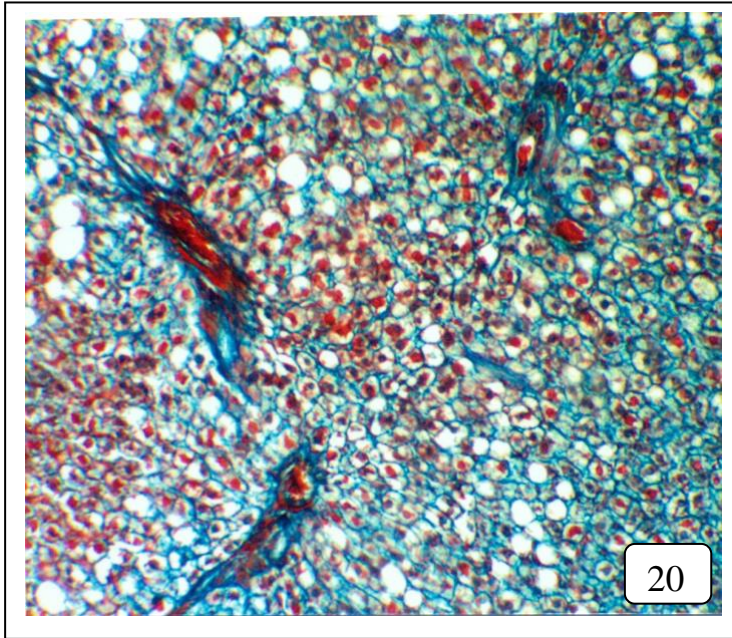


18

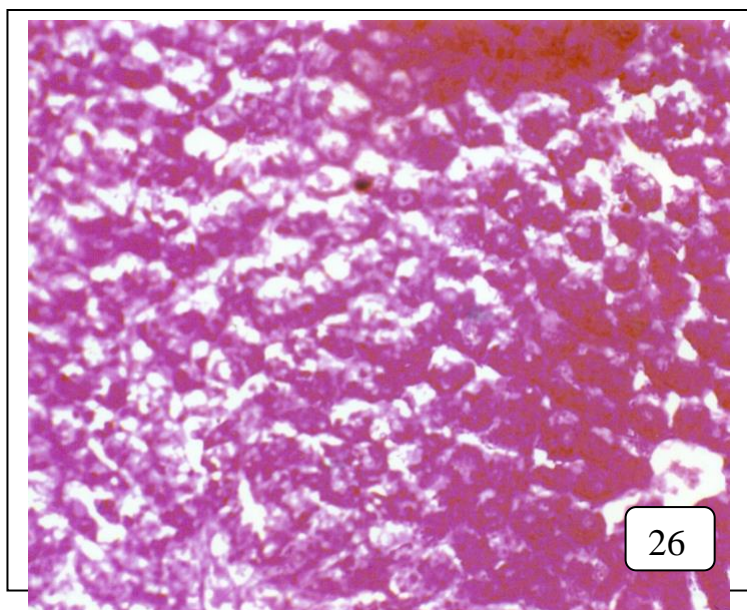
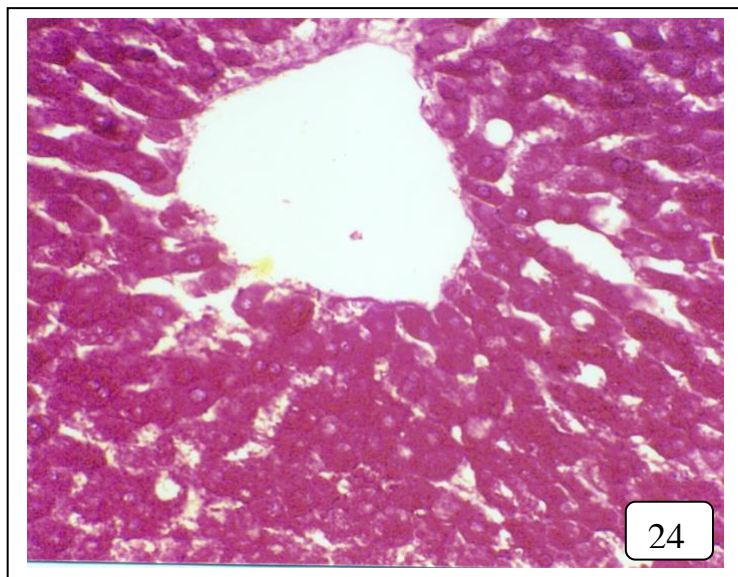


19

- (Fig 16) Photomicrograph of hyperlipidemia for 6 weeks showing marked congestion and fatty changes (Hx. & E stain x300)
- (Fig 17) Photomicrograph of hyperlipidemia for 6 weeks treated by Oat showing good regenerative effect cellular changes (Hx. & E stain x300)
- (Fig 18) Photomicrograph of hyperlipidemia for 6 weeks treated by Fennel showing mild regenerative effect cellular changes (Hx. & E stain x300)
- (Fig 19) Photomicrograph of hyperlipidemia for 6 weeks treated by Triphala showing same changes of fig 18 (Hx. & E stain x300)



- (Fig 20) Photomicrograph of hyperlipidemia for 6 weeks showing marked decreased fibrous elements (Mallory trichrome stain x300)
- (Fig 21) Photomicrograph of hyperlipidemia for 6 weeks treated by Oat showing good restoration of fibrous elements (Mallory trichrome stain x300)
- (Fig 22) Photomicrograph of hyperlipidemia for 6 weeks treated by Fennel showing mild restoration of fibrous elements (Mallory trichrome stain x300)
- (Fig 23) Photomicrograph of hyperlipidemia for 6 weeks treated by Triphala showing mild restoration of fibrous elements (Mallory trichrome stain x300)



(Fig 24) Photomicrograph of hyperlipidemia for 6 weeks shows no changes of PAS+ve content (PAS stain x300)

(Fig 25) Photomicrograph of hyperlipidemia for 6 weeks treated by Oat shows no changes of PAS+ve content (PAS stain x300)

(Fig 26) Photomicrograph of hyperlipidemia for 6 week striated by Fennel shows no changes of PAS+ve content (PAS stain x300)

(Fig 27) Photomicrograph of hyperlipidemia for 6 weeks treated by Triphala showing no changes of PAS+ve content (PAS stain x300)

B) Laboratory changes

Four main parameters were done and including:

- 1- Changes of AST activity (Aspartate transaminase).
- 2- Changes of ALT (Alanine transaminase).
- 3- Changes of GGT (Glutamyl transferase).
- 4- Changes of Serum total hepatic lipids.

Table 1 Changes in the level of Aspartate transaminase (AST) after induction of high fat diet and treatment with the different medicinal plants

	Control	3 weeks				6 weeks			
		Hyper L 3 w	Hyper L 3 w treated by Oat	Hyper L 3 w treated by Fennel	Hyper L 3 w treated by Triphela	Hyper L 6 w	Hyper L 6 w treated by Oat	Hyper L 6 w treated by Fennel	Hyper L 6 w treated by Triphela
Mean	32.5	89.8	50.2	57	53	114.6	80.8	94.2	84.2
SE	0.8	0.96	0.96	1.45	1.96	2.3	0.82	2.3	0.69
P value	0	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
% of change	0	176.3	54.4	75.3	63	252.6	148.6	189.8	159

Table 2 Changes in the level of Alanine transaminase (ALT) after induction of high fat diet and treatment with the different medicinal plants

	Control	3 weeks				6 weeks			
		Hyper L 3 w	Hyper L 3 w treated by Oat	Hyper L 3 w treated by Fennel	Hyper L 3 w treated by Triphela	Hyper L 6 w	Hyper L 6 w treated by Oat	Hyper L 6 w treated by Fennel	Hyper L 6 w treated by Triphela
Mean	23.2	73.4	31.4	50.6	32.4	107.8	35.2	64.6	44.4
SE	1.4	1.8	1.2	1.2	1.6	2.3	2.1	2	1.8
P value	0	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
% of change	0	216.3	35.3	118.1	39.6	364.6	51.7	178.4	159

Table 3 Changes in the level of Glutamyl transferase (GGT) after induction of high fat diet and treatment with the different medicinal plants

	Control	3 weeks				6 weeks			
		Hyper L 3 w	Hyper L 3 w treated by Oat	Hyper L 3 w treated by Fennel	Hyper L 3 w treated by Triphela	Hyper L 6 w	Hyper L 6 w treated by Oat	Hyper L 6 w treated by Fennel	Hyper L 6 w treated by Triphela
Mean	26.2	40.8	32.7	38.4	34	45.4	39.4	44.4	42,6
SE	1.85	0.6	0.675	0.57	0.625	1.35	0.57	0.57	0.75
P value	0	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
% of change	0	55.7	24.8	46.5	29.7	73.2	50.3	69.4	62.5

Table 4 Changes in the level of hepatic total lipid after induction of high fat diet and treatment with the different medicinal plants

	Control	3 weeks				6 weeks			
		Hyper L 3 w	Hyper L 3 w treated by Oat	Hyper L 3 w treated by Fennel	Hyper L 3 w treated by Triphela	Hyper L 6 w	Hyper L 6 w treated by Oat	Hyper L 6 w treated by Fennel	Hyper L 6 w treated by Triphela
Mean	4.52	5.64	3.72	5.34	3.84	7.46	5.42	7.12	6.58
SE	0.21	0.13	0.14	0.125	0.044	0.16	0.12	0.065	0.066
P value	0	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
% of change	0	24.7	17.6	18.1	15.04	65.04	19.9	57.5	45.5

Discussion

High fat diet and hyperlipideamia is the main factor for the increase in the serum level of lipid which may markedly affect the healthy state of blood vessels and increasing the incidence of developing atherosclerosis **Jain et al., 2007**.

Many pharmaceutical medications were

used for lowering the serum level of lipids and cholesterol, but always they causes a great risk of many sides effect especially in their prolonged use.

Herbal medicine today shows higher rate of safety and lower costs **Chattopadhyay and Bhattacharyya, 2007**.

In the present study three medicinal plants are used to detect their protective effects

against induced hyperlipidemia after ingestion with high fat diet, Oat (*Avena sativa*), fennel (*Foeniculum vulgare*) and Triphala (*Terminalia chebula*).

Liver tissue was the tissue of choice in this study for its role as detoxifying organ in all mammalian bodies.

Scientific studies support the view of increasing dietary soluble fibers as a part of hypercholesterolemia and hyperlipidemia treatment.

Fibric acid derivatives act to inhibit the hepatic secretion of VLDL and to promote triglyceride-rich lipoprotein catabolism through induction of lipoprotein lipase gene expression and stimulation of lipoprotein lipase activity

The Oat is a species of cereal grain has potent beneficial health effect in reducing LDL- cholesterol and should be induced in the prudent diet of individuals with hyperlipidemia **Al-Rawi, 2007**.

Rats treated with fat for 3 weeks showed many structural changes in the liver tissue, vacuolation of hepatocytes and some vascular changes. The changes were more observed in 6 weeks treated rats.

Hyperlipidemia is known to enhance the risk of fatty diseases **Festi et al., 2004** and carcinogenesis which is associated with hydroxyl radical formation **Tseng et al., 1996**.

In **2000**, **Ohno et al.**, noticed fatty changes in the liver in shrews suffered from hyperlipidemia with severe insulin-dependent diabetes mellitus.

Low grade inflammation, endothelial dysfunction and decreased fibrinolysis were associated with increased cardiovascular risk caused by hyperlipidemia **Ridker et al., 2002**.

Antolin et al, 2009 stated a reduction between obesity and different degrees of fibrosis and chronic liver diseases and they added that liver transplant patient show increased rates of obesity.

Signs of hepatic recovery were shown after use of Oat (*Avena sativa*) for 3 weeks in rats treated with fat for 3 weeks.

The present study showed that Oat contained several beneficial components such as vitamin E (alpha-tocopherol) phenolic acids, flavonoids, sterol and B-glucan, **Nie et al., 2006; Theuwissen and Mensink, 2008**.

Significant bioactivities of phenolics which found in Oat act as scavenging free radicals, chelating metals, regulating enzyme activity and modulating cell proliferation were observed by **Virgili et al 1998**. The protective effect of Oat observed in the present study may be due to high content of B-glucan in Oat.

According to **Davidson et al.1991** Oats, an important source of water-soluble fibers, have long been recognized as a potential cholesterol-lowering dietary component.

Fennel was observed to have a protective role on the liver cells **Toma et al., 2008** and **Yamini et al (2002)** stated that Fennel is of great effect in treating many digestive disorders.

Hwang and Choi 2004 noticed *Foeniculum vulgare* may act on both the cyclooxygenase and lipoxygenase pathway. They added that lipid peroxidation decreased significantly in rats treated by *Foeniculum vulgare*.

In this study some degenerative changes were observed in liver tissue which may be explained by reduction in lipid peroxidation and augmentation in the antioxidant activity **Birdane et al., 2007**.

A detectable recovery was observed in hepatic tissue of rat treated with fat and Triphala for 6 weeks. The beneficial effects of Triphala were studied by several authors **Jain et al., 2009** and **Saravanan et al., 2007**.

Impairment in vascular changes were noticed in hepatic tissue treated with high fat diet and Triphala in the present study **Jain et al., 2009**.

Results in the present study showed increased staining affinity of collagen fiber in rats treated with high fat diet especially around the hepatocytes.

Horn et al.,1985 reported that the presence of collagen in the presinusoidal spaces might affect the blood supply to liver cells and

would be reduce the exchange of metabolism ,perhaps causing hepatocellular dysfunction and necrosis.

Liver of rats treated with high fat diet for 3 weeks then 3weeks with Oat or Fennel or Triphala showed increased collagen fibers in walls of the central vein. Also in rats treated with high fat diet and Oat for 6 weeks, while those who treated with Fennel showed highly decreased collagen fibers in the wall of central vein .Such collagen increase was observed by both **Rousovan et al., 1992** and **Mervat, 2010**.

Rousovan et al, 1992 stated that the increase in collagen fibers may be due to increase interstitial tissue and the collagenous fibers and may lead to increase the defense reaction against toxic materials. Decreased PAS positive materials were observed in liver tissue of rats treated with high fat diet for 3 or 6 weeks.

Decreased glycogen content observed in hepatocytes after induction of of fat diet may be due to failure of hepatocytes resynthesizes of stored glycogen.

The affected glycogen contents was observed in this study in liver of rats treated with high fat diet may be due to altered insulin level and insulin sensitivity or insulin resistance due to obesity **Han et al., 2007**.

References

Al-Rawi M M(2007):Efficacy of Oat bran (*Avena sativa*) in comparison with atorvastatin in treatment of hypercholesterolemia in albino rat liver Egypt. J. of Hospit. Med.,**29**:511-521.

Antolin G S , Pajares F G and Vallecillo M A(2009):Fibroscan evaluation of liver fibrosis in liver transplantation. Transplant .Unit .Rio Hortegea Unive .Valladolid ,Spain ,**41**:1044-1046.

Bernard J (2008): Free fatty acid receptor family: novel targets for the treatment of diabetes and dyslipidemia. Curr. Opin .Investig. drugs **9**:1078-1083.

Birdane F M , Cemek M, Birdane Y O ,Gulcin I And Buyuroglu M E (2007): Beneficial effect of *Foeniculum Vulgare* on endathol-induced acute gastric mucosal injury in rats. World J. Gastroenternol., **13(4)**:607-611.

Burt A D, Mutton A and Day C P(1998):Diagnosis and interpretation of steatosis

and steatohepatitis. Semin Diagn Pathol., **15**:246-258.

Caldwell S H, Oelsner J C , Iezzoni E E and Hespeneide E H(1999): Cryptogenic cirrhosis: clinical characterization and risk factors for underlying disease. Hepatology., **29**: 664–669.

Chattopadhyay R R and Bhattacharyya S k (2007): Terminalia chebula :an update .Pharmaco .Revi.,**1**:151-156.

Davidson H H ,Dugan L D , Burns J H , Bava J , Story K and Drennan K B (1991): The hypocholesterolemic effect of B-glucan in oat bran .a dose-Controlled study .JAMA .,**265**:1833-1839.

Den Boer M, Voshol F, Kuipers L M , Havekes, and Romijn J. A. (2004):Hepatic steatosis: a mediator of the metabolic syndrome: lessons from animal models. Arterioscler. Thromb. Vasc. Biol., **24**: 1–6.

Drury R and Wallington E (1980):Carleton's Histological Techinque,**4Th** Ed. Oxford Univ. Press ,New York. Toronto.

Farrell GC and Larter CZ (2006): Nonalcoholic fatty liver disease: from steatosis to cirrhosis. Hepatology ., **43**:S99–S112.

Festi D , Colecchia A , Sacco T , Blondi M , Roda E and Marchesini G (2004): Hepatic steatosis in obese patients: clinical aspects prognostic significance. Obesity Reviews ,**5**: 27-42.

Haines, I.A.(2001): Observations of magnetospheric plasma by the radio plasma imager (RPI) on the image mission. Advances in Space Research, **30(10)**:2259-2266.

Han S H , Qu0n M J , Kim J A and Koh k K(2007): Adiponectin and cardiovascular disease: response therapeutic interventions . J. Am .Coll.Cardiol.,**49**:531-538.

Hansen B , Jorde L B and Turco S (2009): Biochemistry and medical genetic lecture notes. Kaplan Medi.USA.

Harrison D , Kathy K G , Hornig B and Drexler H(2003): Role of oxidative stress in atherosclerosis. Amr. J. of Cardio.,**91**:7-11.

Horn T , Jung J and Christoffersen P(1995): Alcoholic liver injury: early changes of the Disse space in acinar zone .Liver ,**6**:301-310.

Hwang J K and Choi E M(2004): Anti-inflammatory analgesic and antioxidant activities of the fruit of *Foeniculum Vulgare* . Fitoterapia J.,**557**-565.

Jain K S , Kathiravan M K , Somani R S and Shishoo C J(2007): The biology of chemistry of hyperlipidemia review .Bioegan. Med.Chem.,**15**:4674-4699.

Jain S ,Yadav P and Gill V (2009): Terminalia

- arjuna as a medicinal plant: Phytochemical and pharmacological profile: *Phytochem. Rev.*, **8**:491-502.
- Khanna A, Chander R and Kapoor N (1996)** : Terminalia arjuna: an ayurvedic cardiotoxic regulates lipid metabolism in hyperlipidemic rats. *Phytotherapy Res.*, **10**:663-665.
- Lee R G (1989)**: Nonalcoholic steatohepatitis: a study of 49 patients. *Hum. Pathol.*, **20**:594-598.
- Lee R G (1995)**: Nonalcoholic steatohepatitis: tightening the morphological screws on a hepatic rambler. *Hepatology.*, **21**:1742-1743.
- Lewis G F, Carpentier A, Adeli A, and Giacca A (2002)**. Disordered fat storage and mobilization in the pathogenesis of insulin resistance and type 2 diabetes. *Endocr. Rev.*, **2**: 201-229.
- Liu L, Ziubik L, Collin F W, Marko M and Meydani M (2004)**: The antithrombotic potential of oat phenolic compound. *Atherosclerosis* ., **175**:39-49.
- Mervat A A (2010)**: Modulation of radiation injury in pregnant rats by bone marrow transplantation. Zoology Depart. Faculty of Science. Al-Azhar Unive. Cairo.
- Mori N, Lee P, Muranaka S and Sagara F (2010)**: Predisposition for primary hyperlipidemia in Miniature Schnauzers and Shetland Sheepdogs as compared to other canine breeds. *Research in Veterinary Science.*, **10**:1-6
- Nie L, Wise M L, Peterson D M and Meydani M (2006)**: Avenanthramide, a polyphenol from oat, inhibits vascular smooth muscle cell proliferation and enhances nitric oxide production. *Atherosclerosis.*, **186**:260-266.
- Ohno T, Horio F and Tanaka S (2000)**: Fatty liver and hyperlipidemia in insulin-dependent diabetes mellitus (IDDM) of streptozotocin treated shrews. *Life sciences.*, **66**(2):125-131.
- Panfili G, Fratianni A and Irano M (2003)**: Normal phase high-performance liquid chromatography method for the determination of tocopherols and tocotrienols in Cereals. *J. Agric. Food Chem.*, **51**:3940-3944.
- Pearse A (1977)**: *Histochemistry, Theoretical, and Applied*. 3 ed., Vol.1. Churchill Livingstone. London.
- Pessayre D, Berson B and Mansouri A (2001)**: Mitochondria in steatohepatitis. *Semin. Liver Dis.*, **21**: 57-69.
- Reihner E, Angelin B, Rudling M, Ewerth S, Bjorkhem L and Einarsson K (1990)**: Regulation of hepatic cholesterol metabolism in human: Stimulatory effects of cholestyramine on HMG-CoA reductase activity and low density lipoprotein receptor expression in gallstone patients. *J. Lipid Res.*, **31**:2219-2226.
- Ridker P M, Rifai N, Rose L, Buring J E and Cook N R (2002)**: Comparison of C-reactive protein and low-density lipoprotein cholesterol level in the prediction of first cardiovascular events. *Nat. Engl. J. Med.*, **347**: 1557-1565.
- Rousovan A, Kanje M and Mild K (1992)**: The stimulatory effect of magnetic field on regeneration of the rat sciatic nerve is frequency dependent. *Exp Neurology.*, **117**:81-84.
- Saravanan S, Srikumar R and Manikandan S (2007)**: Hypolipidemic effect of Triphala in experimentally induced hypercholesteremic rats. *Yakugaku Zasshi. The pharmaceutical Society of Japan.*, **127**: 385-388.
- Schonfeld G, Patterson W D, Yablonskiy T S, Tanoli M, Averna N, Elias P, Yue and Ackerman J (2003)**: Fatty liver in familial hypobetalipoproteinemia: triglyceride assembly into VLDL particles is affected by the extent of hepatic steatosis. *J. Lipid Res.*, **44**: 470-478.
- Tarantino G, Saldalamacchia G, Conca P, Arena A (2007)**: Nonalcoholic fatty liver disease: further expression of the metabolic syndrome. *J Gastroenterol Hepatol* ., **22**:293-303.
- Targher G, Bertolini L, Rodella S, et al (2007)**: Nonalcoholic fatty liver disease is independently associated with an increased incidence of cardiovascular events in type 2 diabetic patients. *Diabetes Care.*, **30**:2119-2121.
- Theuwissen E and Mensink R P (2008)**: Long-chain fatty acid intake and risk of cancers of the breast and prostate. *J. of Nutr.*, **134**:341-342.
- Toma C, Pancan L, Chirita M and Zamfir A (2008)**: Electrospray ionization tandem mass spectrometric investigation of *Melissa officinalis* oil. *Pharma.*, **56**(1) 92-98.
- Tseng T H, Hus J D, Chu C Y and Wang C J (1996)**: Promotion of colon carcinogenesis through increasing lipid peroxidation induced in rats by a high cholesterol diet. *Cancer Lett.*, **100**:81-87.
- Virgili F, Kim D and Packer L (1998)**: Procyanidins extracted from pine bark protect alpha-tocopherol in ECV 304 endothelial cells challenged by activated RAW 264.7 macrophages: role of nitric oxide and peroxynitrite. *FEBS. Letters.*, **431**:315-318.
- Yamini Y, Sefidkon F and Pourmortazavi S (2002)**: Flavour. *Fragr. J.*, 17-345. Cited from: **Choi E M and Hawng J.K. (2004)**: Anti-

inflammatory analgesic and antioxidant activities of the fruit of *Foeniculum vulgare*. *Fitoterapia*, **75**:557-565.

Younossi ZM, Gramlich T, Liu YC, Matteoni C, Petrelli M, Goldblum J, Rybicki L and

McCullough, AJ (1998):Nonalcoholic fatty liver disease: assessment of variability in pathologic interpretations. *Mod Pathol.*, **11**: 560-5.

التغيرات التركيبية والمعملية فى كبد إناث الجرذان البيضاء فى حالات إستخدام غذاء على الدهون التجريبي والدور العلاجي لبعض النباتات الطبية

عزالدين الشرقاوى عبدالله^١ جمال سليمان الغرباوى و مصطفى السعيد الصاوى
من أقسام الهستولوجى بكلية الطب بنين (دمياط والقاهرة) جامعة الأزهر

يعتبر تنظيم عناصر الغذاء المختلفة من الأتجاهات الهامة للحفاظ على صحة الجسم وتفادى إصابته بالأمراض المختلفة. ولعل زيادة نسبة الدهون بالدم يمثل عنصرا خطيرا لتعرض الجسم بالعديد من أمراض العصر الحديث مثل تصلب الشرايين والكبد الدهنى. ولقد إستهدفت هذه الدراسة إلى محاولة إستخدام بعض النباتات الطبية والمعروف عنها بقدرتها على عملية تنظيم نسبة الدهون بالدم. فى هذه الدراسة تم إستخدام 45 من إناث الجرذان البيضاء البالغة والتي تم تقسيمها إلى 9 مجموعات متساوية العدد. إعتبرت المجموعة الأولى مجموعة ضابطة فى حين إعتبرت المجموعة الثانية مجموعة تم تغذيتها بغذاء على الدهون لمدة 3 أسابيع ولم يتم تعريضها إلى العلاج بالنباتات الطبية. أما بالنسبة للمجموعات أرقام 3 و4 و5 فقد تم علاجها بنباتات الشوفان ثم الشمر والهيلينج حسب الترتيب بعد إحداث الزيادة الدموية بها للدهون لمدة 3 أسابيع. وفى المجموعة 6 تم تغذيتها بغذاء على الدهون ولمدة 6 أسابيع ولم يتم تعريضها للعلاج بالنباتات الطبية سالفة الذكر. وفى المجموعات أرقام 7 و8 و9 فقد تم علاجها بنفس النباتات المذكورة وذلك بعد إحداث الزيادة الدموية بها للدهون لمدة 6 أسابيع.

وقد تم تقسيم النتائج إلى إتجاهين, حيث كان الأتجاه الأول هو الدراسة التركيبية لخلايا الكبد فى المجموعات المختلفة وذلك بعد إستخدام الصبغات المناسبة. أما الأتجاه الثانى فكان عمل التحاليل المعملية المناسبة والتي تظهر مدى كفاءة خلايا الكبد فى المجموعات المختلفة.

وقد دلت النتائج على مدى تأثر خلايا الكبد بتأثير زيادة نسبة الدهون بالدم سواء لمدة 3 أسابيع أو لمدة 6 أسابيع وتتلخص هذه التغيرات فى الترسيبات الدهنية بنسب مختلفة داخل الخلايا الكبدية.

كما لوحظ مدى إحتقان الأوعية الكبد وبعض الترسيبات الخلوية الألتهابية فى مناطق الكبد المختلفة. وقد أظهرت نتائج هذا البحث مدى الدور الوقائى لإستخدام النباتات الطبية حيث لوحظ بعض التحسن الواضح فى خلايا الكبد وإختفاء بعض الترسيبات الدهنية بها. وقد أظهرت النتائج المعملية مدى تحسن وظائف الكبد بعد إستخدام النباتات الطبية رغم عدم عودة هذه الوظائف إلى حالتها الطبيعية بالكامل. ويستنتج من هذه الدراسة مدى أهمية الحرص على ضبط كمية ونوع المواد الغذائية تفاديا لحدوث الأمراض الخطيرة المتوقعة وكذلك مدى أهمية الأعتداد على هذه النباتات الطبية لما لها من دور فعال.