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Original Article

The effect of Melatonin Hormone on Formaldehyde-Induced Liver Injury in adult male albino rats: A Light and electron Microscopic Study

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ABSTRACT

Background: It has been detected that general population is exposed to many products of daily used that contain formaldehyde. Numerous studies revealed that formaldehyde- induced major health problems affecting all the body organs especially the liver. Recent studies have shown melatonin to be an antioxidant substance which has been used for the treatment of liver diseases.

Aim of work: This study aimed to investigate histological and biochemical changes in the livers of formaldehyde exposed rats and possible effects of melatonin hormone on these changes.

Material and Methods: Eighteen healthy adult male albino rats were studied. The animals were divided into three main equal groups, six rats each:

Group I: (control group) rats were given tap water.

Group II: rats received 2ml of 0.1% of formaldehyde.

Group III: rats received 2ml of 0.1% of formaldehyde with melatonin (25 mg/kg) diluted in 0.9% of Nacl. After 8 weeks all animals of the three groups were sacrificed. Liver functions were assessed both biochemically and histologically using both light and electron microscopes.

Results: The present study demonstrated variable degrees of hepatic affection after administration of formaldehyde in rats of group II, manifested as biochemical and histological changes. The plasma level of (SGOT) and (SGPT) showed a significant increase. Rats of group III treated with melatonin showed considerable preservation of the liver histology.

Conclusion: Melatonin had a protective role on the liver which may improve the toxic damaging effect of the formaldehyde on the liver cells.

Key Words: Formaldehyde, liver, melatonin

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INTRODUCTION

Formaldehyde (HCHO) is a highly reactive flammable, colorless agent with prominent odor. It is the simplest aldehyde present in nature, cigarette smoke, and in photochemical smog. (IPCS 1991 & Becker, Rosenberg 1990) It has a boiling point of -19°C, a melting point of -118°C, and it doesn't mix with acetone, benzene, diethyl ether, chloroform and ethanol, (*Gardner 1993*).

Under atmospheric conditions, formaldehyde is readily photo-oxidized by sun light to carbon dioxide.

Formaldehyde is very reactive, it auto condenses especially in alkaline conditions. It condenses with numerous compounds to produce methylol or methylene derivatives. It can react with hydrogen chloride to form bis - (chloromethyl) ether, which is a human carcinogen. Formaldehyde is able to catalyze nitrosation of a series of secondary amines to carcinogenic nitrosamines or N-nitroso-compounds, (*Martindale & Reynolds 1993 & Houry et al 1990*).

The hazard of exposure to formaldehyde increases nowadays, either through its natural sources, man - made sources or indoor environmental sources.

The wide use of formaldehyde in many fields is of great significance for human beings. Exposure to formaldehyde occurs as free formaldehyde, easily liberated and affect people (when used as a disinfectant). Formaldehyde is also used in house hold cleaning agents, dish washing liquid, fabric softeners, shoe care agents, car shampoos and waxes, and carpet

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cleaning agent, (*Maurice et al 1986*). It may reach many people via various consumer goods, such as preservatives, pharmaceutical products and cosmetics, (*Rosenberg 1990 & Gardner 1993*). Thus Formaldehyde has many medical uses, it is used for cadaver embalming, organ and tissue fixation, disinfection and sterilization procedures.

Formaldehyde is readily absorbed via respiratory tract, and gastrointestinal routes. Dermal absorption of formaldehyde appears to be very slight, (*Rosenberg 1990 & Maurice et al 1986 & De Groot et al 2009*). The absorbed formaldehyde is rapidly metabolized in human body into formic acid in the liver and erythrocytes. It is excreted by urine, feces, or expiration, (*Jawetz 1989*).

The liver is structurally and functionally heterogeneous and has been considered second to brain in its complexity., the liver has thousands of vital functions including the efficient uptake of amino acids, carbohydrates, bile acids, cholesterol, proteins, lipids and vitamins for storage and metabolism subsequent to release into bile and/or blood, (*Swiecichowski et al 1993*).

Microscopically, each liver lobe made up of hepatic lobules. The lobules are roughly hexagonal, and consist of plates of hepatocytes radiating from a central vein, (*Monticello et al 1991*). The central vein joins to the hepatic vein carry venous blood out from the liver. Portal triad is the distinctive component of the lobule, which consists of a branch of the hepatic artery, a branch of the hepatic portal vein, and a bile duct, as well as lymphatic vessels and a branch of the vagus nerve, (*Pallikaris et al 1992 & Grammer et al 1993*). Liver sinusoids, are enlarged capillaries between the hepatocyte plates through which blood from the hepatic portal vein and hepatic artery enters via the portal triads, then drains to the central vein, (*Liden et al 1993*).

The microscopic anatomy of liver, shows two major cell types: parenchymal cells and non-parenchymal cells. 70–85% of the liver volume is occupied by parenchymal hepatocytes. Non-parenchymal cells constitute 40% of the total number of liver cells, (*Kilburn 1994*). The liver sinusoids are lined with two types of cell, sinusoidal endothelial cells, and phagocytic Kupffer cells. Hepatic stellate cells are non-parenchymal cells found in the perisinusoidal space, between the sinusoid and the hepatocyte, (*Agarwal et al 2003 & Valko et al 2005*). Additionally, intrahepatic lymphocytes are often present in the sinusoidal lumen, (*Valko et al 2005*). (Fig. 1)

Hepatocytes are relatively long-lived for cells associated with the digestive system; their average lifespan is about 5 months. In addition, liver cells are capable of considerable regeneration when liver tissue is lost due to hepatotoxic processes, disease, or surgery, (*Møller et al 2007 & Møller et al 2006*).

Various studies reported the structural and functional disorders of the respiratory, gastrointestinal, reproductive and nervous systems associated with toxic effects of HCHO. Allergic effects of HCHO have also been reported, (*Michael & Ross 2011*).

HCHO has adverse effects on the histological structure and functions of the liver, (*Burt & Day 2002*). The toxic effects of HCHO have been reported in form of structural changes in the epithelial biliary cells and damage intrahepatic and extrahepatic biliary ducts. HCHO exposure has led to disorders of oxidant and oxidant-antioxidant systems of the liver tissue and inflicted oxidative damage. Furthermore, it has been found to decrease the liver weight and triglyceride level, (*Harada et al 1999 & Barbara 2006*).

Melatonin is the chief secretory product of the pineal gland in response to darkness. In addition to the pineal gland, melatonin detected in the retina, intestines, erythrocytes, leucocytes, and many other tissues. The organs and tissues exposed to oxygen radical formation such as the liver, lungs, brain, and skin, produce few amount of intracellular melatonin, (*Chojnacki et al 2014 & Guha et al 2007*).

Melatonin hormone (N-acetyl-5-methoxytryptamine) regulates the endocrine rhythm. It has antigonatropic effects, it protects the nervous system, stimulates of the immune system, and protects the free radicals. Recent studies considers melatonin as an antioxidant substance. Melatonin, which is both water and oil soluble, is available to each organelle of the cell, (MacSween et al 2002).

AIM OF WORK

This study aimed to investigate histological changes in the livers of formaldehyde exposed rats and possible effects of melatonin hormone on these changes.

MATERIAL AND METHODS

This study was carried out on 18 adult male albino rats, each of average weight ranging from 150-200 gm and 6-8 weeks of age. The experimental animals were kept under standard laboratory conditions of temperature and humidity and 12 hours light/dark cycle. The care and use of animals, were done by the Animal House Center, Faculty of Medicine, University of Alexandria. The experimental animals were randomly divided into three main equal groups six rats each:

Group I: (control group) rats were given tap water. Once daily for 8 weeks.

Group II: rats received 2ml of 0.1% of formaldehyde. Once daily for 8 weeks.

Group III: rats received 2ml of 0.1% of formaldehyde with melatonin (25 mg/kg) diluted in 0.9% of Nacl. Once daily for 8 weeks.

The concentration of formaldehyde used in this experiment is 40% dissolved in 4cm tap water. The doses were administered by oro-gastric tube. Once daily for 8 weeks.

To regulate the endogenous secretion of melatonin, all rats were kept in 12-hour dark conditions throughout the experiment.

At the end of the experiment rat anaesthetized by ethyle inhalation, then pressure with thumb caudal to the mandible were applied to exert pressure on the external jugular vein then blood samples were collected from retro-orbital venous plexus of all rats in sterilized dry centrifuge tubes. This was achieved by elevation of the upper eyelid with the index finger, then broke a small piece of the haematocrit tube and inserted the broken edge of the tube into the conjunctiva of the mid –dorsal globe. The hematocrit tube was gently directed in a caudal and medial direction until blood was obtained.

Blood samples were allowed to clot for 35 min at room temperature. Centrifugation was done at 2500 rpm for 15 min, serum was separated and biochemical parameters of serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvate transaminase (SGPT) were estimated by using ELISA technique, Abbot, Austria. At the Clinical Pathology department, Faculty of Science, Alexandria University.

Rats were then sacrificed, thereafter the right lobes liver from all animals were excised by midline incision and divided into 2 specimens. All the specimens were subjected to light and electron microscopic studies: (*Drury & Wallington 1980 & Bozzola & Russell 1992*)

1. The first specimen was immediately fixed in 3% gluteraldehyde solution and processed to get semithin and ultrathin sections for transmission electron microscopic examination.

2. The second specimen was fixed in 10% formal saline and processed to get 6 μm thick paraffin sections. These sections were stained for light microscopic examination.

Histological study:

A- Light microscopic study: (Glauret 1986)

Paraffin sections stained with Haematoxylin and Eosin stain in the Histology and Cell Biology department, Faculty of Medicine, University of Alexandria.

B- Electron microscopic study: (Trevor & Graham 1996)

The grids were examined and photographed by Jeol 100 CX transmission electron microscope at the Electron Microscopy Unit, Faculty of Science, University of Alexandria. II- Histological results

RESULTS

I-Biochemical results

Table 1: Showed the level of SGOT and SGPT in the different studied groups.

	Control (I)	Group (II) with 0.1% formaldehyde	Group (III) with 0.1% formaldehyde and melatonin
SGOT			
Min. – Max.	135.0 – 141.0	177.0 – 184.0	159.0 – 162.0
Mean ± SD	136.21 ± 2.40	179.35 ± 2.45	158.30 ± 1.70
SGPT			
Min -Max	35.0 – 40.0	63.0 – 65.0	52.5 – 62.0
Mean ± SD	38.60 ± 2.35	62.10 ± 2.41	55.30 ± 2.33

p: p value for F test (ANOVA) for comparing between the different studied group.
p1: (<0.001*) p value for Post Hoc test (Scheffe) for comparing between control and each other group
p2: (<0.001*) p value for Post Hoc test (Scheffe) for comparing between group II and group III.
*: Statistically significant at $p \leq 0.05$

II- Histological results

A) Light Microscopic Results

In the control group I, liver appeared with normal architecture; Hepatocytes arranged in cords radiating from the central veins forming the hepatic lobules. They had polyhedral shaped with rounded, vesicular, centrally located nuclei and acidophilic cytoplasm. (fig. 2)

Hepatic sinusoids appeared as narrow spaces between the hepatic cords they lined with flattened endothelial cells and few bulging branching Kupffer cells. (fig. 2)

The portal tracts revealed the normal appearance with branch of portal vein, branch of hepatic artery and one bile duct radical, all were enclosed in scanty connective tissue. (fig.3)

Histological examination of liver sections of group (II) (receiving 2ml of 0.1% formaldehyde) showed hepatic lobules with degenerated hepatocytes, where many of these hepatocytes were polyhedral in shape with vacuolated hyper-eosinophilic cytoplasm and pyknotic nuclei. The hepatocytes appeared disorganized around dilated central veins (Fig. 4). Periportal areas showed Mononuclear cellular infiltration with the congested blood vessels (Figs. 5, 6a, 6b). These hepatocytes were further separated by dilated blood sinusoids (Fig. 5) that exhibited apparent increase in the number of Kupffer cells. (Figs. 4, 5, 6b)

The histological sections of rats of group III (receiving 2ml of 0.1% formaldehyde with melatonin dissolved in water by orogastric tube once daily for 8 weeks) revealed mild affection of the hepatocytes with preserved hepatic architecture. Few periportal hepatocytes showed vacuolated cytoplasm (Fig.7). Hepatocytes in the centrilobular region were polyhedral in shape with acidophilic cytoplasm and central vesicular nuclei. Hepatocytes were arranged in cords radiating from the central vein. The blood sinusoids were lined by endothelial cells (Fig. 8) and few Kupffer cells were observed. (Fig. 7)

b. Electron microscopic results:

The liver of control rats group I revealed normal hepatocytes with rounded euchromatic nuclei. The hepatic nuclei had regular contour and contained one or more nucleoli. The cytoplasm of these cells showed parallel arrays of rough endoplasmic reticulum in close association with mitochondria. The mitochondria were numerous, usually round to oval in shape The cytoplasm appeared to have a finely granular appearance due the presence of numerous free glycogen granules with few lysosomes. (fig.9)

The hepatocytes of group II, revealed degenerative changes, the cytoplasm of some hepatocytes with rough and dense nuclei. The cells also depicted many mitochondria with dense matrix, ill defined cristae and showed variability in size and shape, and many cytoplasmic vacuolation. Many Kupffer cells were seen with irregular nuclei. (Fig.10 & 11).

Sections of liver of rats of group III treated with melatonine, revealed nearly normal hepatocytes. The nuclei were euchromatic with regular contour and some were binucleated. Their cytoplasm showed dilated smooth endoplasmic reticulum, and numerous mitochondria with dense matrix. (Fig.12 & 13).

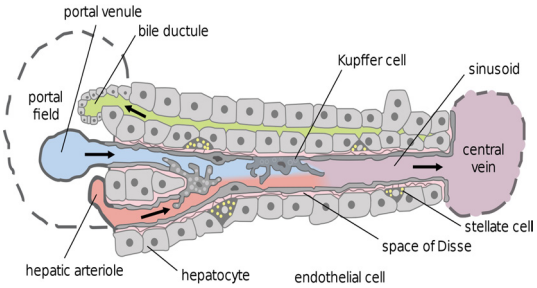

Fig. 1: The microscopic anatomy of liver (*Frevert et al 2005*).

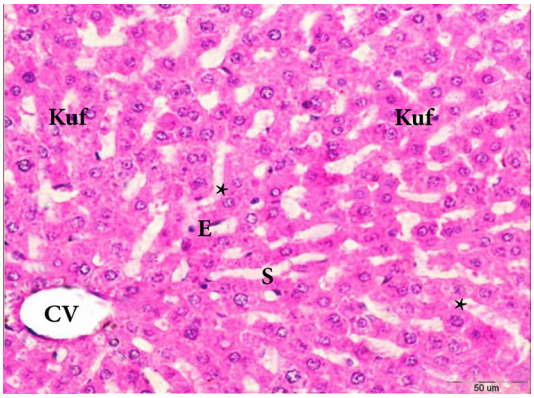

Fig. 2: A photomicrograph of rat liver of group I (control), showing the classical hepatic architecture. Hepatocytes (*) are arranged in cords radiating from the central vein (CV).The cells are polyhedral in shape with acidophilic cytoplasm and central vesicular nuclei .blood sinusoids (s) are lined by endothelial cells (E) and Kupffer cells(Kuf). (H&E stain, Mic. Mag. × 400).

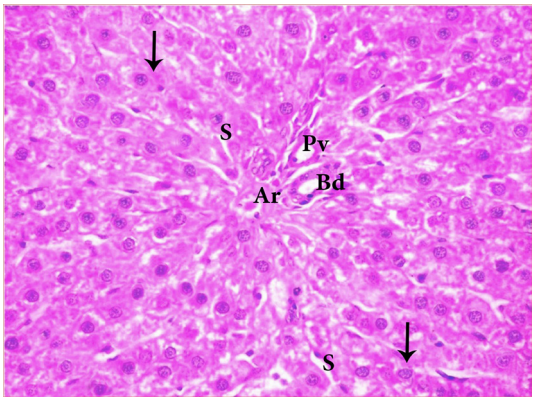

Fig. 3: A photomicrograph of rat liver of group I (control), showing the classical hepatic architecture. The portal tract composed of; branches of portal vein (pv), hepatic artery (Ar) and bile duct (Bd) within scanty connective tissue. Hepatocytes are acidophilic with central vesicular nuclei (arrows). S: (hepatic sinusoid). (H&E stain, Mic. Mag. × 400).

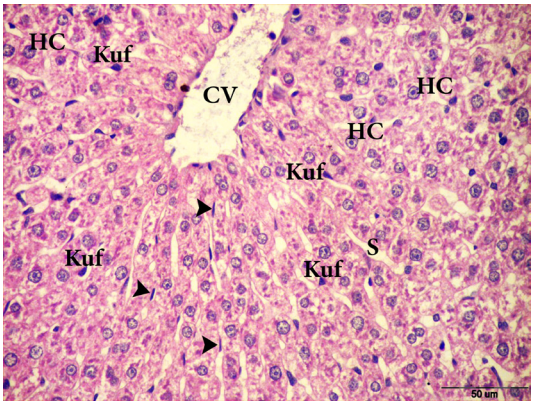

Fig. 4: A Photomicrograph of rat liver of group II, showing the hepatocytes are arranged in cords radiating from the central vein (CV). Many of liver cells (HC) are with dense acidophilic vacuolated cytoplasm and dark pycnotic nuclei. The liver cords are separated by dilated blood sinusoids (S) lined by endothelial cells (arrow head). The Kupffer cells (kuf) are increased in numbers. (H&E stain, Mic. Mag. × 400).

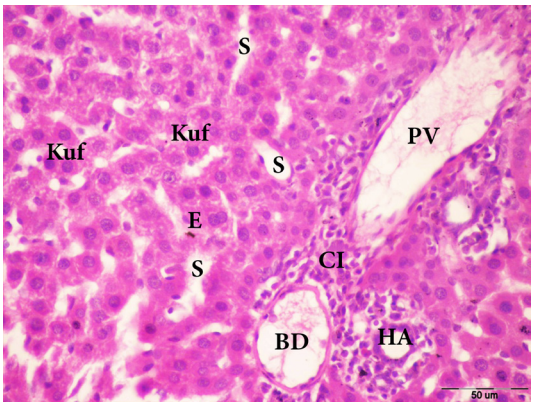

Fig. 5: A Photomicrograph of rat liver of group II, showing Cellular infiltration (CI) around the portal tract, branch of the portal vein (PV), branch of hepatic artery (HA), branch of bile duct (BD).
S: (dilated hepatic sinusoid) k: Kupffer cells
E: endothelial cells. (H&E stain, Mic. Mag. × 400).

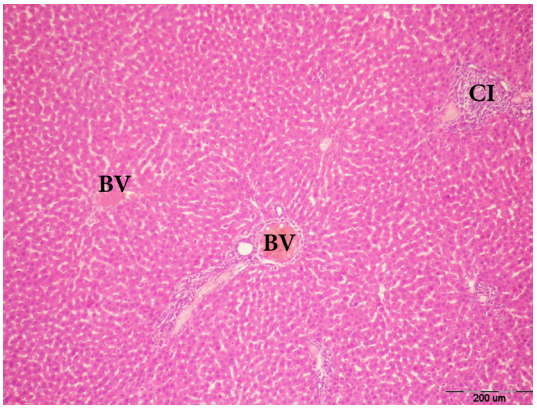

Fig. 6a: A Photomicrograph of rat liver of group II, showing Cellular infiltration (CI) is noticed as well as congested vessel (BV). (H&E stain, Mic. Mag. 100).

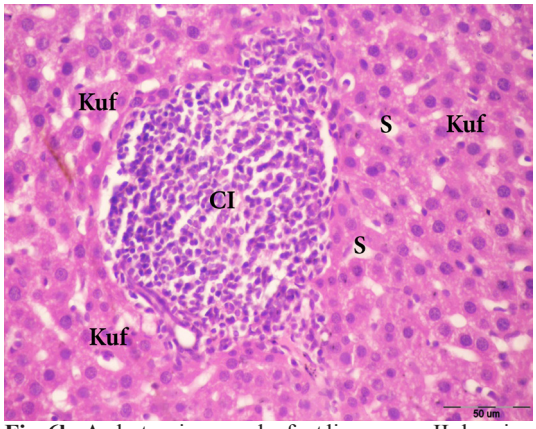

Fig. 6b: A photomicrograph of rat liver group II showing Cellular infiltration (CI), dilated blood sinusoids (s) with increasing number of kupffer cells (kuf). (H&E stain, Mic. Mag. × 400).

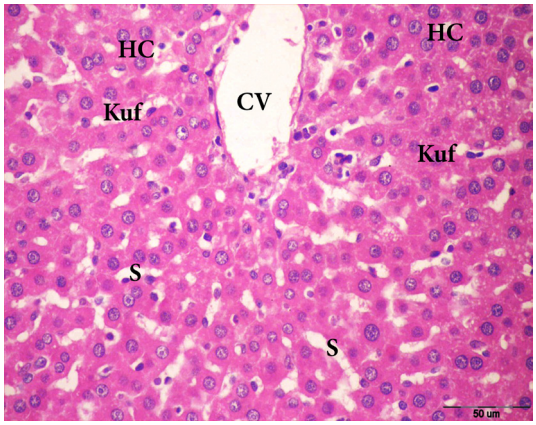

Fig. 7: A photomicrograph of rat liver group III showing preserved hepatic architecture. hepatocytes are arranged in cords radiating from the central vein (CV). Many of liver cells (HC) are with dense acidophilic cytoplasm and dark nuclei. The liver cords are separated by dilated blood sinusoids (s). The Kupffer cells (kuf) are frequently encountered. (H&E stain, Mic. Mag. × 400).

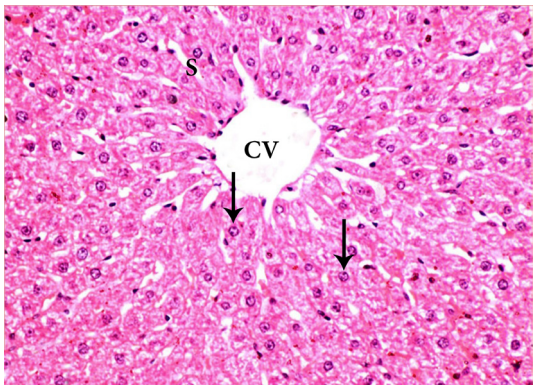

Fig. 8: A photomicrograph of rat liver group III showing preserved hepatic architecture. hepatocytes are arranged in cords radiating from the central vein (CV). Many of liver cells (arrows) are with dense acidophilic cytoplasm and dark vesicular nuclei. The liver cords are separated by blood sinusoids (s). (H&E stain, Mic. Mag. × 400).

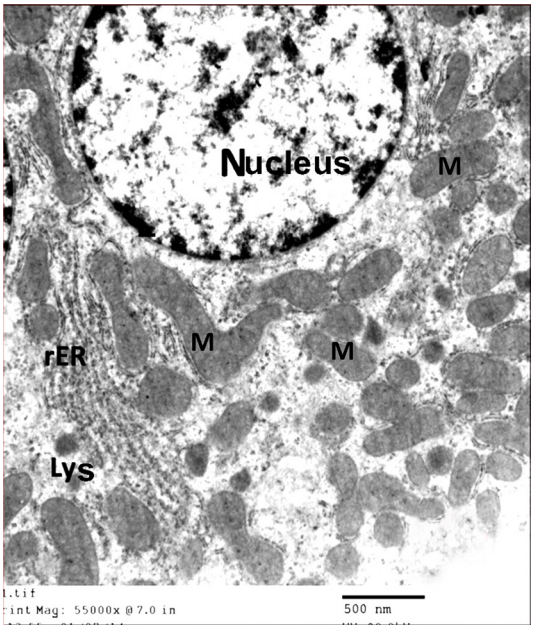

Fig. 9: Electron micrograph of rat liver of control group I showing hepatocytes with smooth contoured euchromatic nucleus (Nucleus), parallel arrays of rough endoplasmic reticulum (rER), numerous lamellar mitochondria(M) and few lysosomes (Lys). Inside the granular cytoplasm. (Mag. × 5000).

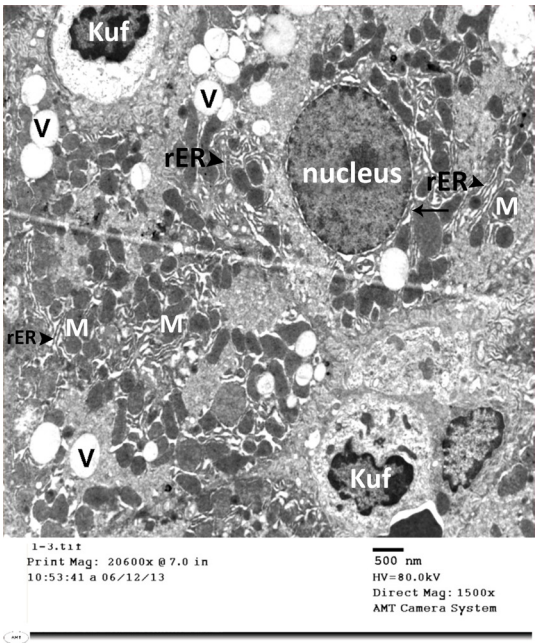

Fig. 10: Electron micrograph of rat liver of group II, revealing hepatocytes with dense nuclei (nucleus) and many lipid droplets (v). Mitochondria with electron dense matrix (M) in close association to dilated profiles of rough endoplasmic reticulum (rER), as well as dilated perinuclear cisternae (arrow) are seen .Notice the increasing number Kupffer cell with its dense irregular nucleus (kuf). (Mag. × 1500).

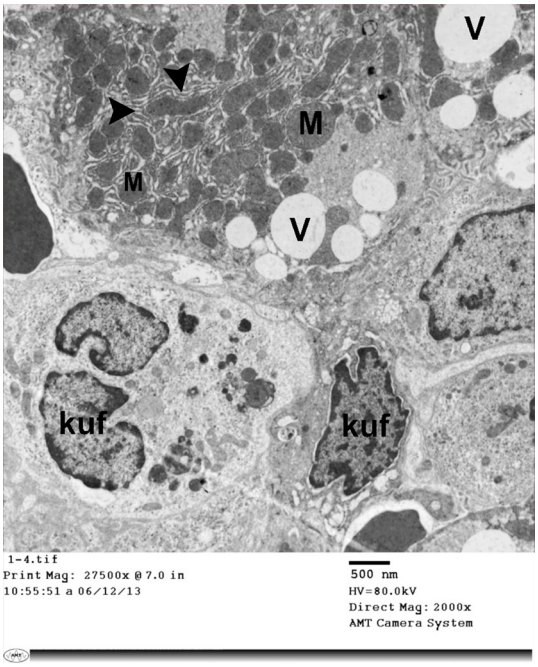

Fig. 11: Electron micrograph of rat liver of group II, revealing many lipid droplets (v), mitochondria with electron dense matrix (M) in close association to dilated profiles of rough endoplasmic reticulum (arrow head). Notice the Kupffer cell with multiple cytoplasmic processes and irregular dense nucleus (kuf). (Mag. × 2000).

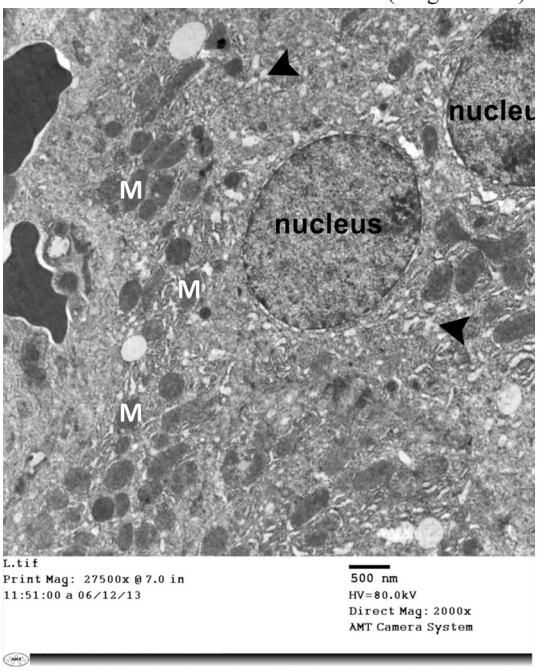

Fig. 12: Electron micrograph of rat liver of group III, showing hepatocytes with binucleated euchromatic nuclei (nucleus), dilated smooth endoplasmic reticulum (arrow head) and numerous mitochondria with electron dense matrix (M). (Mag. × 2000).

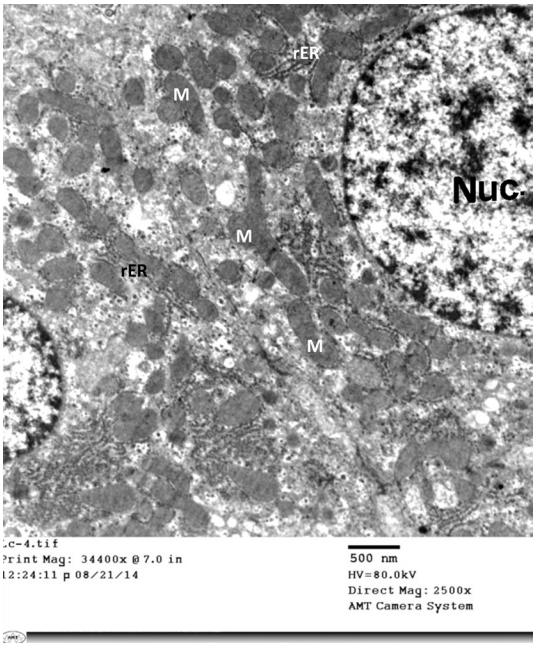

Fig. 13: Electron micrograph of rat liver of group III, showing a binucleated hepatocyte with normal rounded nuclei (Nuc.).The cytoplasm contains normal profiles of rough endoplasmic reticulum (rER), mitochondria (M). (Mag. × 2500).

DISCUSSION

Formaldehyde is used in many fields as in house hold cleaning agents, preservatives, pharmaceutical products and cosmetics. Also it has many medical uses, it is used for cadaver embalming, organ and tissue fixation, disinfection and sterilization procedures, (*Husted & Lentsch 2006 & Olson & Ley 2002*). The maximum authorized concentration of free formaldehyde according to the Council of the European Union (EU) when used as a preservative is 0.2%, (*Lawson et al 2000 & Jaeschke & Smith 1997*). There are no specific regulations concerning its use as an antibacterial for oral hygiene and cosmetic products where the maximum concentration of free formaldehyde may exceed 0.1%, (*Jaeschke 2000*).

The liver was selected in the present study as it is the largest parenchymatous organ in the body, and it is highly vulnerable to toxic injury, due to its role in the detoxification and metabolism, (*Jaeschke et al 2002*). The liver plays a key role in the detoxification of numerous molecules, which results in the formation of an excessive number of toxic reactive oxygen species. This results in oxidative damage to the hepatocytes, which when severe, compromises

the function of this critical organ, (*Chojnacki et al 2014*). The toxic effects of HCHO have been reported to cause hepatocyte affection, and liver pathogenesis, which generally, ranging from reversible degeneration up to irreversible necrosis and replacement of the damaged cells by connective tissue that ends by fibrosis, (*Mukaida & Baba 2012*).

Melatonin is an important immunomodulator and antioxidant agent. It has an ability to work via electron donation to detoxify a variety of reactive oxygen and nitrogen species, including the highly toxic hydroxyl radical, (*Pekmez et al 2008*). So the aim of this study was to investigate the histological changes in the liver of formaldehyde exposed rats and the possible effects of melatonin hormone on these changes.

In the present study the control group with both light and electron microscopic examination revealed normal liver histological aspect both centrilobular and periportal. This is reported by many researchers, (*Burt & Day 2002 & Harada et al 1999*).

Examination of liver cells of group II treated with formaldehyde (0.1%) showed all animals with less preserved hepatic architecture and degenerative changes of the hepatocytes as compared with those of control (group I). EM revealed degenerative changes, the cytoplasm of some hepatocytes with dilated rough ER and dense nuclei. The cells also had many mitochondria with dense matrix and variability in its size and shape. There were many cytoplasmic vacuolation. Moreover, liver sections of animals in this experimental group II (0.1 %) showed variable degrees of cellular infiltration that was periportal as well as between the hepatocytes. In addition, the dilated blood sinusoids were lined by prominent Kupffer cells and the centrilobular hepatocytes showed dense acidophilic cytoplasm and small dense nuclei.

These in agreement with Chargui et al, who explained the vacuolation of cytoplasm in the degenerated hepatocytes might be due to accumulation of fat droplets or due to disturbance of ATP dependent sodium pump at the cell membrane, resulting in accumulation of sodium intracellularly and consequent entry of water into the different cellular compartments which results in cellular swelling, (*Chargui et al 2012*).

Other researchers explained the loss of radial arrangement of hepatocytes, cytoplasmic vacuolization with small dense nuclei, dilated central vein and cellular inflammatory response, were due to hepatotoxins that caused focal hepatocellular necrosis, and cell death, (*Tuzmen et al 2008 & Saiman & Friedman 2012*).

Hepatotoxins, rapidly induces proinflammatory cytokines, such as TNF-α and IL-1β, this inflammatory response, via paracrine production of cytokines as well as chemokines, attract the circulating immune cells, further amplifying an inflammatory response, (*Karlmark et al 2009*). This leading to leukocyte maturation, and activation, (*Kobayashi 2008*).

In the present study light and electron microscopic results of the formalin treated rats showed prominent Kupffer cells in the liver sinusoids. In EM results, the cells showed multiple cytoplasmic processes and irregular heterochromatic nuclei.

Cellular infiltration were detected in the present study and could be attributed to the same causes These were similar to previous works, (*Michael et al 2011*).

Administration of formaldehyde showed histological changes in liver parenchyma of treated rats. These changes in a previous study were clearly evident by substantial augmentation in plasma levels of transaminases that was associated with the severity of the damage, (*Hong et al 2009*). The biochemical changes in animals of group II revealed significant increase in the serum level of aminotransferase as compared to the control (group I). It was documented in a previous study that plasma (SGOT) and (SGPT) were sensitive inductors of hepatocellular damage under oxidative stress, which histologically presented as cytoplasmic vacuolization, (*Wasmuth et al 2010 & Lu & Cederbaum 2008*). In addition, increased activity of hepatic aminotransferases reflects genetic abnormality in their production in order to overcome oxidative stress, (Pablo et al 2009 & Li et al 2012). The determination of plasma (SGOT) and (SGPT) in rats treated with formaldehyde showed a significant increase of SGOT&SGPT after 8 weeks and deduced that the elevated levels of transaminases, which were located primarily in the cytosol of hepatocytes, was a

sign of damage which leads to liver dysfunction in treated rats. (*Bhattacharya et al 2011*)

The histological and biochemical results in the present work are in agreement with results obtained by other researchers. They showed similar changes and they referred these changes to the oxidative stress, (*Lu & Cederbaum 2008 & Li et al 2012*). The histological examination and the liver biopsy is a reliable indicators of chronic liver damage rather than the classical biochemical parameters such as serum aminotransferase activities. (*Usanmaz et al 2002*)

In liver sections of animals (group III) received 2ml of 0.1% of formaldehyde with melatonin (25 mg/kg) diluted in 0.9% of Nacl. The histological structure of most of the animals were similar to the control. Only few animals showed focal degenerative changes that was limited to the periportal zone of the affected lobules more than the centrilobular zones, that showed light and electron microscopic feature like that of the control.

Melatonin is a naturally occurring hormone in the body that is responsible for maintaining sleep. It is used as a supplement to help sleep or to help with jet lag. It is now being studied for more than just sleep functions, as it has potential as an antioxidant, (*Vijayalaxmi et al 2004*).

The hepatoprotective effect of melatonin have been reported to be due to its antioxidant effect that reduces the production and / or accumulation of toxic metabolites. In addition results of another study exhibited that melatonin possesses the highest superoxide radical scavenging activity, (*Pekmez et al 2008*). A variety of antioxidants protect the liver from free radical-mediated damage, the best of them is melatonin. Clinical studies have confirmed the melatonin, as well as it precursor tryptophan, protect the liver from non-alcoholic liver disease, and also during the surgical procedure of partial liver resection, (*Chojnacki et al 2014*). Melatonin has an effective role in combating oxidative stress-induced apoptosis, and liver damage during malaria infection, (*Guha et al 2007*).

In a study published in 2010 in "Free Radical and Biology Medicine," oxidative stress was found to be compounded by a substance called asymmetric dimethylarginine, which inhibits nitrous oxide synthase, an important part of cell structure, and is also responsible for many systemic diseases. The study found that melatonin prevented ADMA increases in rat livers. This information suggests that melatonin may be a potential therapy for different diseases with elevated cellular ADMA, but more research is needed before melatonin can be marketed for this use, (*Vijayalaxmi et al 2004*).

Lipid peroxidation occurs in the liver and is associated with the impairment of protein functions located in the membrane environment, according to an article published in "Current Molecular Medicine" in 2007. Lipid peroxidation can lead to free radical damage in cells, and melatonin has been shown to help reduce peroxidation, (*Guha et al 2007*). A study that focused on melatonin and lipid peroxidation was published in 2010 in "Neuro Endocrinology Letters." It was found that melatonin injections prevented lipid peroxidation in lung cells, particularly peroxidation induced by potassium bromate. The study published in "Current Molecular Medicine" also showed that melatonin was helpful in preventing lipid peroxidation, (*Vijayalaxmi et al 2004 & Longoni et al 1998*).

CONCLUSION

Melatonin has a protective role on the liver that may improve the toxic damaging effect of the formaldehyde on the liver cells.

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تأثير هرمون الميلاتونين على إصابة الكبد الناتجة من الفورمالديهايد في ذكور الفئران البيضاء البالغة: دراسة بالميكروسكوب الضوئى والإلكترونى

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ملخص البحث

خلفية البحث: تأكد أن عموم السكان معرضين لكثير من المنتجات المستعملة يوميا التى تحتوي على الفورمالديهايد. وأظهرت العديد من الدراسات أن المشاكل الصحية الرئيسية التي تؤثر في جميع أجهزة الجسم وخاصة الكبد يسببها الفورمالدهيد وقد أثبتت الدراسات الحديثة أن الميلاتونين مادة مضادة للأكسدة ويمكن استخدامها لعلاج أمراض الكبد.

الهدف من العمل: هدفت هذه الدراسة إلى التحقق من التغيرات النسيجية والكيميائية الحيوية في الفئران المعرضة للفورمالديهايد مع دراسة التأثيرات المحتملة لهرمون الميلاتونين على هذه التغييرات.

المواد والطرق: تمت دراسة ثمانية عشر ذكور الجرذان البيضاء البالغين. وقسمت الحيوانات إلى ثلاث مجموعات متساوية الرئيسية على ستة فئران فى كل منها:

المجموعة الأولى: (مجموعة المراقبة) الفئران أعطيت ماء الصنبور.

المجموعة الثانية: تلقت الفئران 2مل من 0.1 ٪ من الفورمالديهايد.

المجموعة الثالثة: تلقت الفئران 2مل من 0.1 ٪ من الفورمالديهايد مع الميلاتونين (25 ملغ / كلغ) المخفف في 0.9٪ من كلوريد الصوديوم لمدة 8 أسابيع تم ذبح الحيوانات فى المجموعات الثلاثة. وتم تقييم وظائف الكبد بيوكيميائيا ونسيجيا باستخدام كل من المجاهر الإلكترونية والضوئيه.

النتائج: أظهرت الدراسة الحاليه درجات متفاوتة من تأثر الكبد بعد تعرض الفئران للفورمالدهيد فى المجموعة الثانية التى ظهرت فى صوره تغيرات بيوكيميائية ونسيجية، مع زيادة كبيرة فى مستوى البلازما (SGOT) و (SGPT). وأظهرت الفئران المجموعة الثالثة المعالجه بالميلاتونين حفاظ كبيرا على الأنسجة الكبديه.

الاستنتاجات: : الميلاتونين له دور وقائي على الكبد التي قد تؤدي إلى تحسين التأثير السمى الضار للفورمالديهايد على خلايا الكبد.