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Influence of Carcinogenic Substance (7, 12 Dimethylbenz [A] Anthracene (DMBA)) on Tissue, Hematology Character and Enzyme Activity in Rat

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Abstract

This study designed to investigate the effects of 7,12 dimethylbenz [a] anthracene (DMBA)on some blood parameters and hepatic histopathology in rats and antioxidant enzyme. twenty female Wistar albino rats, weighing 180–200 g, were randomly divided into two group 1- DMBA group (positive group) who received 20 mg DMBA/kg body weight/ (single Douse) 2-Control group (negative group) doesn't receive any item. The animals in these groups were sacrificed at the end of the 90 days:The histological structure of the liver tissues in the control group was normal. the liver exhibited hydropic degeneration and coagulation necrosis in hepatocytes, severe dilation in the sinusoids, congestion in the central and portal regions , DMBA groups, was degenerative and necrotic changes were detected.MDA levels increased in the DMBAgroup , compared to the control group, Antioxidant activity CAT, SOD and GPX, the results showed increased enzyme activity in positive control compared with negative groups , ,the hematological parameter was increase in WBC, PLT, GRA, and LYM and decrease in RBC value .

Keywords: *7,12-dimethylbenz[a]anthracene (DMBA); Blood parameters; Antioxidant enzyme ; MDA ; Rat.*

Introduction

Malignant neoplasm, is that diseases in which a crowd of cells illustrate abnormal growth, invasion and sometimes called metastasis [1] .This disease begins in the moment that cells in body start to grow without control [2]. More than 100 kinds of neoplasm are identified [3]. The stimulation of tumors is named carcinogen, that have the capacity to change DNA in behavior that are inherited by daughter cells which called mutagens. Most of these tumors are associated to ecological, life, or expected behaviors [4]. The statement "ecological", as used by cancer investigators, means everything outside the body that reacts with humans [5]. On the other hand some chemicals, like benzene, ketones, vinyl chloride, ethylene bromide, and dichloro-diphenyl-trichloroethane (DDT), known as carcinogens [6]. When multiple factors are accumulated, altered genes and carcinogens change a normal cell into a cancerous one. Carcinogens which promote cancer have various precursors [7]. exogenous and endogenous factor lead to cause Cancer development [8] such as nutritional habits (food preservation and preparation), socio-economic status, way of life, physical agents (ionising and non-ionising radiation), chemicalcompounds (natural and synthetic) and biological agents (Helicobacter pylori, Epstein Barr virus, human T lym-photropic viruses I and II, human papilloma virus and thehepatitis B virus [9].

Material and Method

Experimental animals and Tumor induction in rats:

Twenty female of Wistar albino rats and aged between (7-8) week were weighing between 150 – 250 g used in this study. All they were kept in ventilated cages, with temperature of 25±2C°. A 12:12 h light:dark cycle is regulated for the animals. Balanced rodent food and water is provided. The rats were randomly assigned to 2 groups, every group of 10 rats.

The following groups:

Group 1: Taking one dose of DMBA (positive control) 20 mg DMBA/kg body weight/ (single dose)

Group 2: Did not received any treatment (negative control).

DMBA administration :breast cancer that induced by 7, 12-

Dimethylbenz (a) anthracene (DMBA) [10]. One dose of DMBA dissolved within corn oil and given orally to each groups with the syringe and needles. DMBA was taken from Sigma Aldrich and melted in corn oil. The concentration of the mixture was 20 mg DMBA per 1 ml corn oil for each rat [10] .

Preparation of tissue sample

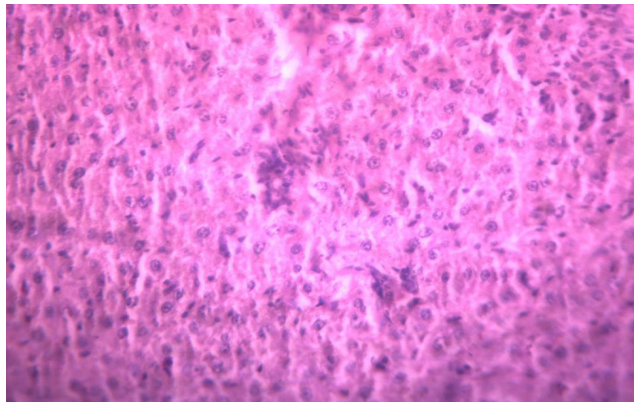
The liver was exteriorized and excised. All samples in the same time fixed in 10% formaldehyde. And then they processed in known method, and placed in paraffin for histopathological testing for liver. A scoring system (of no abnormalities, mild, moderate, severe) was used to classify the liver changes according to the severity of the damage and extent of histological changes. The histological sections were evaluated by a pathologist without prior knowledge of the treatment given to the animals [11].

Blood parameters were determined in whole blood by the applying rat method of veterinary practice with a blood cell counter (Abocus Junior Vet-5, Austria). Measurements of biochemical parameters were made with a Modular PP autoanalyzer (Mindray BS800, China).

Result

Histopathological findings: In the DMBA group, the livers exhibited dilatation of the sinusoids, cholangiohepatitis in the portal region, and congestion in the sinusoidal and portal regions (Figure 1A). The control group showed normal histological structure in the liver tissue (Figure 1B).

hematological parameters also change in negative group compared of positive group Table 1 , in positive group : white blood cell (WBC) , LYM, MON ,GRA and PLT while other parameter such as RBC was decrease. The state of free radicals and antioxidants is given in Table 2. As seen in Table 2, the levels of MDA increased in liver groups in compare with control group, also SOD, GSH-Px, CAT, and GSH values decreased .



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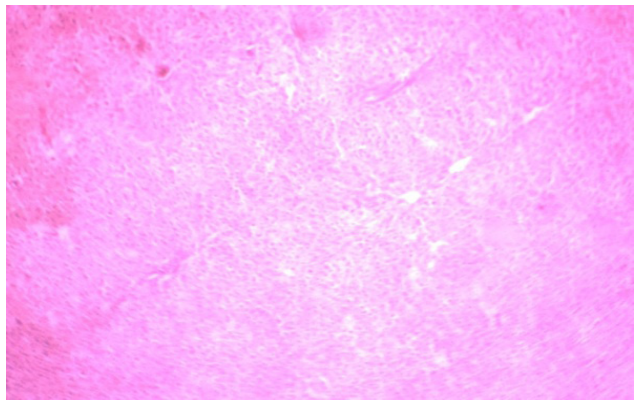

B

Figure1; A:DMBA group showing colangiohepatitisin portal region, mild dilation in sinusoids, hyperemia, and hydropic degeneration in hepatocytes;

B: manage group viewing liver tissue with a normal histological structure

Table 1. Some hematological parameters in the groups (values are mean n=4)

No.	Parameter	Negative control	Positive control
1	WBC(103 /mm3)	8.2	15.1
2	RBC(103 /mm3)	8.8	1.4
3	LYM %	67%	78.5 %
4	MON%	1	0.9
5	GRA %	18.8 %	94 %
6	MCV(fl)	56.6	58.7
7	MCH(Pg)	16	21
8	MCHC(g/dl)	32.3	32.8
9	PLT(105 /mm3)	338	737

Table 2. Some biochemical parameters in the groups (values are mean n=4)

Treatments	Conc. of GPx(IU/mg)	Conc. Of SOD(IU/mg)	Conc. of CAT(IU/mg)	Conc. of MDA(nmol/mg)
Negative group	127	458	122	134
Positive group	312.3	567	187	267

Discussion

7, 12-dimethylbenz (α) anthracene (DMBA) is a famous carcinogen and immunosuppressor used in rodent model to learn tumor[12]. DMBA is report to make mutations by creation DNA adducts [13, 14]. while, it is a well known skin carcinogen, however lots of researchers have reported the harmful result of DMBA in liver [15, 16]. Liver is the main site of metabolism and is frequently prone to injure by xenobiotics. obviously, liver cancer is the second most general source of cancer deaths universal [17].

a number of haematological and haematochemical parameters were altered when treated with DMBA and establish that DMBA caused hepatocellular carcinoma. new studies showed that DMBA-induced skin, oral, mammary and ovarian tumors [18].

The carcinogenic and mutagenic effect of DMBA needs to its metabolic activation by mixed gathering oxidases. The hydroxylation of DMBA at 7-methyl collection is a critical step towards its carcinogenesis [19]. additional metabolism of DMBA leads to development of a large range of metabolites with changeable toxicity. along with these, trans-3,4-dihydrodiol-1,2-epoxide is the carcinogenic result of DMBA [20, 21]. The metabolic products of DMBA, when present within body, hampers ROS-antioxidant balance by overproduction of free radicals and the body go round reacts by modulating activities of antioxidant enzymes to control the destructive effects of an enlarged ROS [22].

Hematological and biochemical parameters may be affected by a variety of factors such as race, age, gender, pregnancy, lactation, muscular activity, region, season, environmental heat, maintenance, and nutrition. In the present study, the effects on blood parameters and hepatic, histopathology of fluoride .

Oxidative products derived as of mutagen metabolism , for instance DMBA , might impair critical cellular function by damage proteins and lipid membranes . therefore , these alterations induced by the chemical carcinogen 7,12-dimethylbenz[a]anthracene, have been reported to be leukemia, and the growth of anemia [23] .Reactive oxygen species (ROS) are significant as pathological agents for numerous diseases. Increased oxygen radical production and lipid peroxidation are connected with the pathogenesis of lots of diseases and the toxic effects of a wide range of compounds increase in whole leukocyte count (WBC), eosinophil, neutrophil and monocyte values for rats exposed to DMBA was also reported by [24].

Hematological and biochemical parameters may be affected by a variety of factors such as race, age, gender, pregnancy, lactation, muscular activity, area, season, environmental heat, maintenance, and nutrition.

a significant increase in the GPX, CAT, SOD level in rat treated with DMBA only was reported by [25]. On other hand [26] find MDA substance increase significantly with rat treated with DMBA only.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the University of Warith Al-anbiya'a , Iraq, Iraq and all experiments were carried out in accordance with approved guidelines.

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