Amygdalin and magnetic water ameliorate histological changes in liver induced by 1, 2 dimethyl hydrazine

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Summary

This study aimed at evaluating the ameliorative effect of amygdalin and magnetic water on 1,2-dimethyl hydrazine induced toxic damage in tissues and oxidative stress in rat liver. Seven groups of ten rats each were selected for the study. Group I animals were treated as control. Group II rats received 1,2-dimethyl hydrazine (20 mg/kg body weight) injections subcutaneously once a week for 16 consecutive weeks and then kept without any treatment untill the end of the experimental period. Group III rats received amygdalin (20 mg/100 mg) daily via Oro-gastric tube. Groups IV rats were given magnetic water freely. Group V rats were given 1,2-dimethyl hydrazine + amygdalin. Group VI rat were given 1,2-dimethyl hydrazine + magnetic water Group VII rats were given 1,2-dimethyl hydrazine + amygdalin + magnetic water. Liver histological changes were studied. Degenerative changes were observed in different areas of liver tissue in 1,2-dimethyl hydrazine group, and these changes include: Fibrosis with the appearance of cell necrosis, hemorrhage, fatty infiltration and pleomorphic nuclei. While other groups showed normal appearance of the hepatic cells but some changes were observed in 1,2-dimethyl hydrazine + amygdalin + magnetic water group include: Fibrosis with the appearance of cell necrosis, hemorrhage, fatty infiltration and pleomorphic nuclei but changes in this group were less than in 1,2-dimethyl hydrazine group. In conclusion, the present results suggest that the amygdalin and magnetic water have the potential to ameliorate carcinogen 1,2-dimethyl hydrazine induced hepatotoxicity by antioxidant and antiinflammation activity.

Keywords: Amygdalin, Magnetic water, 1,2-dimethyl hydrazine, Rat liver.

Introduction

1,2 Dimethylhydrazine (DMH) is a potent colon carcinogen, inducing colorectal tumors in experimental animals (1 and 2) and is the most widely used model of chemically induced colon carcinogenesis. 1,2-dimethylhydrazine (DMH) induce oxidative stress to both liver and colon tissues (3). Liver is a major organ in which most of the chemicals, drugs and carcinogens undergo metabolism (4). Active metabolite of DMH is metabolized in liver to form azoxymethane and methylazoxymethanol which is further transported to colon via bile or blood to generate its ultimate carcinogenic metabolite, diazonium ion which elicits an oxidative stress by methylating biomolecules of colonic epithelial cells and leads to promutagenic events as a result of inflammation and tumor promotion (5). Amygdalin is a natural compound whose anticancer, anti-inflammatory activity and other medicinal benefits have been known for many years. It is a major component of the seeds of prunasin family plants, such as apricots, almonds, peaches, apples, and other rosaceous plants. Amygdalin is composed of two molecules of glucose, one of benzaldehyde, which induces an analgesic action, and one of hydrocyanic acid, which is an anti-neoplastic compound. It has been used as a traditional drug because of its wide range of medicinal benefits. Amygdalin can be used in medicine for preventing and treating hypertension, chronic inflammation and other reaction source diseases (6). The body consists mainly of water and all living process are strongly dependent on water, which is secret of life that leads to investigate the possibility of improving quality of water by passing it through a magnetic field with different devices and strength. This water treatment process has small installation fees, no energy requirements and creates no pollutants **(**7**)**. The structure of the water is more stable and the ability of the water molecules to form hydrogen bonds is enhanced when a magnetic field is applied. In addition, the behavior of the water molecules changes under the influence of a magnetic field (8). Since magnetic field has an impact

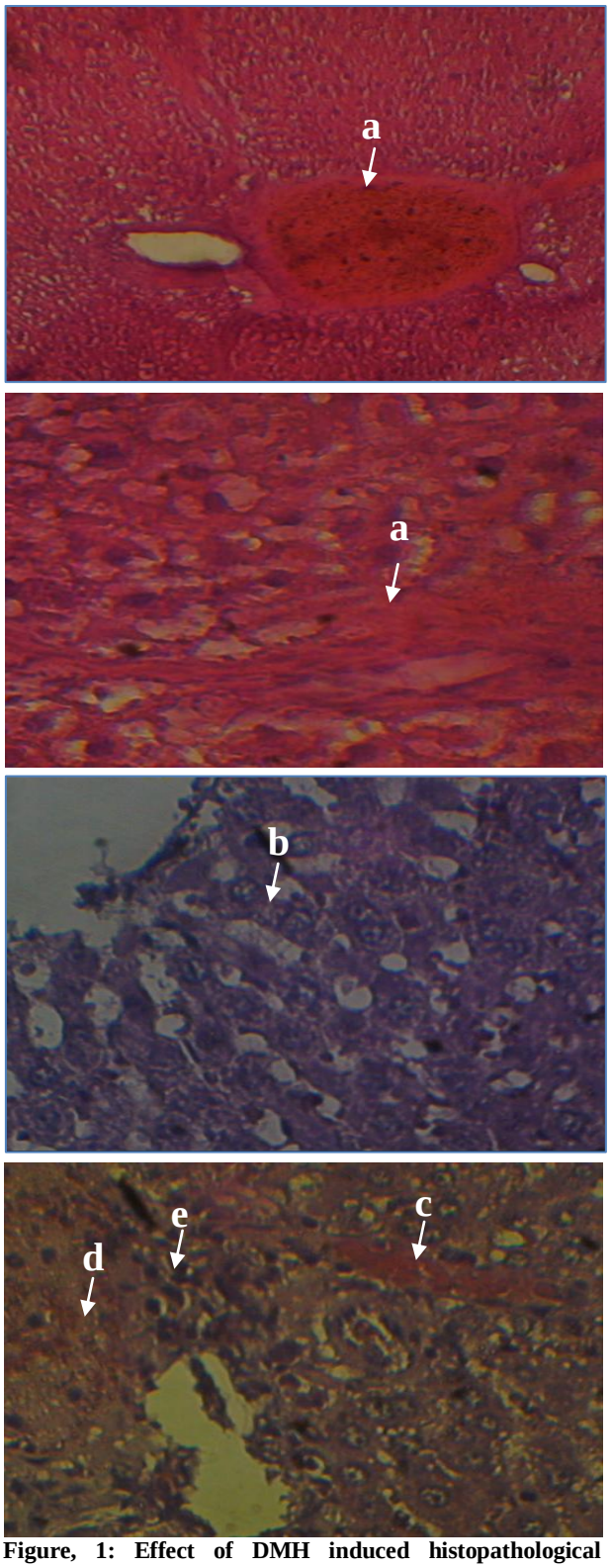
on biochemical reactions that involve more than one unpaired electron, superoxide dismutase (SOD), one of the enzymes responsible for antioxidant system, was measured under magnetic fields. There has been a significant increase of SOD activity when passed 0, 1, 9 and 15 times at 2.9-4.6 mT magnetic field density for 0, 2.2, 19.8 and 33.0 seconds respectively **(**9**)**.

Materials and Methods

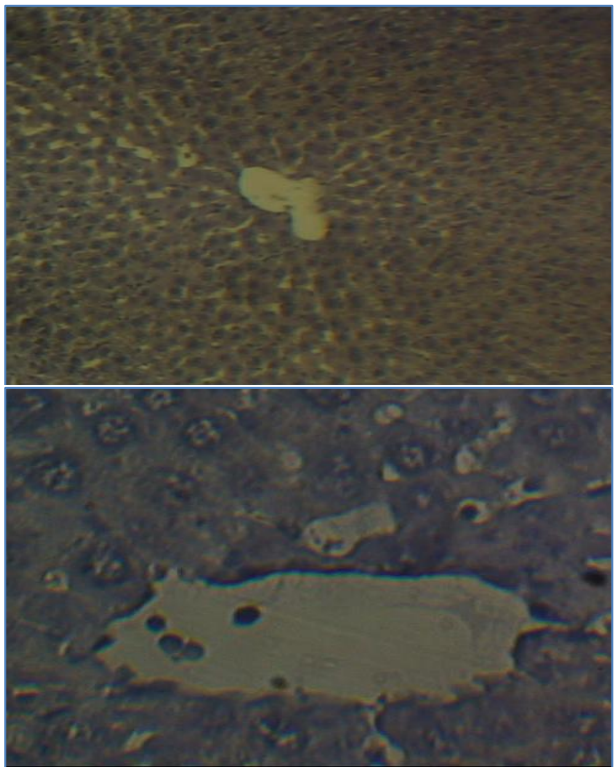
Albino rats were purchased from Pharmacology College/ Baghdad University. Amygdalin isolation in ministry of science and technology from apricot kernel. Water was magnetized in laboratory by passing through magnetic field for three hours. Seventy prepubertal albino female rats were used in this study; they were weighed and randomly divided into seven groups as follows: Control group were treated with distal water. DMH group was given subcutaneous injection 20 mg/kg 1,2-dimethylhydrazine weekly for 16 week. Amygdalin (Amg) group was given 20 mg/100 mg amygdalin daily via Oro-gastric tube. Magnetic water (M.W.) group was given magnetic water freely. DMH+Amg group was given 1,2-dimethylhydrazine and amygdalin. DMH+ M.W. group was given 1,2-dimethyl hydrazine and magnetic water. Finally, DMH+ Amg+ M.W. group was given 1,2-dimethyl hydrazine, amygdalin and magnetic water. DMH was dissolved in 1mM EDTA just prior to use and the pH adjusted to 6.5 with 1mM NaOH and administered subcutaneously in the right thigh of rats at a dose of 20 mg/kg body weight once a week for the first 16 consecutive weeks. All animals were sacrificed at end of experimental period of seven month. Small pieces of liver tissues fixed in fifteen percent buffered formalin were processed for embedding in paraffin. Sections of 4–5 µm were cut and stained with hematoxylin and eosin and examined for histopathological changes.

Results and Discusion

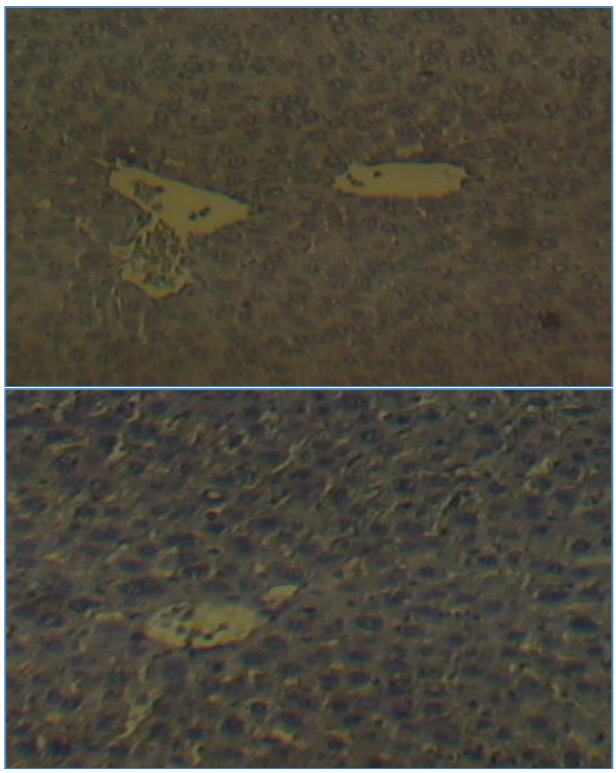
Rats treated alone with DMH (group II) showed significantly histological changes in liver, including fibrosis (a), with the appearance of cell necrosis (b), hemorrhage (c), fatty infiltration (d) and pleomorphic nuclei (e) (Fig. 1). While other groups showed normal appearance of the hepatic cells and normal architecture pattern (Fig.2 and 3). Although, some histopathological changes were observed in DMH+Amg+M.W. group include: Fibrosis with the appearance of cell necrosis, hemorrhage, fatty infiltration and pleomorphic nuclei but changes in this group were less than in DMH group (Fig. 4).



Figure, 1: Effect of DMH induced histopathological changes in rat liver tissue of DMH group.

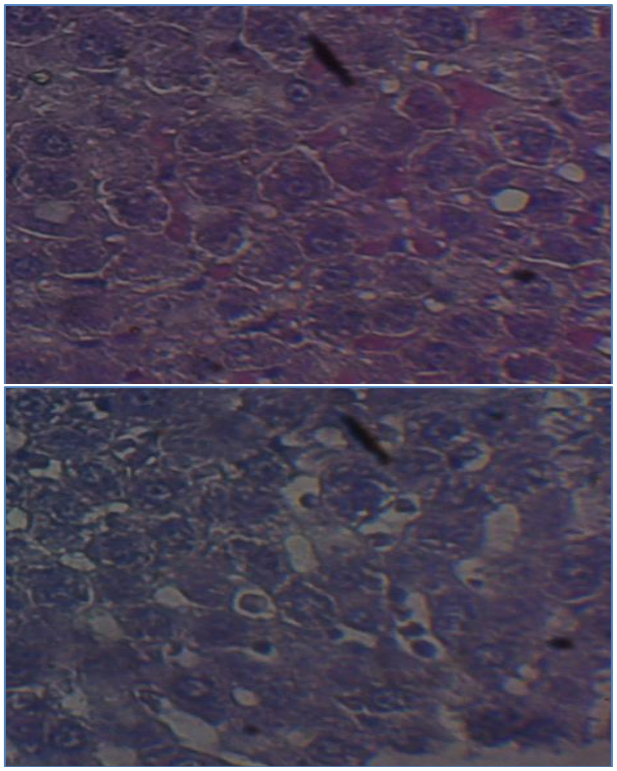


Figure, 2: Left: Liver of amygdalin group, Right liver of magnetic water group. (Normal)



Figure, 3: Left: Liver of DMH+Amg group , Right liver of DMH+M.W group. (Normal)

1,2-dimethylhydrazine (DMH) induce oxidative stress to both liver and colon tissues (3). In the present study, subcutaneous injection of DMH (20 mg/kg body weight) once a week for 16 consecutive weeks led to hepatic damage, which has been proven by the significant histopathological changes, include necrosis, fibrosis and fatty infiltration. These results agree with results (10).



Figure, 4: Liver of DMH+Amg+M.W group. (Fibrosis, necrosis, hemorrhage and polymorphic nuclei).

DMH is metabolized in the liver into methylazoxymethanol (MAM), which is catalyzed by the enzyme cytochrome P450. Metabolic activation of MAM to highly reactive carcinogenic electrophiles (methyl-diazonium ion and carbonium ion) occurs in the liver and colon, which is known to elicit oxidative stress (11). Antioxidant and detoxification enzymes can block necrosis by acting as inhibitors to oxidants. Hence, enhancement of these enzymes by a natural or synthetic component might result in the amelioration of carcinogen induced hepato -toxicity and inhibition of extra hepatic tumorigenesis (12). Amygdalin could be used as antianflammation and anticancer in body. In addition to other medicine benefits (6). Study reported that magnetic field increase SOD enzyme (antioxidant) **(**9**)**. Magnetic water do as antioxidant (13). Treatment with each amygdalin and magnetic water produced a better results in liver tissues than amygdalin with magnetic water in same time, show the response action of the against DMH induced increase of fibrosis, necrosis, fatty changes and

polymorphic nuclei. This could be related to the interaction between amygdalin and magnetic water assist to hepatic tissue damage due to DMH.

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تحسين الامكدالين والماء الممغنط للتغيرات النسجية للكبد المعرض للمركب ثنائي مثيل الهيدرازين

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الخلاصة

تهدف هذه التجربة إلى دراسة التأثيرات العلاجية المفيدة للامكدالين والماء الممغنط لتثبيط الجهد التأكسدي الذي يولده المركب المسرطن ثنائي مثيل الهيدرازين في كبد الجرذ مما يؤدي إلى تغيرات نسجية. استعمل سبعين جرذاً من الإناث وُزّعت توزيعاً عشوائياً متساوياً على سبع مجموعات، وكانت على النحو الآتي: مجموعة السيطرة (المراقبة) ومجموعة المركب المسرطن ثنائي مثيل الهيدرازين فقط ومجموعة الامكدالين فقط ومجموعة الماء الممغنط ومجموعة المركب المسرطن والامكدالين معاً ومجموعة المركب المسرطن والماء الممغنط معاً وأخيراً مجموعة المركب المسرطن والامكدالين والماء الممغنط معاً. حُقِنَ المركب المسرطن ثنائي مثيل الهيدرازين تحت الجلد اسبوعياً بتركيز 20 ملغم/كغم (جرعة/وزن) في الجرذ على مدى 16 أسبوعاً متتابعاً، أما مركب الامكدالين فقد جُرّع في الحيوانات عن طريق انبوب المعدة تجريعاً يومياً وبمقدار 20 ملغم/100ملغم (جرعة/وزن)، أخيراً الماء الممغنط فيعطى بدل ماء الشرب إعطاءً مستمراً. استمرت التجربة لمدة سبعة أشهر، قُتِل بعد ذلك الحيوان واستؤصل الكبد لدراسة التغيرات النسجية. أظهرت النتائج النسجية للكبد وجود تغيرات نسجية واضحة إذ اتصف النسيج الكبدي بالتنكس وتليف اجزاء من الكبد كما اظهرت النتائج وجود ارتشاح دهني في خلايا الكبد في مجموعة الحيوانات المعاملة بالمركب المسرطن ثنائي مثيل الهيدرازين ولم تُلحظ هذه التغيرات في باقي مجاميع التجربة إلّا في مجموعة الحيوانات المعاملة بالمركب المسرطن والامكدالين والماء الممغنط معاً إذ لوحظ في هذه المجموعة وجود تنكس في الخلايا ووجود تليف وارتشاح دهني ولكن بصورة اقل مما هو عليه في مجموعة الجرذ المعاملة بالمركب المسرطن. واخيراً يوصى بإستعمال كل من الامكدالين والماء الممغنط كمضادات للأكسدة او كمحفزة للمركبات المضادة للأكسدة أو كمضادة للالتهابات وحماية انسجة الجسم من الإجهاد التأكسدي.

الكلمات المفتاحية: الامكدالين، الماء الممغنط، ثنائي مثيل الهيدرازين، كبد الجرذ.