Histopathological Study of Amoxicillin Drug Derivative on Rats Treated with Sodium Nitrite.

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الملخص:

الخلفية: نيتريت الصوديوم يؤثرعلى الثدييات وموثق بأن له تأثير سمي على الكبد ويقلل المعاييرالكيميائية الحيوية للكلية وهذا يعكس الضررالحاصل في الكلية.

الهدف: التحري عن التأثيرالسلبي لنيتريت الصوديوم وامكانية تحسين هذا التأثير من خلال مشتق الأموكسيسيلين على الجرذان المختبرية.

المواد وطرق العمل: تم أستخدام ٢٤ من ذكور وإناث الجرذان المختبرية وقد قسمت إلى أربعة مجاميع متساوية. المجموعة الأولى: مجموعة السيطرة وقد تم حقنها يوميا في غشاء الجدارالبطني بمادة DMSO وبتركيز ٠,٥مل ولمدة ١٥ يوم. المجموعة الثانية: وقد تم حقنها يوميا في غشاء الجدارالبطني بنيتريت الصوديوم المذاب في ٠,٥ مل من الماء المقطر وبجرعة ١,٤٢٨ملغم / كغم ولمدة ١٥ يوم. المجموعة الثالثة: وقد تم حقنها يوميا في غشاء الجدارالبطني بعُشر الجرعة النصف قاتلة من المركب المصنع. المذاب في٠,٥ مل من DMSO وبجرعة ٨,٢١٣ ملغم / كغم ولمدة ١٥يوم. المجموعة الرابعة: وقد تم حقنها يوميا في غشاء الجدارالبطني بنيتريت الصوديوم المذاب في ٠,٥مل من الماء المقطر وبجرعة ١,٤٢٨ ملغم /كغم وبعد ساعة تم حقنها في غشاء الجدارالبطني بعُشرالجرعة النصف قاتلة من المركب المصنع المذاب في ٠,٥ مل من DMSO وبجرعة ٨,٢١٣ ملغم / كغم ولمدة ١٥ يوم.

النتائج : تقييم تأثيرنيتريت الصوديوم النسيجية المرضية على الكبد للجرذان المعاملة بنيتريت الصوديوم اشارت الى احتقان وتنخروكذلك التهاب فيه بينما الكلية حدث فيها تنخرواحتقان بالمقارنة مع مجموعة السيطرة ومن جهة ثانية اظهرت نتائج ايجابية للكبد والكلية للمجموعة المعاملة بالمركب المصنع.

ABSTRACT:

Background: Sodium nitrite effects on the mammals which documented to be hepatotoxic and decrease the biochemical parameters of kidney which reflects the damage occurring in kidney.

Objective: To investigate the effect of sodium nitrite and the possible ameliorative effect of amoxicillin derivative on rats.

Material and Methods: 24 adult male and female rats were divided into 4 groups, group 1 received dimethyl sulfoxide (DMSO) intraperitonially (IP) at dose 0.5 ml for 15 days, second group treated with sodium nitrite ($NaNO_2$) with (0.5ml) at dose of (1.428 mg/kg). Third group: rats treated with (1/10 LD50) of synthesized compound by (0.5ml) at dose of (8.213 mg/kg), while fourth group treated with ($NaNO_2$) at dose of (1.42 mg/kg) then after 1 hour. Rats were injected with synthesized compound at dose (8.213 mg/kg) for 15 days. All groups were injected (IP).

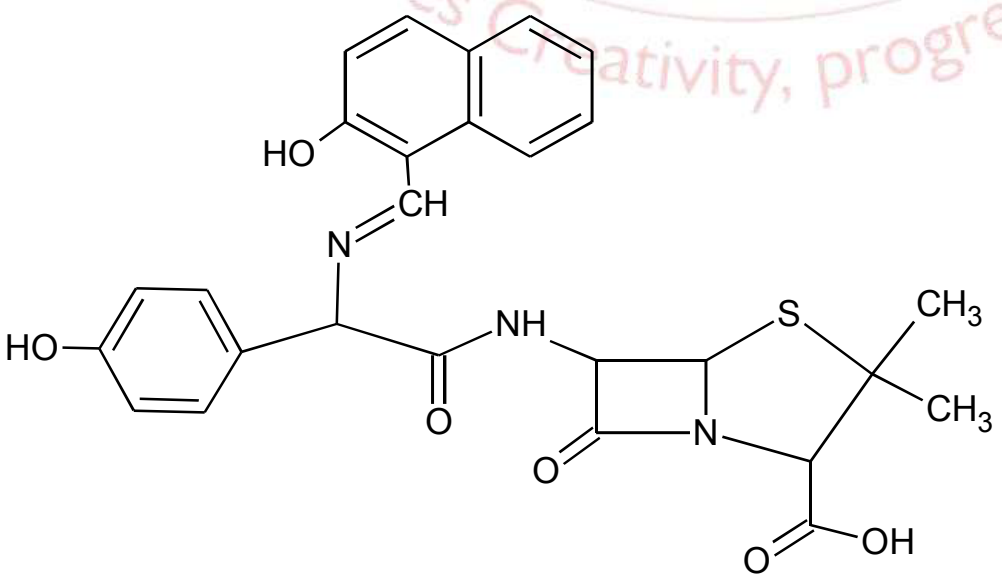
The results: Histopathological evaluation of liver of nitrite exposed rats indicated that there was congestion, necrosis and inflammation while the kidney that group had necrosis and congestion in comparison with the control group. On the other hand the liver and kidney which was treated with synthesized compound showed positive effects.

Key words: *Amoxicillin, Histo-pathological study, Hepatotoxicity, Sodium nitrite, Oxidative Stress.*

INTRODUCTION:

Sodium nitrite ($NaNO_2$) is widely used in the food industry as color fixative and preservation of fish and meat products also the ($NaNO_2$) has been in human and veterinary medicine as hypoxia potentiate vasodilators in ischemic condition [1] and used as a pharmacological agent in poisoning with cyanide [2]. The presence of amines in the food causes the reaction with nitrites to form potentially cytotoxic and carcinogenic nitrosamines [3]. The nitrites and nitrates are environmental pollutants present in food and water, and it's suggested that they may contribute to the etiology of liver and kidney disease and problems related to immunity in domestic fowls [4]. The other effects of ($NaNO_2$) on the mammals which is documented to be hepatotoxic and decrease the biochemical parameters of kidney which reflects the damage occurring in kidney [5]. The present work describes the effect of amoxicillin modified [6] on rats which treated with sodium nitrites.

AIM OF STUDY: To investigate the effect of sodium nitrite and the possible ameliorative effect of amoxicillin derivative on rats.



Scheme 1: Chemical structure of amoxicillin derivative [6].

MATERIALS AND METHODS:

Preparation of animals: Twenty four adult rats male and female were divided into four groups as following:

First group: considered as control group received 0.5 of DMSO (IP) for 15 days.

Second group: rats were injected (IP) by $NaNO_2$ with 0.5 ml at dose of (1.428 mg/kg) for 15 days.

Third group: rats were injected (IP) by a synthesized compound with (1/10 LD50) at dose of (8.123 mg/kg) at the same period. At the end of experiment, the liver and kidney were isolated for the histopathological examination.

Fourth group: rats were treated with ($NaNO_2$) at dose (1.42 mg/kg) then after one hour treated with new compound at dose (8.123 mg/kg).

Histological Analysis: Rats of each group were scarified at 15 days. The liver and kidney were excised and fixed in (10%) formalin, dehydrated in ascending concentration of ethanol, paraffin sections were stained with haematoxyline and eosin [7], and the histological changes studies.

RESULTS:

Histopathological examination in Fig. 1 show normal liver of control group, hepatocyte are arranged in hepatic cord radiating from central vein toward the periphery of lobule, the hepatocyte cords are separated by sinusoid, ($NaNO_2$) causes congestion, necrosis and inflammation in Figs.2 and 3 respectively.

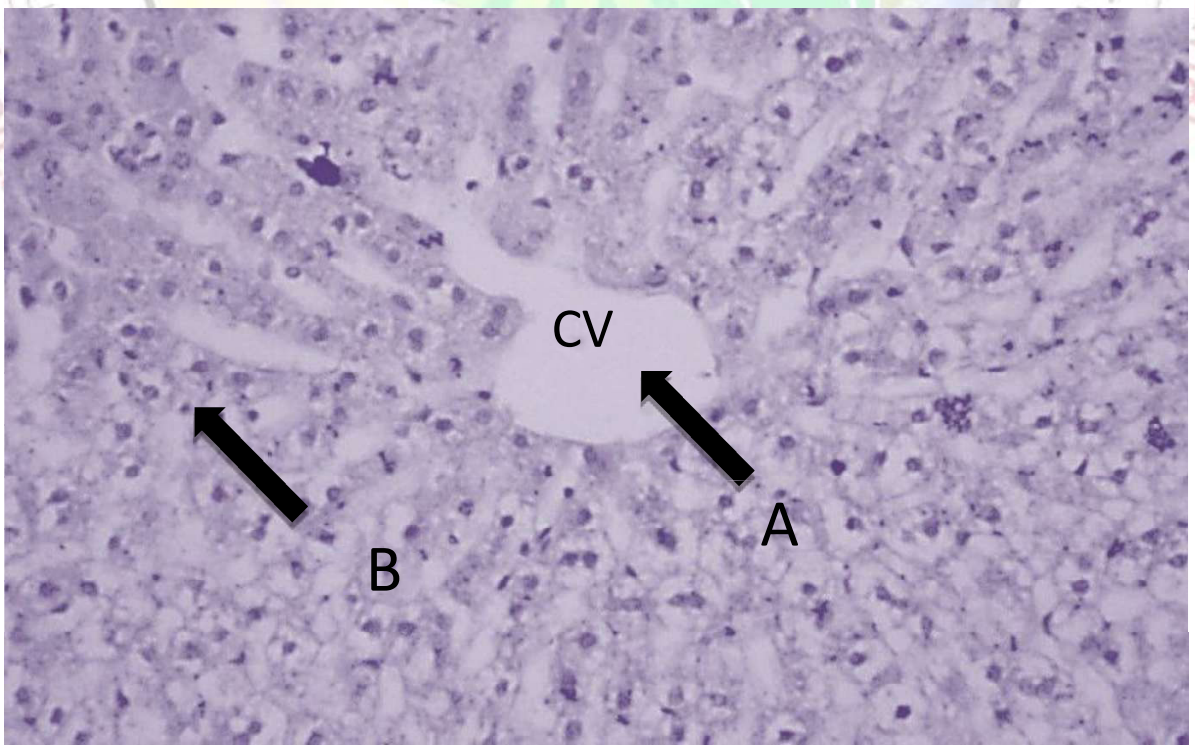


Fig. (1): Transverse section in the liver of the Control Group (C) shows a normal central vein (CV) A and normal hepatocytes (HC) B (H&E, 40x).

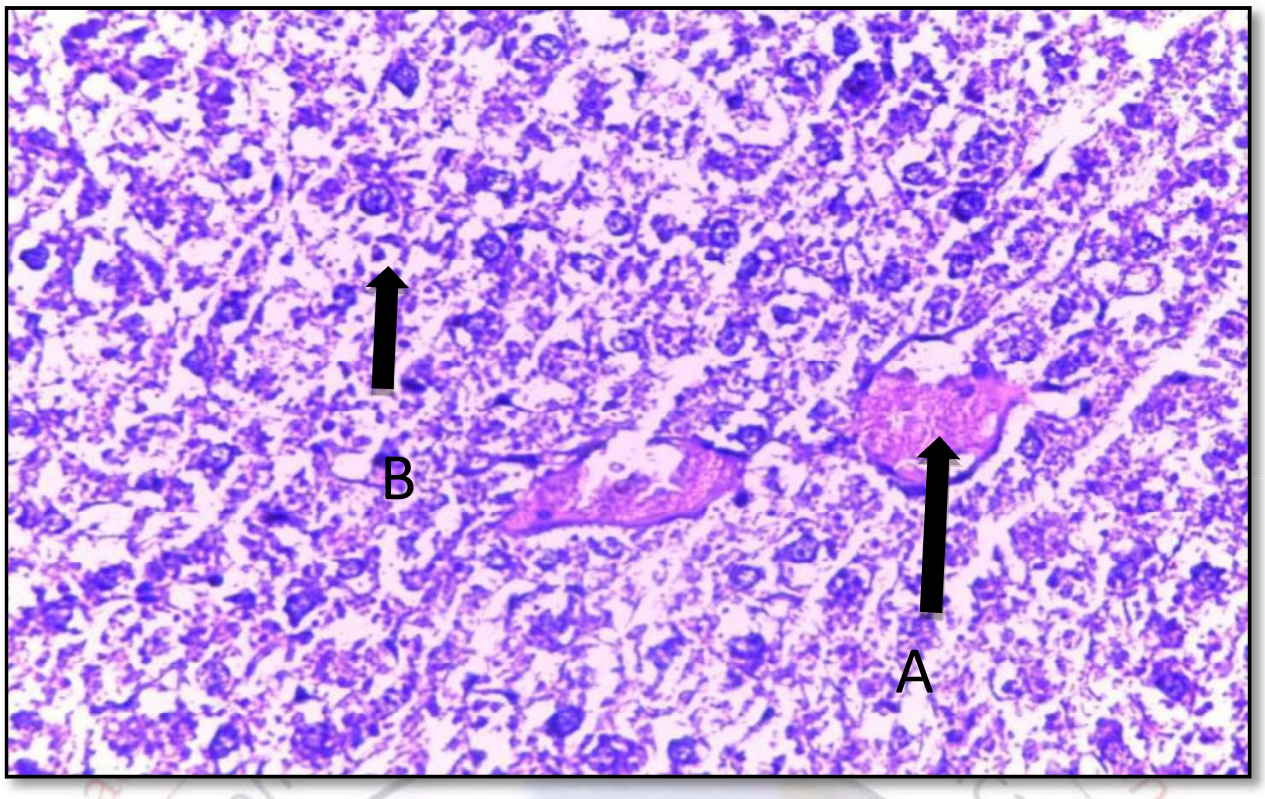


Fig (2): Cross section of liver in rat exposed to (NaNO2) showing congestion (A), necrosis of hepatocytes (B). (40X, H&E).

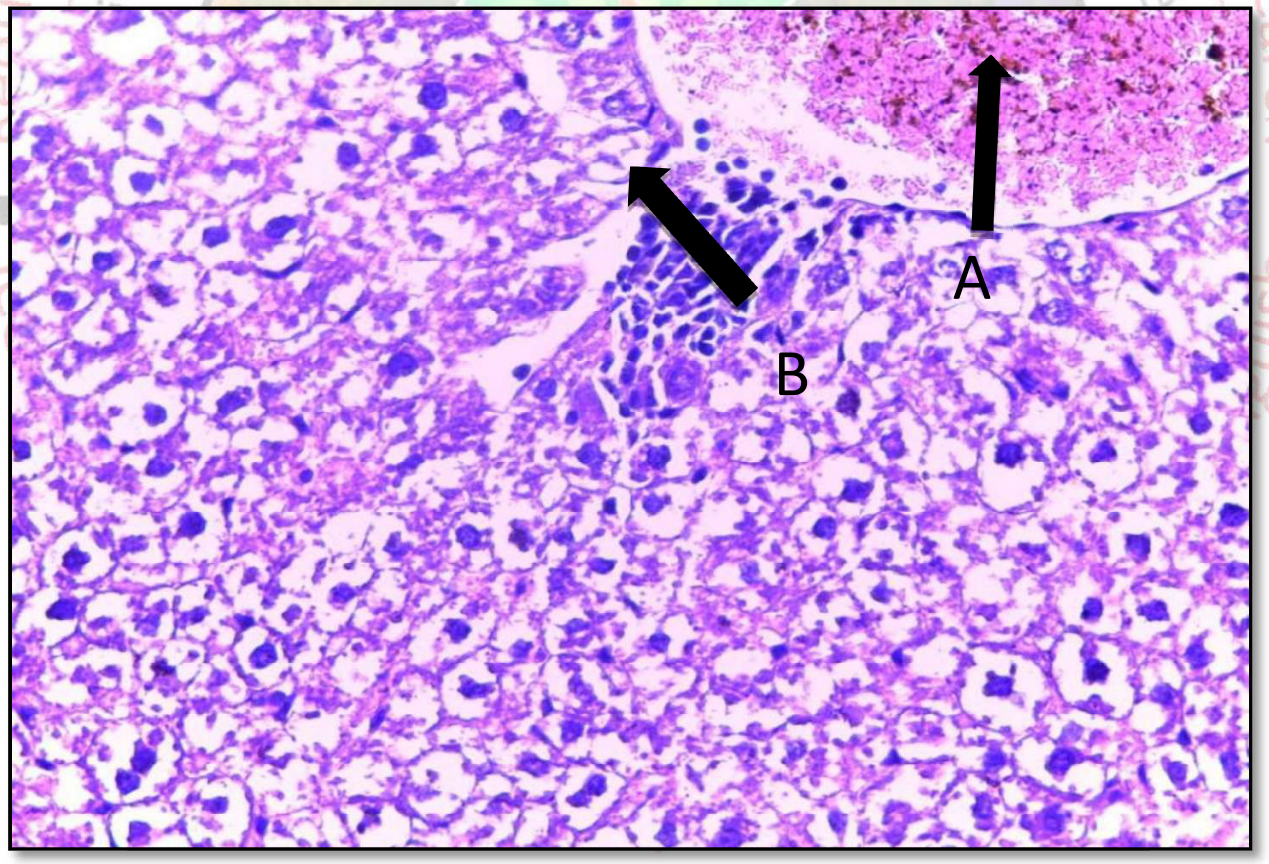


Fig (3): Cross section of liver in rat exposed to ($NaNO_2$) showing congestion (A), Inflammation (B). (40X, H&E).

Microscopically histopathological examination of kidney in Control group showed in Fig.4, normal glomerulus and normal renal tubules, while the rats treated with $NaNO_2$ for 15 days showed alteration of renal tissue such as necrosis and congestion as shown in Fig.5 and when the synthesized compound was administered after one hour of

$NaNO_2$ it exerts a very clear effect when the liver and kidney tissue is near or like control.

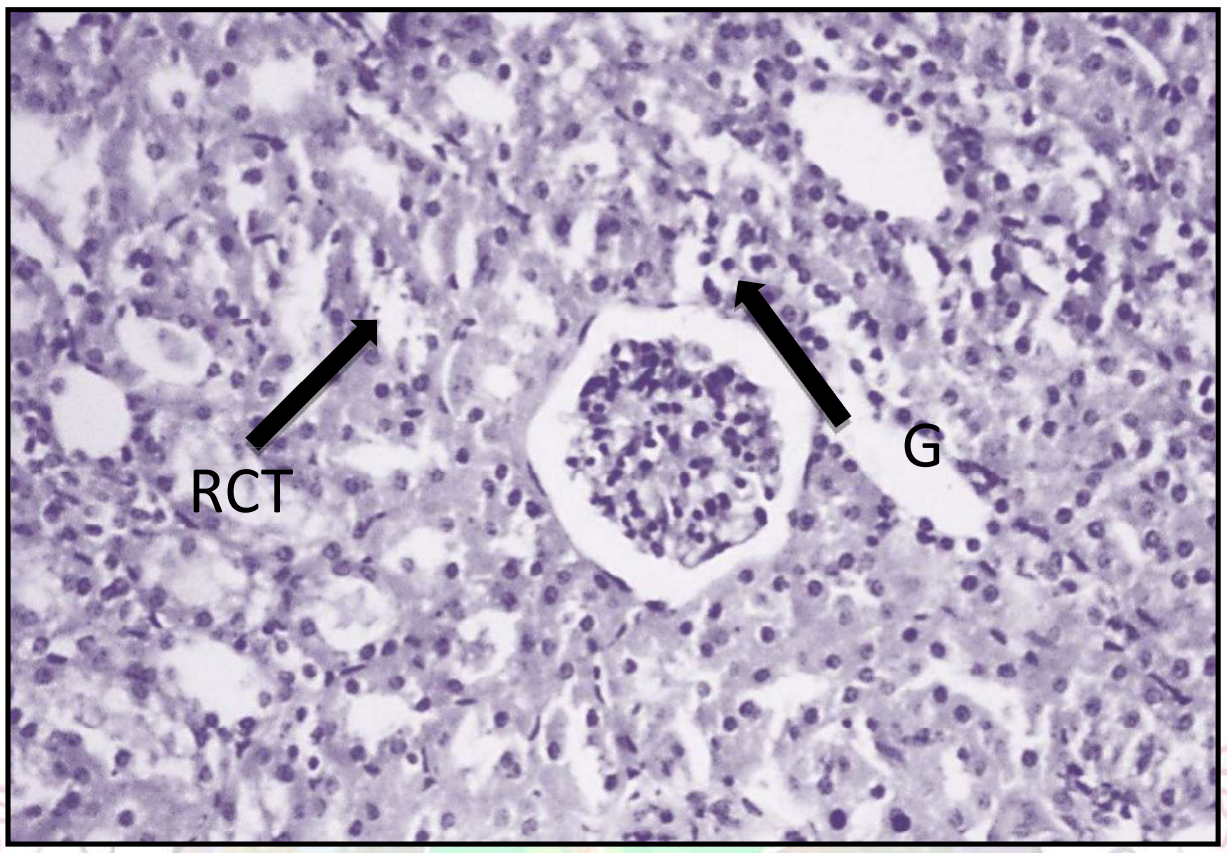


Fig.(4): Transverse section in the Cortex of kidney of Control Group (C) show normal Glomrulus (G) and normal Renal Cortical Tubules (RCT). (H&E, X40)

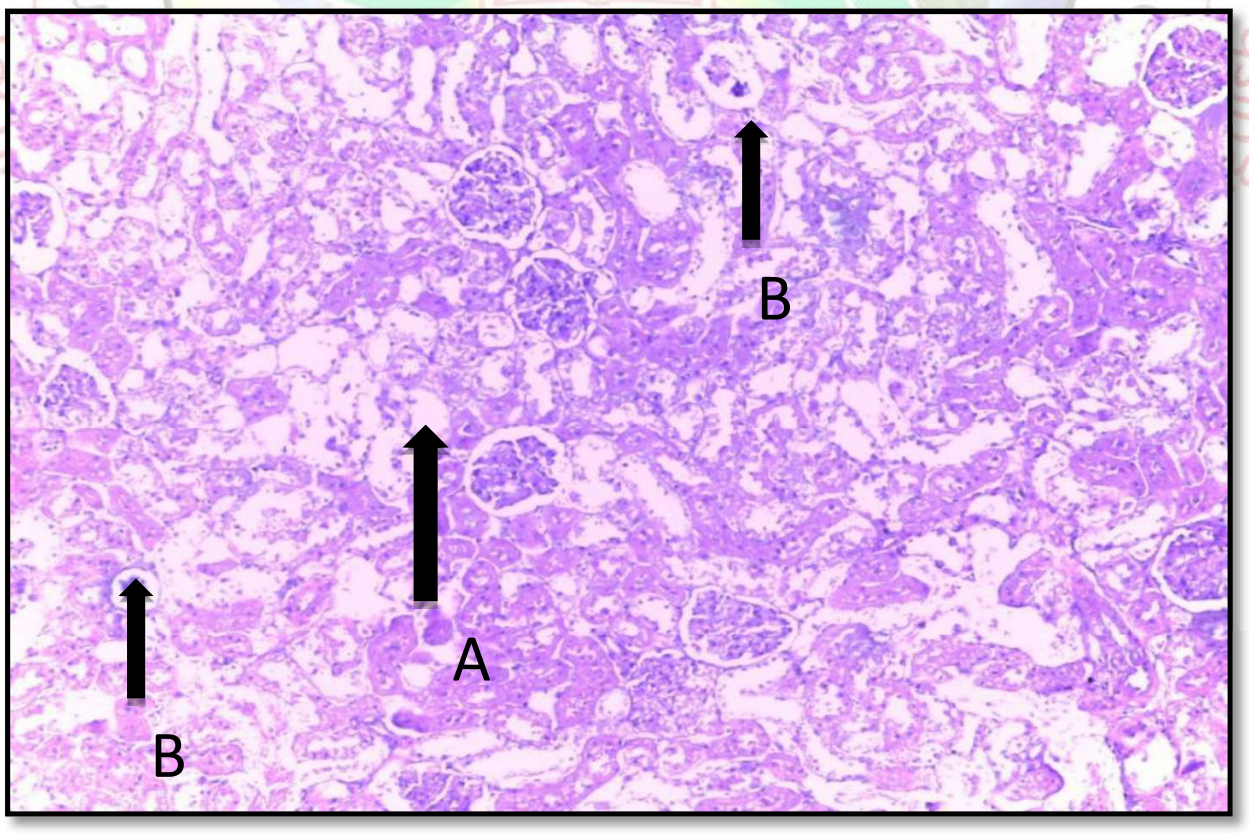


Fig (5): Cross section of kidneys in rat exposed to (NaNO2) showing necrosis of tubules (A), atrophy of glomerulus (B) (10X H&E).

DISCUSSION:

Histopathological finding of tissue showed significant histological changes in organs (liver and kidney) after 15 days post sodium nitrite treatment. The effect of $NaNO_2$ was very obvious and deleterious on the liver such as congestion, necrosis and inflammation [8]. The disturbances in the liver histopathology reflect the heavy toxic effect [9]. Observed the dilation of the blood vessels to the direct toxic effect of toxin. This agrees with Aziz [10] who mentioned that the hepatic congestion as a result from the direct effect on the blood vessels wall or the feedback of pressure inside the portal area.

In the present study the rats were treated with $NaNO_2$ causes necrosis in the hepatocytes, this accordance to [11] the necrosis lesion might be the rupture of lysosome that led to amorphous eosinophilia cytoplasm as initials in the sequence of hepatocytes before shrinking [12]. Moreover the result revealed infiltration of inflammatory cells, this is due to hypersensitivity to the heavy metal that characterized the role of neutrophil and mononuclear cells in the liver mediated cytotoxicity [13]. On the other hand the pathological changes in the kidney showed alteration of most of these changes were congestion and necrosis, the result is similar to [14] which may be to depletion of (ATP) that leads to the necrosis and death cells, also [15,16] mentioned the congestion of blood vessels due to the nitric oxide (NO) formation which causes vascular smooth relaxation and dilation of the lumen causes increase in blood flow. The results of histopathological effects of the liver and kidney which treated with synthesized compound revealed the beneficial changes, this due to the presence of Schiff base (azomethine) group.

CONCLUSION:

The synthesized compound by the insertion of (azomethine) group causes a positive effect on the liver and kidney tissue, so the results which obtained from this research provide to the use of this compound in the treatment of pathological disease arising from oxidative stress.

RECOMMENDATION:

More studies should be done to fix synthesized compound as drug for antitumor and further study about adverse effect of synthesized compound on the all organ of body.

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