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Beneficial effect of *Alhagi maurorum* on rats submitted to sulfadimidine-induced kidney injury

Nada Mahdi Alkhafaji[1], Hussein Jasim Alharbi[1,*]

[1]Department of Biology, College of Science, University of Babylon, Hillah, Iraq

***Corresponding author:** Hussein Jasim Alharbi, Department of Biology, College of Science, University of Babylon, Hillah, Iraq; Tel.: +964-(0)7811436990
E-mail: husseinjasim1967@gmail.com

Abstract

Alhagi maurorum is one of the many plants that have proven effectiveness in folklore medicine and that are still utilized to treat disease or disorders, thanks to their phytochemical compounds and other secondary metabolites. Sulfadimidine, chemical known as 4-amino-*N*-(4,6-dimethylpyrimidin-2-yl)benzene-sulfonamide, is an antibacterial drug that has side-effects on organs such as the kidney. In this study, the unwanted acute effect of this sulfonamide and of its metabolites was recorded in the form of rat interstitial nephritis and as an increase in creatinine and blood urea nitrogen (BUN) levels. Results showed a significant (P<0.05) decrease in BUN levels in rat groups treated with the ethanolic extract of *Alhagi maurorum* as a therapy, but there were no significant differences observed in terms of the creatinine levels in these groups. The undertaken histological study revealed an almost normal histological appearance of the kidneys in the two groups of rats that were treated with the plant extract as a therapy after the damage that occurred as a result of the drug injection (interstitial nephritis, infiltration lymphocytes, and mild tubular atrophy). Our study suggests a potential benefit from natural plants in the treatment of drug-related adverse effects.

KEYWORDS
Alhagi maurorum, sulfadimidine, kidney damage, creatinine, rat

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1. INTRODUCTION

Phytochemical analyses of medicinal plants like those belonging to the *Alhagi* species have revealed a content of alkaloids, phenol, tannin, steroids, carbohydrate, lipids, and terpenoids; these chemical components have been extensively studied for their biological activity [1]. In a study by Varshochi and Asadollahi [2], it was revealed that the phytochemical contents of *Alhagi* can be used as a remedy for the removal of urinary tract stones; moreover, *Alhagi maurorum* (AM) had the highest number of mentions related to the claim that the plant's components can reduce the concentration of oxalates and calcium oxalate stones. On the other hand, sulfonamides and their metabolites are known to be able to cause severe interstitial nephritis or tubular necrosis [3].

2. MATERIALS AND METHODS

Plant extract: The plant was harvested from Hillah (Iraq). The taxonomy of the plant was carried out in a herbarium affiliated with the College of Science of the University of Babylon. The AM extract was prepared, the 2,2-diphenyl-1-picrylhydrazyl (DPPH) antioxidant assay was carried out on it, and so was a screening for some major phytochemical substances (such as flavonoids, phenols, alkaloids, glycosides, and tannins), as previously described [4].

Animals used: A total of 48 male albino rats of the species of *Rattus*, weighing between 180 to 250 gr, and aged between two and three months were used. The animals were bred in the animal house that belongs to the Department of Biology of the College of Science of the University of Babylon. The animals were subjected to the same conditions throughout the experiment with standard feed and water. At the end of the experiment, the animals were sacrificed by using anesthetic chloroform, and their blood was collected through a heart puncture with a sterile syringe.

Experimental design: The rats in the experiment were divided into eight groups of six rats each (n=6) as follows: (i) group 1 (G1) as a control group (rats received distilled water), (ii) group 2 (G2) in which the rats were injected with 40 mg/kg of sulfadimidine (SDD), (iii) group 3 (G3) in which the rats were given 300 mg/kg of the AM extract, (iv) group 4 (G4) in which the rats were given 600 mg/kg of the AM extract, (v) group 5 (G5) in which the rats were given 300 mg/kg of the AM extract and were then injected with SDD (40 mg/kg), (vi) group 6 (G6) in which the rats were given 600 mg/kg of the AM extract and were then injected with SDD (40 mg/kg), (vii) group 7 (G7) in which the rats were injected with SDD (40 mg/kg) and were then given 300 mg/kg of the AM extract, and (viii) group 8 (G8) in which the rats were injected with SDD (40 mg/kg) and were then given 600 mg/kg of the AM extract.

Biochemical analyses and histological study: Blood samples were collected in order to determine the blood urea nitrogen (BUN) and creatinine levels based on the protocol of the Sunlong Biotech Co., Ltd ELISA kit. The histological processing was performed according to a previous study [5], and the tissues were stained with haematoxylin / eosin.

3. RESULTS

Biochemical analyses: Our study has found a significant increase (P<0.05) in the creatinine (11.16±1.1 nmol/mL) and BUN (827.30±10.2 nmol/mL) levels in the group that was injected with SDD. There were no significant differences observed in terms of the creatinine levels in all other groups. When comparing the BUN levels between groups G5, G6, G7, and G8, we noted a significant decrease (P<0.05) in the groups receiving the AM extract after the SDD injection (G7: 659.2±9.7 and G8: 687.4±8.2 nmol/mL, respectively) as compared to those receiving the AM extract after the SDD injection (G5: 733.7±15.2 and G6: 779.5±11.4 nmol/mL, respectively).

Phytochemical analysis and determination of antioxidant activity: The phytochemical screening of the ethanolic extract of the plant revealed the following compounds: phenols, tannins, alkaloids, glycosides, and glycosides. The plant extract inhibited 37.5% of the DPPH radicals.

Histological study: The G1 rat kidneys exhibited normal tissues with preserved glomerular and tubular structures that were covered by an epithelial layer and displayed no signs of congestion, haemorrhage, or interfacial damage. The kidneys of the G2 rats (that were injected with SDD) exhibited interstitial nephritis (infiltration by lymphocytes) with tubular atrophy. The kidneys of the G3 and G4 rats (that were treated with 300 and 600 mg/kg of the AM extract) exhibited normal glomerular and tubular structures, as in the control group. The kidneys of the G5 and G6 rats (that were treated with 300 and 600 mg/kg of the AM extract, respectively, before being injected with SDD) exhibited signs of interstitial nephritis (infiltration by lymphocytes) with mild tubular atrophy and frequent eosinophils. Finally, the kidneys of the G7 and G8 rats (that were treated with 300 and 600 mg/kg of the AM extract, respectively, after being injected with SDD) exhibited preserved glomerular and tubular structures (Figure 1).

4. DISCUSSION

It appears that the results of our biochemical analyses are supported by those of our histological study in terms of the kidney function. The observed atrophy of some renal tubules, along with the observed inflammation and the proliferation of lymphocytes and of some eosinophils, might be due to a state of chronic inflammation as a result of the injection of SDD. Mustafa *et al*. [6] suggest that sulfa drugs increase deposition in the kidneys, thereby impairing their function and secretion, and then worsening their accumulation in the urinary system and elevating the risk of developing severe interstitial nephritis and even necrosis of the urinary tubes. These changes could lead to the development of drug-induced acute interstitial nephritis [7].

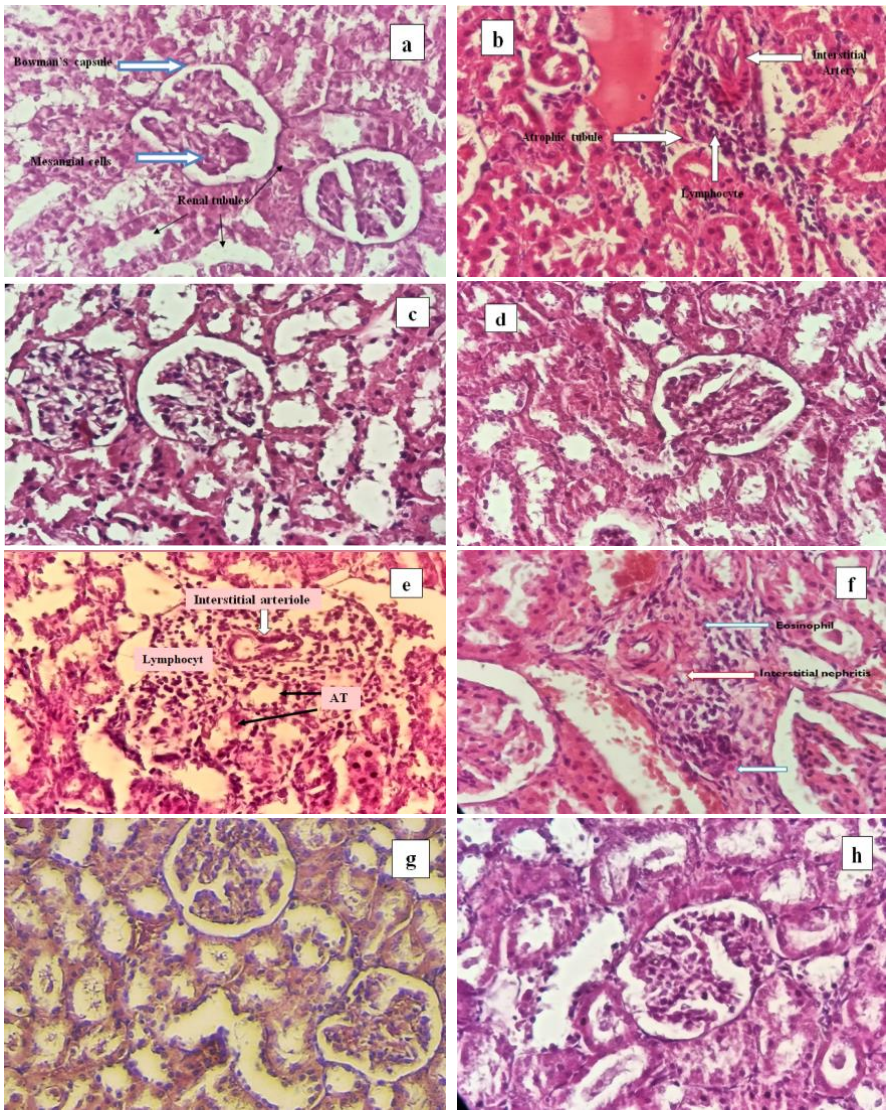

Figure 1. Kidney tissues of male rats stained with haematoxylin and eosin (×400): (**a**) the G1 rat kidneys exhibited normal tissues with preserved glomerular and tubular structures that were covered by an epithelial layer and displayed no signs of congestion, haemorrhage, or interfacial damage; (b) the kidneys of the G2 rats (that were injected with SDD) exhibited interstitial nephritis (infiltration by lymphocytes) with tubular atrophy; (**c** and **d**) the kidneys of the G3 and G4 rats (that were treated with 300 and 600 mg/kg of the AM extract) exhibited normal glomerular and tubular structures, as in the control group; (**e** and **f**) the kidneys of the G5 and G6 rats (that were treated with 300 and 600 mg/kg of the AM extract, respectively, before being injected with SDD) exhibited signs of interstitial nephritis (infiltration by lymphocytes) with mild tubular atrophy and frequent eosinophils; (**g** and **h**) the kidneys of the G7 and G8 rats (that were treated with 300 and 600 mg/kg of the AM extract, respectively, after being injected with SDD) exhibited preserved glomerular and tubular structures.

Our study confirmed through histopathological observations that in the rat groups treated with the AM extract after the SDD injection, the kidneys were nearly identical to those of the control group, and except for some inflammatory cells, the glomerulus and the tubules appeared normal. These findings might be due to phytochemical compounds identified in the AM extract (such as phenols and flavonoids) [8].

The antioxidant activity of the AM extract could work against the oxidative stress resulting from the drug administration, and this is in agreement with

the findings of a previous study [9]. Additionally, the herein studied plant has shown diuretic properties, which have led to the mitigation of the pH and of crystalluria, as well as to the excretion of sodium and potassium and the bulk of the volume of urine [10].

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CONFLICT OF INTEREST STATEMENT
The authors declare no conflicts of interest.

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