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Original Article

Alhagi maurorum aqueous extract protects against norfloxacin-induced hepato-nephrotoxicity in rats

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ABSTRACT

Objectives: While the protective effects of *Alhagi maurorum* have been shown against various ailments, its role against norfloxacin-induced adverse effects has not been studied. The current study was conducted to determine the effect of *A. maurorum* aqueous extract against norfloxacin-induced side effects in rats.
Methods: Twenty-four male albino rats were randomly assigned into four groups, which received normal saline, norfloxacin (50 mg/kg b.wt orally once a day), *A. maurorum* aqueous extract (300 mg/kg b.wt orally once a day), and norfloxacin with *A. maurorum* aqueous extract by the same previous mentioned dosages. Blood samples were collected for hematological examination to evaluate liver and kidney function tests. Hepatic and renal tissue samples were obtained to assess antioxidant activity and histopathological examination.
Results: *A. maurorum* aqueous extract significantly ameliorated norfloxacin-induced elevation in tissue malondialdehyde, and reduction in tissue antioxidant enzymes such as catalase, glutathione peroxidase, and superoxide dismutase activities as well as reduced glutathione concentration. Concurrent administration of *A. maurorum* aqueous extract with norfloxacin significantly reduced serum alkaline phosphatase, aminotransferases, urea, creatinine, and uric acid and increased RBCs count, Hb concentration, PCV, leucocyte, and monocyte counts compared with the norfloxacin-treated group. Co-administration of *A. maurorum* aqueous extract with norfloxacin prevented the degenerative changes induced by norfloxacin alone in liver and kidney tissues. The phytochemical profile of the extract showed the presence of carbohydrates, alkaloids, saponins, tannins, phenolics, and flavonoids.
Conclusion: These findings indicated that *A. maurorum* possesses potent antioxidant activities and could be used to attenuate norfloxacin-induced side effects.

1. Introduction

Alhagi maurorum Boiss (Akool) is a spiny deep-rooted perennial shrub, with roots that can reach six or seven feet into the ground. It has small pink to red pea flowers, and brown legume pods (Muhammad, Hussain, Anwar & Gilani, 2015). Several studies have shown the medicinal properties of *A. maurorum* in folk medicines to be used as diaphoretic, diuretic, expectorant and anti-ulcerogenic drug (Olas, Hamed, Oleszek & Stochmal, 2015; Shaker et al., 2010). In addition, the plant can be used as a laxative in the treatment of urinary and hepatic diseases (Marashdah, AL-Hazimi & Abdallah, 2008). Moreover, the oil extracted from the *A. maurorum* leaves has been demonstrated to exert beneficial effects in the treatment of rheumatism, and its flowers for the treatment of piles migraine and warts (Atta, Nasr, & Mouneir, 2010). Furthermore, the antioxidant and antiviral activities of *A. maurorum* have been reported to protect animals from foot and mouth diseases (Shakiba, Rezatofighi, Nejad & Ardakani, 2016). It has been reported that *A. maurorum* is rich in phenolic and flavonoid compounds (more than 12 different isolated flavonoids) (Al-Jaber et al., 2011). These compounds have been recorded to possess various therapeutic benefits such as antibacterial, anti-inflammatory, anti-aging, antimutagenicity, and anticarcinogenic activities via their abilities to reduce the oxidative damage or stress induced by free radical generation (Borchardt et al., 2008; Kiselova et al., 2006; Middleton, Kandaswami & Theoharides, 2000; Parthasarathy et al., 2009; Rice-Evans, Miller, Bolwell, Bramley & Pridham, 1995; Scalbert et al., 2005; Tarawneh, Irshaid, Jaran, Ezealarab & Khleifat, 2010).

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The norfloxacin, an antibiotic of the second generation quinolones (fluoroquinolones), possesses a wide range of activities against gram-negative and gram-positive bacteria and mycoplasma (Appelbaum & Hunter, 2000; Schem & Ziv, 1993). Norfloxacin has been used in controlling infections from pathogenic organisms including *E. coli*, Pasteurella, Salmonella, and Haemophilus (Wolfson and Hooper, 1985). It is also associated with serious side effects including leucopenia, decrease in hemoglobin and hematocrit values, thrombocytosis, eosinopenia, elevation of liver and kidney enzymes, arthropathy, and oxidative stress in different vital organs such as cerebral and hepatic tissues (Hillel, 1988; Gurbay & Hincal, 2004; Kim, 2010). Nevertheless, the effect of *A. maurorum* on norfloxacin-induced side effects has not been studied.

Given the findings of these reports, the current study was conducted to evaluate the protective role of *A. maurorum* aqueous extract against the adverse effects of norfloxacin using the rat as an animal model.

2. Materials and methods

2.1. Plant and chemicals

A. maurorum was collected from Salehia, faqous, El-sharkia governorate. It is a spiny deep-rooted perennial shrub, with small, pink to red pea flowers, and brown legume pods. Norfloxacin (Mycomas® 20%) was obtained from Univet, pharmaceutical Co., Ireland. Each 1 mL vial contains 200 mg norfloxacin. The kits to measure ALT, AST, ALP, serum creatinine, serum urea, and serum uric acid were procured from BioMerieux, France, and for SOD, GPx, MDA was from Bio-Diagnostic, Egypt. Other chemicals used in this study were of analytical grades.

2.2. Preparation of A. maurorum plant extract

A. maurorum plant extract was prepared according to the method described by Naderah Fathi (Nadheerah, 2012). The whole green plant was washed thoroughly, and then boiled in 3 L of distilled water for 1 h, the dark brown colored solution was obtained (the plant still green and intact), and the solution was dried by reduced pressure (lyophilization). The powder was kept in a sterile container and stored at −4 °C until used.

2.3. Animals

A total of 24 adult male albino rats of 150−200 g average body weight were obtained from the Faculty of Veterinary Medicine, Zagazig University. All animals were kept under the hygienic condition and acclimatized for one week before starting the experiment. These rats were given standard diet and water *ad-libitum*. The experimental protocol was approved by the Ethics Committee of the Faculty of Veterinary Medicine, University of Zagazig, Egypt.

2.4. Experimental design

These rats were randomly divided into four groups with six rats per experimental groups and assigned as follow: Group 1 (Control) received orally physiological saline. Group 2 (Norfloxacin) was treated with 50 mg/kg norfloxacin by oral gavage once a day (Sen, Jaiswal, Yanpallewar & Acharya, 2007). Group 3 (*A. maurorum*) received an aqueous extract of *A. maurorum* at a dose of 300 mg/kg once a day (Naseri & Mard, 2007). Group 4 (Norfloxacin + A. *maurorum*) received both norfloxacin and *A. maurorum* aqueous extract at the same previous dosages. The treatment was continued for 14 successive days.

2.5. Collection of samples and tissue preparation

At the end of the experiment (14 d), rats were sacrificed by decapitation, blood samples were collected in clean tubes containing EDTA used in hematological examination and other blood samples were collected in centrifuge tubes, allowed to clot and then centrifuged at 3000 rpm for 20 min to separate the sera, which were preserved at −20 °C until used for biochemical assays. Liver and kidneys were immediately removed and washed in physiological saline. A half gram of each tissue samples was homogenized in 5 mL of phosphate buffer (pH 7.4) on ice, using an electric homogenizer. Homogenates were then centrifuged at 3000 rpm for 15 min at 4 °C and the resulting supernatants were kept at −20 °C until later use. The remaining liver and kidney specimens were immediately fixed in 10% neutral buffered formalin for histopathological examination.

2.6. Assessment of oxidative/antioxidant status

Liver and kidney homogenates were used for assessment of antioxidant enzymes activity. Catalase (CAT) was measured according to the method of Aebi (1984), superoxide dismutase (SOD) according to the method illustrated by Kakkar, Das & Viswanathan (1984), and glutathione peroxidase (GPx) according to Paglia and Valentine studies (Paglia & Valentine, 1967). Reduced glutathione (GSH), a non-enzymatic antioxidant biomarker, was assessed according to the method of Beutler, Duron & Kelly (1963). Lipid peroxidation was evaluated by measuring the malondialdehyde (MDA) concentration according to the method developed by Uchiyama & Mihara (1978).

2.7. Assessment of serum biochemical parameters

The stored sera were used for an evaluation of liver function tests: ALT and ALP according to method of Tietz (1976), and ALP according to the method described by Belfield & Goldberg, n.d.), and kidney function tests; serum creatinine according to the method of Henry (1974), serum urea according to the method illustrated by Vassault et al. (1986), and serum uric acid according to the method developed by Henry, Cannon & Winkelman (1957).

2.8. Hematological studies

Total erythrocyte counts (TEC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), total and differential leukocytic counts were evaluated by using an automated hematology analyzer (Hospitex Hema Screen 18 analyzer, Italy).

2.9. Phytochemical screening

The extract of *A. maurorum* was screened for the presence of alkaloids, carbohydrates, saponins, phenols, flavonoids, and tannins according to standard procedures used by Alex et al. (2012).

2.10. Statistical analysis

All values were expressed as the mean ± SEM. The data were analyzed by F-test (ANOVA) using the statistical software program (SPSS, ver. 16.00, USA). Results were statistically significant at $P \leq 0.05$. All analyzes were conducted using the GraphPad Prism software (Version 8, GraphPad Software Inc.).

3. Results

3.1. Phytochemical profile of A. maurorum

The extract of *A. maurorum* was positive for alkaloids, saponins, tannins, phenolics, carbohydrates, and flavonoids. According to Al-Jaber et al. (2011), 12 flavonoids were isolated from *A. maurorum*. These flavonoids were identified as tamarixtin-3-*O*-dirhamnoside, isorhamnetin 3-*O*-glucosylneohesperidoside, isorhamnetine 3-*O*-robinoside, isorhamnetin 3-*O*-rotinoside, quercetin 3-*O*-rhamnoside, kampferol 3-*O*-galactoside, quercetin 3,7-diglycoside, isorhamnetin 3-rutinoside, daidzein 7,40-dihydroxyisoflavone, calycisin 30-hydroxyformononetin, isorhamnetin and tamarxtin aglycones.

3.2. Effect on liver and kidney antioxidant biomarkers activities and lipid peroxidation

Oral administration of norfloxacin in rats induced a significant decrease in the activities of CAT, SOD, GPx and GSH concentration (Fig. 1) with an increase in MDA level (lipid peroxidation marker) (Fig. 2) in the liver and renal tissues compared to control group ($P \leq 0.05$). However, the concurrent administration of *A. maurorum* with norfloxacin induced a significant ($P \leq 0.05$) increase in antioxidant enzymes of CAT, SOD, and GPx activities and non-enzymatic antioxidant biomarker GSH (Fig. 1) and with a reduction in MDA level (Fig. 2) in liver and kidney tissues compared to norfloxacin treated group. The concurrent administration of *A. maurorum* with norfloxacin showed a non-significant difference in the value of antioxidant biomarker (Fig. 1) in the liver and renal tissues ($P > 0.05$) when compared with the control group. Norfloxacin-treated rats induced a significant increase in MDA level in liver and renal tissues compared to control group (Fig. 2) ($P \leq 0.05$). The concurrent administration of *A. maurorum* with norfloxacin showed a non-significant difference in the value of MDA biomarker in renal tissues (NS = $P > 0.05$) while showing a significant increase in the value of MDA biomarker in liver tissues ($P \leq 0.05$) (Fig. 2) compared to control group.

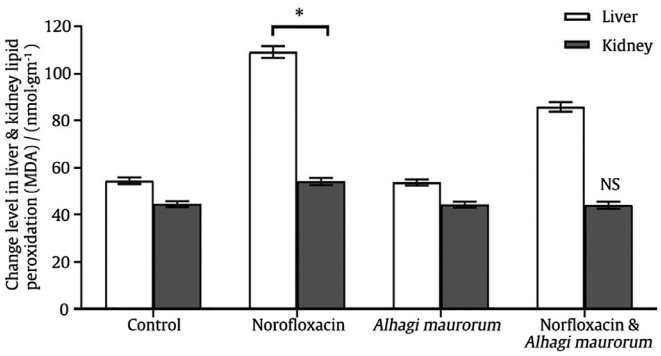

Fig. 2. Effect of oral administration of norfloxacin and *A. maurorum* aqueous extract on lipid peroxidation (MDA) level in liver and kidney of male rats.
Note: Norfloxacin-treated rats induced a significant increase in MDA level in liver and renal tissues compared to control group ($^*P \leq 0.05$). The concurrent administration of *A. maurorum* with norfloxacin showing non-significant difference in the value of MDA biomarker in renal tissues (NS = $P > 0.05$), while showing a significant increase in the value of MDA biomarker in liver tissues ($^*P \leq 0.05$) compared to control group. The value of MDA Malondialdehyde was measured by nmol/gm. Data represent mean values from six independent experiments, error bars indicate standard error of mean (SEM), $n = 6$.

3.3. Serum biochemical analysis

Administration of norfloxacin alone, or the combination of norfloxacin with *A. maurorum* aqueous extract in rats for fourteen days exhibited significant ($P < 0.05$) elevation in serum levels of liver function parameters of ALT and AST, and non-significant difference ($P > 0.05$) in the ALP value compared to control rats (Fig. 3)

Administration of norfloxacin alone exhibited a significant ($P < 0.05$) elevation in serum levels of kidney function parameters of creatinine, urea, and uric acid (Table 1) compared to control rats. Meanwhile, rats treated with norfloxacin with *A. maurorum* aqueous extract for 2 weeks showed a significant ($P < 0.05$) reduction in the levels of these parameters, when compared to norfloxacin treated rats. Comparing the concurrent administration of norfloxacin with *A. maurorum* aqueous extract with the control group showing a non-significant difference ($P > 0.05$) in the value

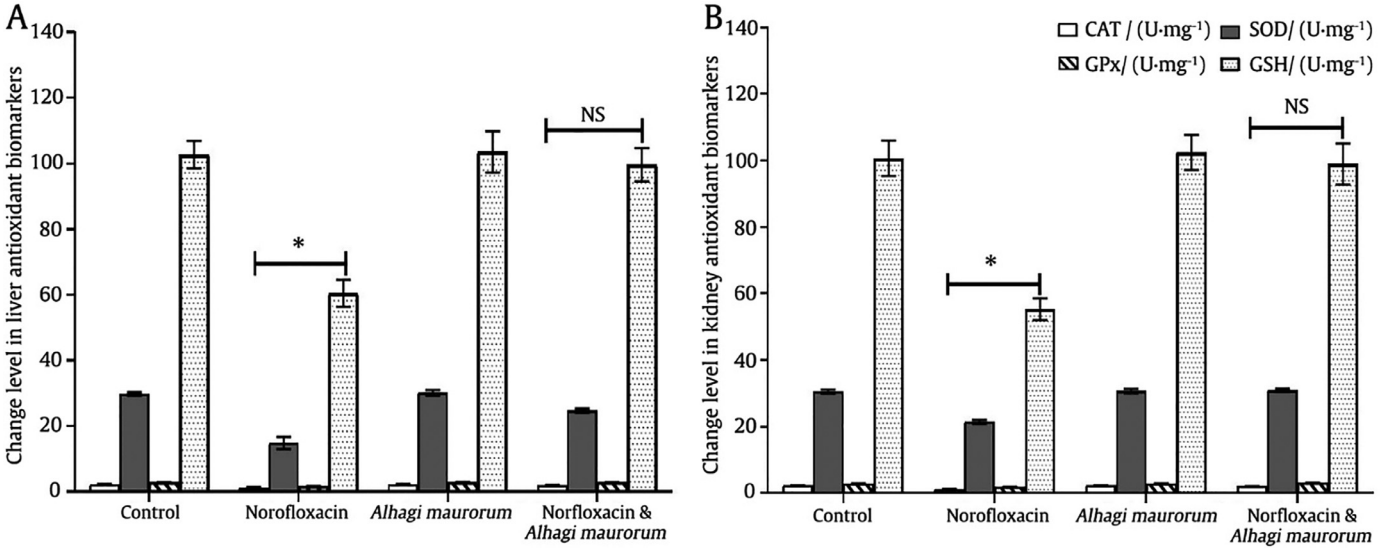

Fig. 1. Effect of oral administration of norfloxacin and *A. maurorum* aqueous extract on antioxidant biomarkers levels of liver (A) and kidney (B) in male rats.
Note: Norfloxacin treated rats induced a significant decrease in the activities of CAT, SOD, GPx and GSH concentration in liver and renal tissues compared to control group ($^*P \leq 0.05$). The concurrent administration of *A. maurorum* with norfloxacin showing non-significant difference in the value of antioxidant biomarker in liver and renal tissues (NS) compared to control group. The value of CAT Catalase, SOD Superoxide dismutase, GPx Glutathione peroxidase, antioxidant was measured by U/mg and GSH Reduced glutathione by mg/g. Data represent mean values from six independent experiments, error bars indicate standard error of mean (SEM), $n = 6$.

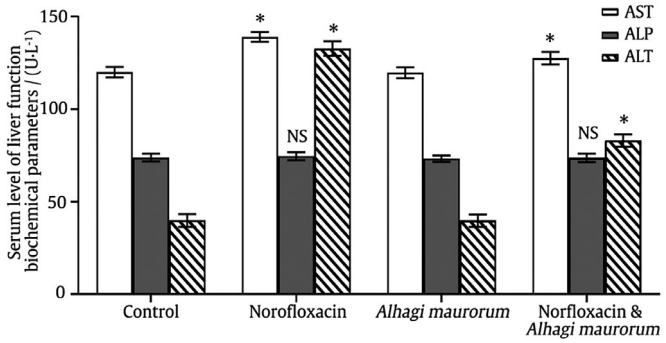

Fig. 3. Effect of norfloxacin and *A.* maurorum aqueous extract on selective liver function tests (AST, ALP, and ALT) in male rats.
Note:Administration of norfloxacin alone, or the combination of norfloxacin with Alhagi maurorum aqueous extract in rats exhibited a significant ($^*P < 0.05$) elevation in serum levels of liver function parameters; ALT and AST, and non-significant difference (NS = $P > 0.05$) in the ALP value compared to control rats. The value of AST aspartate aminotransferase, ALP alkaline phosphatase, and ALT alanine aminotransferase was measured by U/L. Data represent mean values from six independent experiments, error bars indicate standard error of mean (SEM), $n = 6$.

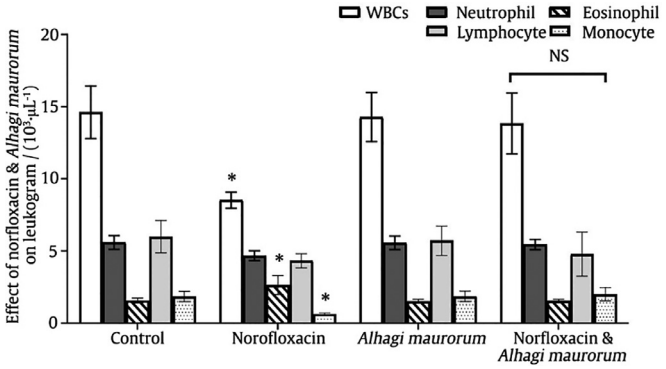

Fig. 4. Effect of oral administration of norfloxacin and *A. maurorum* aqueous extract on leukogram in male rats.
Note:Norfloxacin treated group exhibited a significant reduction ($^*P < 0.05$) in leucocytic and monocyte counts with an increase in eosinophils when compared with control rats. Concurrent administration of Alhagi maurorum aqueous extract with norfloxacin showing non-significant difference (NS= $P > 0.05$) when comparing with the control group.
The value of WBCs, neutrophil, eosinophils, lymphocyte, and monocyte was measured by 10^3/ µL. Data represent mean values from six independent experiments, error bars indicate standard error of mean (SEM), $n = 6$.

of creatinine and still significant increase ($P \leq 0.05$) in the value of urea, and uric acid (Table 1).

3.4. Hematological analysis

Rats treated with norfloxacin orally for fourteen days showed a significant decrease ($P < 0.05$) in RBCs count, Hb concentration, and PCV compared with control rats. However, co-administration of *A. maurorum* aqueous extract with norfloxacin in rats elicited a significant elevation ($P < 0.05$) in these parameters compared with norfloxacin treated rats and non-significant difference ($P > 0.05$) when compared with the control group (Table 2). Furthermore, administration of norfloxacin exhibited a significant reduction ($P < 0.05$) in leucocyte and monocyte counts with an increase in eosinophils when compared with control rats. Concurrent administration of *A. maurorum* aqueous extract with norfloxacin improved all these alterations induced by norfloxacin alone and these parameters showing non-significant difference ($P > 0.05$) when compared with the control group (Fig. 4).

The basophil counts in the different treatment groups (control rats, norfloxacin treated rats, *A. maurorum* treated rats, and rats treated with concurrent administration of *A. maurorum* aqueous extract with norfloxacin) showing non-significant difference ($P > 0.05$) with values (0.01 ± 0.006), (0.01 ± 0.013), (0.01 ± 0.000), and (0.00 ± 0.000103)/µL respectively (data not shown)

3.5. Histopathological examination results

The examination of liver and renal H&E sections revealed normal morphological features in control and *A. maurorum* group (Fig. 5a,b,g,h). In norfloxacin treated rats, liver sections showed focal interstitial lymphocytic aggregations, dilated central vein and hepatic sinusoids with acute cell swelling or scattered apoptotic bodies in the hepatic parenchyma (Fig. 5c). Some portal areas showed edema, lymphocytic infiltration and fibroblast proliferation and proliferative bile ductules (Fig. 5d). Kidney sections revealed

Table 1
Effect of norfloxacin (50 mg/kg b.wt orally once a day), *A. maurorum* aqueous extract (300 mg/kg b.wt orally once a day), and their combinations on some kidney function tests in male albino rats.

Groups	Parameters		
	Creatinine/(mg·dL^{-1})	Urea/(mg·dL^{-1})	Uric acid/(mg·dL^{-1})
Control	0.71 ± 0.05^b	40.09 ± 1.72^c	1.58 ± 0.027^c
Norofloxacin	0.92 ± 0.02^a	52.37 ± 4.49^a	1.78 ± 0.081^a
A. maurorum	0.69 ± 0.05^b	39.54 ± 1.38^c	1.56 ± 0.021^c
Norfloxacin + A. *maurorum*	0.68 ± 0.04^b	47.45 ± 2.17^b	1.67 ± 0.040^b

Data are expressed as mean ± SE ($n = 6$). Values having different alphabetic superscripts within the same column are significantly different ($P \leq 0.05$).

Table 2
The effect of norfloxacin (50 mg/kg b.wt orally once a day), *A. maurorum* aqueous extract (300 mg/kg b.wt orally once a day), and their combinations on erythrogram and platelets count male albino rats.

Groups	Parameters					
	RBCs/ (10^{12}·L^{-1})	Hb /gm%	PCV/%	MCV/fL	MCHC/%	Platelets/ (10^9 ·L^{-1})
Control	10.17 ± 0.307^a	17.88 ± 0.772^a	66.78 ± 1.38^a	66.00 ± 2.50^a	26.90 ± 1.37^a	263.00 ± 8.92^a
Norofloxacin	7.99 ± 0.136^b	13.95 ± 0.335^b	57.91 ± 1.60^b	62.83 ± 2.32^a	27.61 ± 1.24^a	257.67 ± 4.09^a
A. maurorum	9.61 ± 0.478^a	18.49 ± 0.982^a	68.15 ± 0.684^a	68.66 ± 1.94^a	25.60 ± 1.58^a	263.00 ± 8.32^a
Norfloxacin + A. *maurorum*	9.53 ± 0.428^a	17.66 ± 0.571^a	65.66 ± 1.75^a	63.00 ± 1.36^a	26.40 ± 0.187^a	260.83 ± 11.12^a

Data are expressed as mean ± SE ($n = 6$). Values having different alphabetic superscripts within the same column are significantly different ($P \leq 0.05$).

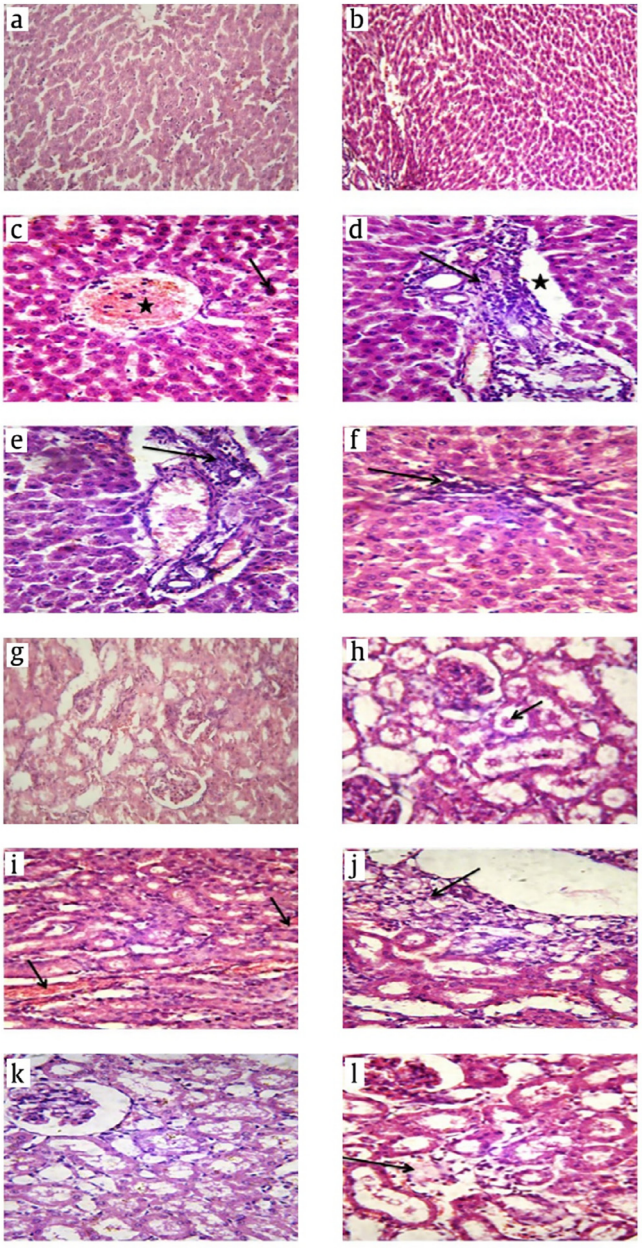

Fig. 5. Photomicrographs of liver and kidney tissues revealed histopathological examination results from different treatment stained by H&E (× 1200). (a) Liver section from control rat demonstrating normal hepatic parenchyma. (b) Liver section from *A. maurorum* treated rats showing normal hepatic parenchyma. (c) Liver section from norfloxacin rats showing dilated central vein (star) and sinusoids with scattered apoptotic bodies (arrow). (d) Liver section from norfloxacin rats revealing portal edema (star), lymphocytic infiltrations and proliferative bile ductules (arrow). (e) Liver section from norfloxacin + *A. maurorum* rats displaying a few lymphocytes (arrow) and proliferative bile ductules in portal area beside normal hepatic parenchyma. (f) Liver section from norfloxacin + *A. maurorum* rats showing lymphocytosis of the portal vessels (arrow) and normal hepatic cells. (g) Kidney section from control rats showing apparently normal renal parenchyma. (h) Kidney section from *A. maurorum* treated rats revealing normal renal parenchyma except a few granular casts in some renal tubules (arrow). (i) Kidney section from norfloxacin rats showing congestion and hemorrhage in renal medulla (arrows). (j) Kidney section from norfloxacin rats demonstrating perivascular necrotic renal tubules infiltrated by lymphocytes (arrow). (k) Kidney section from norfloxacin + *A. maurorum* rats revealing normal renal parenchyma. (l) Kidney section from norfloxacin + *A. maurorum* rats showing mild degenerative changes and necrosis in renal cortex (arrow).

congested renal blood vessels and inter renal capillaries beside hemorrhage were common in the renal medulla (Fig. 5i). Kidney sections showed Focal tubular degenerative changes or necrosis of some renal tubules, which usually infiltrated with lymphocytes in the renal cortex (Fig. 5j). In rats treated with norfloxacin + A. *maurorum*, liver sections exhibited normal hepatic parenchyma except a few lymphocytes and proliferative bile ductules could be seen in some portal area (Fig. 5e). Other portal areas had fibroblast proliferation and lymphocyte aggregations together with lymphocytosis of the portal vessels and hepatic sinusoids (Fig. 5f). The majority of the renal parenchyma in both cortex and medulla in kidney sections appeared normal (Fig. 5k). Mild degenerative changes and necrosis in some renal cortex were also observed (Fig. 5l).

4. Discussion

Oxidative stress is an important contributor to the pathophysiology of various ailments including cardiovascular dysfunction, glomerular diseases, renal ischemia, atherosclerosis, inflammation, carcinogenesis, drug toxicity, reperfusion injury, nephrotoxicity, hepatotoxicity, diabetes, and neurodegenerative diseases (Aruoma, 1998).

The current study has clearly demonstrated the ability of norfloxacin to induce oxidative stress in liver and kidney tissues of rats as evidenced by a significant decrease in CAT, SOD and GPx activities and GSH concentration with an increase in MDA level in liver and kidney tissues compared to control group. These impaired antioxidants activities could be attributed to free radical generation induced by norfloxacin. Norfloxacin has been shown to produce reactive oxygen species (ROS; singlet oxygen, superoxide radical, hydroxyl radical and hydrogen peroxide) in phagocytic cells (Jansen Van Rensburg, Joone & Anderson, 1990; Shakiba et al., 2016). Increased generation of ROS *in vivo* can lead to the depletion of one or more antioxidants which can be measured an index of oxidative stress (Halliwell and Gutteridge, 1998).

Our results are in agreement with previous studies demonstrating that chickens treated with enrofloxacin exhibited an increase in oxidative stress, which was mediated by increased MDA level in the serum and intestines, and decreased activity of CAT in liver and intestine and GPx in erythrocytes (Benzer et al., 2009). Administration of ciprofloxacin and levofloxacin to rats have been shown to result in a significant increase in MDA level, and decrease in glutathione peroxidase activity in brain tissue compared to the control group (Rawi, Mourad, Arafa & Alazabi, 2011), and administration of moxifloxacin in rats showed a significant reduction in the activities of CAT, SOD, and GST with an increase in MDA level in the liver tissues (Ore & Olayinka, 2015).

The present study revealed that administration of norfloxacin exhibited significant alterations in liver and kidney function parameters as evidenced by an increase in serum AST, ALT, creatinine, urea, and uric acid levels compared to the control group. In addition to the degenerative histopathological changes in liver and kidney tissues, these biochemical and histopathological alternations may be due to the oxidative stress induced by norfloxacin. Notably, the generation of oxidative radicals leads to mitochondrial damage, RNA processing, transcription and inflammation that could serve as a mechanism for hepatotoxicity induced by fluoroquinolones (Labbe, Pessayre & Fromenty, 2008). Our data are consistent with previous studies, which demonstrated that liver enzymes (AST and ALT), and kidney function parameters (urea, uric acid, and creatinine) were increased significantly after fluoroquinolones administration (Hirsch & Lundquist, 2009; Ibrahim, Abd-El-Rehim & Abeer, 2011; Ore & Olayinka, 2015; Sureshkumar, Sarathchandra & Ramesh, 2013).

In the present work, rats treated with norfloxacin showed a significant decrease in the total RBCs count, Hb concentration, PCV, leucocytic and monocyte counts compared to normal rats. Fluoroquinolones have been reported to suppress the growth and differentiation of hematopoietic progenitor cells like erythroid precursors or depress bone marrow (Axel & Itamar, 2003; Niyogi & Bhowmik, 2003). Other studies have also demonstrated that norfloxacin and other fluoroquinolones significantly decreased erythrocyte, catalase, and GPx activities (Altinordulu & Eraslan, 2009; Benzer et al., 2009).

Similarly, previous studies have demonstrated that administration of norfloxacin resulted in a significant decrease in total erythrocyte count, Hb concentration, hematocrit value, and PCV in dogs and rats (Rashmi, Jayakumar, Narayana Swamy & Bayer, 2012; Scott, Jonathan & Johna, 1990). Importantly, norfloxacin therapy has been shown to induce leucopenia and eosinophilia in human patients (Hillel, 1988).

Plant constituents with antioxidant activities have been reported to protect biological systems against oxidative stress. Natural antioxidants increase the antioxidant capacity and reduce the risk of diseases such as cancer, heart diseases, and stroke. The secondary metabolites like phenolics and flavonoids from plants have been reported to be the potent free radical scavengers, which are present in all parts of plants such as leaves, fruits, seeds, roots and bark (Narayanan, Joshi & Maunder, 1984; Russo et al., 2002). These phenolics interfere with mechanisms of free radicals production both by chelating transition metals as well as inhibiting enzymes involved in the initiation reaction (Russo et al., 2002). Two flavonoids, quercetin, and catechin that were isolated from *A. maurorum* were found to be associated with antioxidant and free radical scavenging activities (Sairam et al., 2002). Flavonoids have been reported to possess anti-inflammatory, antioxidant, antiallergic, hepato-protective, antithrombotic, antibacterial, antifungal, antiviral, and cancer protective properties, and also to protect against cardiovascular diseases (Ferenci et al., 1989; Knekt, Jarvinen, Reunanen & Maatela, 1996). In the present study, concurrent administrations of *A. maurorum* with norfloxacin induced a significant increase in antioxidant enzymes of CAT, SOD, and GPx activities and reduced GSH concentration with a significant decrease in MDA level in both kidney and liver tissues. In addition, significant improvements in kidney and liver function tests, as well as histopathological examination, were noticed by *A. maurorum* treatment compared to the norfloxacin-treated group. These data suggest the protective ability of *A. maurorum* in attenuating norfloxacin-induced deleterious effects. The protective effect of *A. mmaurorum* against norfloxacin induced oxidative damage may be imputed to the facts that *A. maurorum* has free radical scavenging activities (Awaad, El-Meligy & Qenawy, 2011; Ghassan, 2016; Shakiba et al., 2016; Soni, Jain, Dobhal, Parasher & Dobhal, 2015) due to its high content of phenolic and flavonoids (Gargoum et al., 2013). Phenolic compounds can act as reducing agents, free radical scavengers, hydrogen donators and inhibitors of pro-oxidative enzymes (Cai et al., 2004; Gawlik-Dziki et al., 2012). It has been reported that flavonoids, which contain hydroxyl groups are responsible for the radical scavenging effects in the plants (Das & Pereira, 1990; Younes, 1981) and implicate a possible therapeutics effects against free radicals mediated diseases (Vinayagam & Sudha, 2011).

5. Conclusion

As *A. maurorum* effects on norfloxacin-induced side effects were not clear, our study demonstrates that *A. maurorum* aqueous extract possesses a potent antioxidant activity, and concurrent administration of *A. maurorum* aqueous extract with norfloxacin may reduce the oxidative stress, hepatorenal damage, and hematological alternations induced by norfloxacin. Our findings indicate that *A. maurorum* reduced norfloxacin-induced adverse effects including hepato-nephrotoxicity and hematological alternations. The protective effects of *A. maurorum* were mediated via its antioxidant properties.

Declaration of Competing Interest

The authors report no declarations of interest.

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