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Submission date: 28-Oct-2022 03:33PM (UTC+0800)

Submission ID: 1937662187

File name: ct_of_Cayratia_trifolia_on_Histologically_Kidney_Mouse_Model.pdf (3.26M)

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To cite this article: Djoko Santoso *et al* 2020 *J. Phys.: Conf. Ser.* **1665** 012023

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Effect of Ethanolic Extract of *Cayratia trifolia* on Histologically Kidney Mouse Model

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Abstract. This study was conducted to determine the effect of *Cayratia trifolia* ethanolic extract on histological mouse kidney models. A total of 12 adult male Balb/c mice were randomly divided into two groups, comprising six mice in each group. The first group of 6 mice provided as the control group and received 25 ml/kg BW orally sodium carboxymethylcellulose during 6 days. The second group, 6 mice was administered 50 mg/kg BW of *C. trifolia* ethanolic extract in sodium carboxymethylcellulose orally during 6 days. The present study, we have performed histological kidney mice evaluation after 6 days of *C. trifolia* ethanolic extract administration. The histological mice kidney was quantified in term of tubular epithelium, glomerular and focal mononuclear infiltrate. The effect of administration of *C. trifolia* ethanolic extract on histological kidney of mice appeared normal tubular morphology in cortical and medullary regions of kidney in administered *C. trifolia* ethanolic extract mice, there was no kidney change histologically showed normal architecture of the glomerulus and tubules, while in control mice group, kidney histologically first marked with mononuclear cell infiltration, tubular necrosis, glomerular congestion and hyaline casts. The study results exhibit that relatively sufficient in histopathological changes in the corticomedullary junction of mice kidneys, including tubular epithelial damage, tubular dilatation and intratubular cast formation.

Keywords: Balb/c mice, *C. trifolia* ethanolic extract, kidney

1. Introduction

Several natural substances are possessed the medicinal plants, one of those medicinal plants is *C. trifolia*. A large number of compounds contained in *C. trifolia* plants include bioactive compounds such as yellow wax oil, steroids, terpenoids, flavonoids, and tannins [1]. Phenols, flavonoids, and tannins are gaining attention because they have natural qualities in preventing disease, promoting health, and anti-aging substances as natural antioxidants [2]. Antioxidants can function to reduce oxidative damage caused by free radicals and reactive oxygen species under conditions of oxidative stress in humans [3]. Several parts of *C. trifolia* such as stems, leaves, and roots are reported to have hydrocyanic acid and delphinidin. Leaves of *C. trifolia* have been reported to contain several flavonoids such as cyanidine [1].

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Kaempferol, myricetin, quercetin, triterpenes and epifriedelanol are contained the aerial parts of the plant; the seeds and fruits contain cyanogenic compounds; and the leaves also contain stilbenes such as piceid, resveratrol, viniferin and ampelopsin [4].

Patients with diabetes in order to check sugar levels of blood traditionally can be given infusion of seeds along with extract of tubers orally. In several cases such as diuretics, tumors, neuralgia and splenopathy can be medicated to used the whole plant [5]. The presence of alkaloids and flavonoids in the ethanolic extract of *C. trifolia* can be used for good free radicals scavenging activity. Antioxidants that contained the ethanolic extract of *C. trifolia* exhibits a good free radical scavenging activity [6]. Many of the properties of this plant have been reported in previous studies such as antibacterial, antifungal, antiprotozoal, antiviral, hypoglycemic, anticancer, antioxidant, anti-inflammatory, and diuretic properties. This study aims to know indirect effect of antioxidants and anti free radical scavenging activity of the *C. trifolia* ethanolic extract by inducing sodium carboxymethylcellulose that can influence histologically kidney feature in mouse model.

2. Materials and Methods

A total of 12 adult male Balb/c mice were randomly divided into two groups, comprising six mice in each group. The first group of 6 mice provided as the control group and received 25 ml/kg BW orally sodium carboxymethylcellulose during 6 days. The second group, 6 mice was administered 50 mg/kg BW of *C. trifolia* ethanolic extract in sodium carboxymethylcellulose orally during 6 days. The present study, we have performed histological kidney mice evaluation after 6 days of *C. trifolia* ethanolic extract administration. The histological kidney mice was quantified in term of tubular epithelium, glomerular and focal mononuclear infiltrate.

3. Results and Discussion

In *C. trifolia* ethanolic extract administration mice group (Group 2), relatively well morphology of tubular was appeared in cortical and medullary regions of kidney in that mice group, there was no kidney injury histologically with normal architecture of the glomerulus and tubules. While in sodium carboxymethylcellulose administration mice group (without *C. trifolia* ethanolic extract, Group 1) kidney injury histologically first marked with mononuclear cell infiltration, tubular necrosis, glomerular congestion and hyaline casts in the lumen of tubular (Table 1 and Figure 1).

Table 1. Scoring of the histological features of the mice kidney tissue sections in effect of Ethanolic Extract of *C. trifolia* and sodium carboxymethylcellulose induced nephrotoxicity

Histopathological features	Group 1	Group 2
Glomerular congestion	++	+
Tubular necrosis	+++	+
Tubular casts (hyaline)	++	+

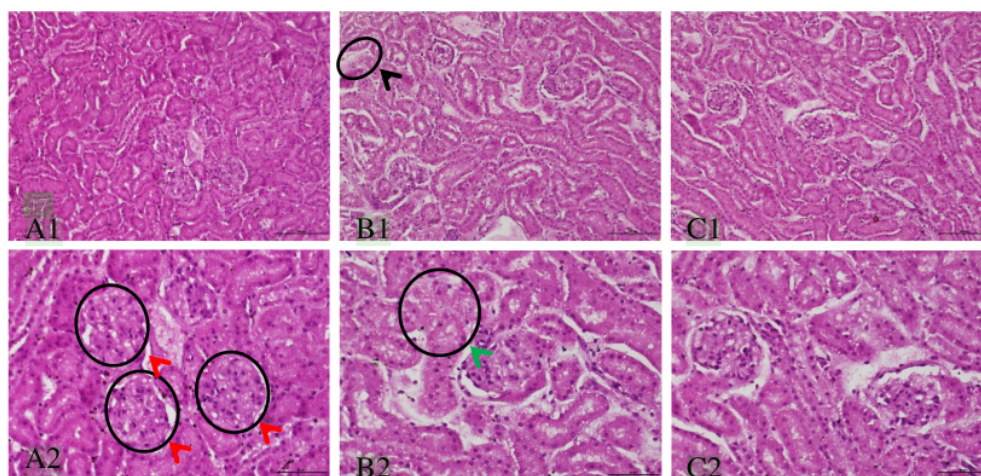


Figure 1. The kidney tissue in group 1 showing glomerular congestion, mononuclear cell infiltration, tubular necrosis and hyaline casts, Group 2 occurred increasing quality architecture of kidney tissue [H&E, A1, B1, C1 (x200); A2, B2, C2 (x400)]. black head arrow, casts hyaline; green head arrow, damaged tubular cells; red head arrow, glomerular congestion.

The use of pro-inflammatory agent is single as well as multiple often generate impact, one of which is nephrotoxicity. Various responses of the use of that agent is important to know including frequency of administration, the dosage and cumulative dose of agent, response of animals is different severity can be occurred acute (early) and chronic (advanced) kidney injury [7]. It appears that the use of carboxymethylcellulose can trigger increased production of pro-inflammatory cytokines, reactive oxygen species, and proteolytic enzymes.

Previous studies of chronic wound environments demonstrated ongoing inflammation with matrix degradation and other accompanying sequelae [8]. Some conditions including serious side effects such as risk of kidney failure, gastrointestinal damage, and prolonged bleeding time due to impaired coagulation often result from the use of proinflammatory agents. [9]. For this reason, nonpharmacological strategies and topical agents to achieve optimal to reduce stimulation of inflammation. Administration of sodium carboxymethylcellulose resulted in histopathological changes at the corticomedullary junction of the mouse kidneys, including tubular epithelial damage, tubular dilatation and formation of casts in the tubular lumen (Figure 1).

Nephropathy in rodents is histologically characterized by degenerative changes in the proximal tubule consisting of hydropic degeneration, pycnotic nuclei, increased cytoplasmic vesicles, cytoplasmic vacuolization, loss of brush border, necrosis and apoptosis of tubular cells, and desquamation of necrotic epithelial cells of tubular lumens and forming hyaline casts. [10]. The effect of the use of sodium carboxymethylcellulose occurs through increased oxidative stress, tubulo-interstitial inflammation and apoptosis. The results of the present study indicated that sodium carboxymethylcellulose may induce free radical production that could cause tubular damage due to sodium carboxymethylcellulose intoxicated animals, which was resulted through the increase of oxidative stress, inflammation and apoptosis in the kidneys [11]. One of the most commonly used strategies is saline hydration and forced diuresis. Despite saline hydration and forced diuresis, nephrotoxicity is in the range of 20–30% [12].

4. Conclusion

Cayratia trifolia ethanolic extract supplementation may reduce sodium carboxymethylcellulose induced nephrotoxicity. The study results demonstrated that relatively sufficient in histopathological changes in the corticomedullary junction of the mice kidney, including damage to the tubular epithelium, tubular dilatation and formation of an intratubular cast. We suggest that the *Cayratia trifolia* Ethanolic extract modulates oxidative stress in the kidney.

Acknowledgement

This study was funded by Directorate of Higher Education, Ministry of Education and Culture of the Republic of Indonesia, Excellence Research Grant of Higher Education for a research contract number: 560/UN3.14/PT/2020.

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