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Research Article
Study of *Anthurium schlechtendalii* Kunth Extract Effects on Nephroprotective or Renal Damage Remission Capacity

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Abstract

Background and Objective: Since the beginning of mankind, plants have been regard as allies used in study. Several traditional medication systems employ herbal medicines for nephroprotection. This study was aimed at investigating the nephroprotective potential of *Anthurium schlechtendalii* (*A. schlechtendalii*) Kunth root consumption as a traditional medicine for kidney disease in Mexico. **Materials and Methods:** Oral administration of adenine (0.75%) induced chronic kidney disease and solid and aqueous extract from plant root. These were tested at doses of 125 mg kg^{-1}/day and 1.8 mg mL^{-1}/day, respectively in the animal model used in 4 weeks experiment. Growth parameters, liquid consumption, 24 h urine volume, kidney weight, creatinine, creatinine clearance, blood urea nitrogen (BUN) and urine proteins were determined and also statistically recognized by variance analysis procedures (one-way ANOVA), with a *post hoc* Tukey multiple range test for comparison of means ($p<0.05$). **Results:** The study shows that in groups IRDG, PG1 and PG2, body weight loss, increased fluid intake and also urine output were all observed to show significant differences in comparison to the other experimental groups. The mean kidney weight in these three groups was significantly greater, 3.1 and 3.3 fold for the right and left kidney, respectively. Induced renal damage was revealed by significantly higher levels of serum creatinine: 6.6 fold (IRDG) and 5.6 fold (PG1 and PG2), BUN levels were 15.1, 11.7 and 14.5 times higher and 24 h proteins were 15.4, 17.2 and 15 fold higher for IRDG, PG1 and PG2, respectively. Creatinine clearance levels decreased significantly: 12.8 fold (IRDG and PG2) and 15 fold (PG1). **Conclusion:** Using adenine-induced renal damage as a model and specific dose and administration time of *A. schlechtendalii* Kunth polar extract, the potential for its nephroprotective action or remission capacity was not evident in the animals under study. There must be more studies to follow this first one in order to accrue enough scientific knowledge that can support or reject medico-ethnobotanical uses or claims of *A. schlechtendalii* Kunth, particularly those linked with the renal or urinary system.

Key words: *Anthurium schlechtendalii* Kunth root, chronic kidney disease, phenolic compounds, nephroprotective action, renal damage

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Chronic Kidney Disease (CKD) is a national and global public health problem. According to the Mexican Secretary of Health[1], CKD is defined as "the decrease in renal function expressed by a glomerular filtration rate (GFR) <60 mL min^{-1} 1.73 m^{-2}, or as the presence of persistent kidney damage for at least three months". Franco-Marina *et al.*[2] stated that the mortality rate and prevalence of terminal CKD for 2005 in Mexico were 407-374 and 1209-1242/million inhabitants for the group of states with very high and high levels of marginalization, respectively. Its projection for 2025 shows substantial increases ranging from 57-142%. The State of Veracruz is located in the highly marginalized group along with 7 other states[2].

The CKD etiology is varied, with diabetes and hypertension being two chronic-degenerative diseases that contribute to morbidity and mortality. According to the WHO and IPCS[3], certain heavy metals are nephrotoxic, scientific evidence also points to pesticides and certain drugs, among other nephrotoxic agents. The Pan American Health Organization (PAHO)[4] stated that in the last two decades the number of patients in Central America diagnosed with CKD has been increasing. This organization also reported that the most affected are male farmers under 60 years old and that the etiology in this case is not the common diabetes and hypertension, rather it has been linked to "toxic-environmental and occupational factors, also to harmful habits such as the intake of nephrotoxic drugs". For its part, the Ministry of Health of El Salvador[5] indicated that this phenomenon occurs in the South of Mexico in addition to Central America, fitting in with the projection made by Franco-Marina *et al.*[2], where the Southern and South-Eastern Mexican states are among the groups with very high and high levels of marginalization and in turn of higher mortality, incidence and prevalence of CKD.

It has been shown that traditional medicine, particularly in China, provides CKD remission through phytochemicals[6]. A plant that has proven active against CKD is *Acacia senegal* (L.) Willd, particularly for its exudate known as gum Arabic[7]. Mexico continues to be a country with high biodiversity, particularly plants, including those used in traditional medicine. Through ethnobotany research in the Papaloapan Basin (Veracruz and Oaxaca states), a list of native plant species with traditional uses for the care of kidney ailments and with properties of a nephroprotective capacity was established. One specie that has been shown to have such properties in traditional medicine is *Anthurium schlechtendalii* Kunth used as drinking water (root infusion) for the regional population of Veracruz, in particular in Hueyapan de Ocampo and Catemaco[8]. It belongs to the *Araceae* family and is mainly tropical with a greater diversity of species in Asia and tropical America[9]. Mexico has recorded 121 species and 18 genera. Endemic status of *Araceae* in Mexico is high, especially in the *Anthurium* genus where of a total of 41 species, 26 are endemic[9-11]. The state of Veracruz is home to approximately 45% of the total Mexican species[12].

Scientific evidence associates the presence of antioxidants and phenolic-type compounds as responsible for the anti-inflammatory potential and oxidative deterioration reduction in the organic root and leaf extracts of *A. schlechtendalii* Kunth[13].

The renal damage induced by the oral administration of adenine has been explained by the precipitation in the form of acicular crystals of the metabolic product 2,8-Dihydroxyadenine in the epithelium of the proximal tubule. This occurs particularly in the microvilli and in the apical region which causes degenerative changes in the cells of these tissues[14]. This model of Chronic Kidney Disease (CKD) induced by adenine remains a benchmark for preclinical studies[15-17]. The intraperitoneal route, rather than oral administration, has also been developed[18].

However, so far, phytochemical or phytopharmacological studies involving *A. schlechtendalii* Kunth do not exist in the scientific literature referring to managing the problem of renal diseases. Its long term use by locals of the Papaloapan Basin area as a palliative treatment for kidney ailments, based on traditional knowledge, gave grounds for carrying out this study.The aim of this research was to determine the potential of *A. schlechtendalii* Kunth (stone root) polar extract in the prevention or remission of renal damage induced by adenine in a murine model under the applied conditions in the preclinical study (dose, administration time, among others).

MATERIALS AND METHODS

Materials: The study was carried out from June, 2014-June, 2016.

Collection of plant material, classification and treatment: The root of *A. schlechtendalii* Kunth (104 kg) was harvested in the municipality of Actopan, in the state of Veracruz, Mexico. Taxonomic identification and classification was performed by Dr. Sergio Avendaño Reyes, curator of the Xalapa Herbarium of the Ecology Institute (INECOL, Xalapa, Veracruz, Mexico) and a specimen of the plant used in this study was deposited in the INECOL Herbarium. The plant material was cleaned and washed to remove impurities and

cut into pieces of approximately 2 cm with a stainless steel knife. Subsequently it was dried at room temperature for a week.

Methods

Determination of humidity and total solids: Using the Gravimetric method, 5 g of plant material were weighed in triplicate on an analytical balance (Mettler, H80, Germany). Samples were placed in porcelain crucibles at constant weight and subjected to a temperature of 50°C and a vacuum pressure of 120 mbar or 90.07 mmHg (Gallenkamp Vacuum Oven, VL-570 030D, England) for periods of 5-12 h until constant weight was achieved (±0.002 g).

Obtaining extracts from *A. schlechtendalii* Kunth: The plant material used was reduced to approximately half its weight (% moisture) to obtain the extracts, using the percentage of moisture and solids at the time of receiving the lot as a reference.

Extraction by infusion: An infusion extraction was performed using a 1:5 w/v plant-water ratio. The plant material was weighed in a portable electronic scale (Ohaus, Scout Pro SP601, China), cleaned for a second time, placed in a plastic sieve, sprayed with deionized water using a wash bottle and scrubbed with a clean brush to remove residual impurities from the root. The material was then cut into approximately 1 cm long fragments, then placed in a plastic sieve, rinsed with deionized water, draining as much water as possible. The plant material was placed in a 1 L beaker, covered with boiling deionized water, placed on a magnetic stirring-heating plate (Gallenkamp, 400, England), boiled for 1 min and left standing for an additional 13 min. The vessel was removed from the heat and the contents filtered through a plastic sieve to separate the material from the infusion then allowed to cool to room temperature. The infusion was then passed through a filtration system (a Kitasato flask assembly and Büchner funnel) using Whatman No. 2 filter paper, aided by a water-suction vacuum pump (Cole Parmer, 7049-50, USA) and the liquid obtained was again filtered through a 0.45 µm pore size mixed cellulose esters membrane (Millipore, HAWP04700, USA) using glass microfiltration equipment (Millipore, USA) pre-sterilized in a dry heat oven (Riossa, HS, Mexico) with the aid of a vacuum pump (Edwards, MF20, England).

Lyophilisation of aqueous extract: Lyophilisation was carried out in order to convert part of the aqueous extract (infusion) into solid material. The microfiltered extract was placed in previously weighed and identified glass vials. The frozen samples were lyophilized (Labconco Freeze Dry System, 4.5, USA), at a pressure of 133×10^{-3} mbar (0.133) and a temperature of -40°C. At the end of the process, the material was weighed and transferred to Falcon type sterile conical tubes (Axygen, SCT-50 ML-25-S).

Animals and diet: About 30 male Wistar rats (9-10 weeks old, weighing 240±10 g) were purchased from Harlan Teklad, Mexico and individually placed in stainless steel boxes in a temperature controlled room (26±2°C) with a 60% relative humidity and a 12 h light-dark cycle (7 AM-7 PM). The animals had free access to both a standard (commercial) powder diet and drinking water throughout the experimental period. The standard diet contained 0.75% phosphorus, 0.95% calcium, 0.20% magnesium, 23% crude protein and 3.3 IU g^{-1} vitamin D3 (5012-Rat Diet, Lab Diet USA). Experiments with animals were approved by the Animal Ethics Committee, Chemical Biology Department, University of Veracruz (Program: Chronic Renal Disease CKD Part I 2013-2016).

Design of the experiment: After seven days of adaptation, the animals were weighed and redistributed with a number (1-30) and an individual letter (A, B, C, D, E and F) assigned by a draw. They were then randomly divided into 6 groups of 5 animals each. The designation and redistribution was carried out by a person outside this investigation. Each cage was previously numbered and represented in a draw with numbered spheres inside a tombola drum. In another drum were 5 spheres that represented a letter corresponding to each experimental group. Thus, a number and a letter were selected for each animal, which generated a specific key, generating the following experimental groups: Group A or control (CG) which received a standard diet and water *ad libitum*, Group B or induced renal damage group (IRDG), standard diet supplemented with adenine 0.75% w/w, water *ad libitum*, Group C or solid extract group (SEG), standard diet supplemented with solid extract and water *ad libitum*, Group D or solid and aqueous extract group (SAEG), standard diet supplemented with solid and aqueous extract, Group E or prevention group 1 (PG1), standard diet supplemented with adenine 0.75% w/w plus solid extract and water *ad libitum* and Group F or prevention group 2 (PG2), standard diet supplemented with adenine 0.75% w/w plus solid and aqueous extract. The experimental diet was the standard powdered diet plus solid *A. schlechtendalii* Kunth root extract (125 mg kg^{-1}/day) and/or aqueous extract (1.8 mg mL^{-1}/day) for each experimental diet, respectively. The animals received the respective experimental diet and the aqueous extract for 4 weeks, each prepared once a week and kept refrigerated

until use. The preparation of the diets, the aqueous extract and the feeding of the animals was performed by a person outside the study which ensured that the researcher did not know which animals belonged to which study group and thus avoid the error of prejudice. Body weight (g), food (g) and fluid (mL) intakes were recorded daily. During the last day of experimentation the animals were individually placed in metabolic boxes to collect 24 h urine. At the end of the study the animals were slaughtered by decapitation and the blood was collected. In addition, both kidneys were extracted for further analysis. Serum creatinine, creatinine clearance, blood urea nitrogen (BUN) and urine proteins were determined.

Assays: Urine (creatinine clearance) and serum creatinine, blood urea nitrogen (BUN) and urine protein were analysed by colorimetric and enzymatic methods on a Vitros 250 kit (J. and J., Ortho Clinical Diagnostics, USA) using the corresponding dry chemical reagents (microslides).

Statistical analysis: The data were expressed as the mean±standard deviation ($\bar{x}\pm SD$). Statistical significance was determined with analysis of variance procedures (one-way ANOVA), with *post hoc* Tukey multiple range tests for comparison of means ($p<0.05$). Spearman rank tests were applied to data concerning food intake and weight changes, also liquid intake and 24 h urine volumes, for correlation between these factors. Data were analysed using SPSS version 20.0[19].

RESULTS

Determination of moisture content and total root solids of *A. schlechtendalii* Kunth: The gravimetric analysis of plant material (mean of three replicates) contained 93% moisture and 6.56% solids.

Obtaining the solid and aqueous extracts from *A. schlechtendalii* Kunth: Eight kilogram of the plant material underwent extraction by aqueous infusion in a 1: 5 w/v ratio to obtain the solid extract. The aqueous extract was lyophilized yielding 39.17 g. Of this total, 17.5 g were allocated to be administered to 20 study rats. Additionally, 7.8 kg of the same batch of plant material from which 50% of the original moisture had also been removed, was used to obtain the aqueous extract, generating 32 L, which were administered to the rats whose diet included this type of extract.

Parameters of growth, diet and liquid consumption, 24 h urine volume and kidney weight: The parameters of growth, food and fluid intake, urine volume and kidney weight for the control group (CG) and 5 experimental groups (IRDG, SEG, SEAG, PG1 and PG2) supplemented with *A. schlechtendalii* Kunth and with or without adenine are shown in Table 1. No statistically significant differences were found in relation to initial weight between the control and experimental groups. However, at week 4 of the study, the SEG and SEAG weights resembled that of the control group (CG) exhibiting a very significant increase ($p<0.01$) compared to their respective initial weights. The IRDG, PG1 and PG2 groups showed a highly significant ($p<0.01$) body loss compared to their initial weights. A Spearman correlation test between weight changes and food intake showed that gain or loss is significantly related ($p<0.01$) to higher or lower food intake, respectively. On the other hand, PG1 and PG2 groups consumed significantly ($p<0.05$) more liquid and produced significantly ($p<0.05$) a higher 24 h urine volume than CG, SEG and SEAG groups, this increased fluid consumption and volume reached a very significant difference ($p<0.01$) in the IRDG group. The Spearman correlation between fluid intake and 24 h urine showed significantly ($p<0.01$) that higher fluid intake leads to greater urine volume. With reference to the parameters mentioned above, it was found that the SEG and SEAG groups did not show statistically significant differences when compared to the CG group. Regarding right and left kidney weight, SEG and SEAG groups were found not to present a statistically significant difference when compared to the CG group. However, the kidneys of the PG2 group had a significant ($p<0.05$) higher weight and this weight increase became highly significant ($p<0.01$) for both kidneys in the IRDG and PG1 groups in comparison with the CG, SEG and SEAG groups.

Body and kidney weights: The changes in body and kidney weight are shown in Table 2. When the initial and final body weight was compared between all groups where adenine was administered (IRDG, PG1 and PG2) and control (CG), a progressive decrease in body weight of about 35% was observed in all adenine administered groups. On the other hand, in the groups where the diet was supplemented only by solid extract (SEG, 125 mg kg^{-1} of weight) and aqueous extract (SEAG, 1.8 mg mL^{-1}) of *A. schlechtendalii* Kunth, a weight increase of 33 and 34% was observed, respectively, equivalent to that of the control group (35%). Additionally, it was observed that the weight gained in the kidneys was very significant ($p<0.01$) in the IRDG and PG1 groups and only significant ($p<0.05$) in the PG2 group.

Biochemical measurements: The results of murine biochemical parameters supplemented with *A. schlechtendalii*

Table 1: Growth parameters, urine volume and kidney weight in rats treated with *A. schlechtendalii* Kunth root, with or without adenine administration

Parameters	CG	IRDG	SEG	SAEG	PG1	PG2
Initial body weight (g)	210±2	214±5	208±2	221±6	211±4	221±5
Final body weight (g)	284±7	162±9**	280±2**	293±21**	161±8**	144±7**
Food intake (g)	19.1±1	6.8±0.5**	19.1±0.9	19.9±0.2	6.8±0.8**	6.5±0.5**
Liquid consumption (mL)	34.1±1.6	52.9±4.2**	37.4±4.3	33.7±2.8	43.1±0.7*	42.9±1.9*
Urine volume 24 h (mL)	7.6±2.1	25.7±9.0**	5.9±3.0	9.3±4.9	20.3±5.7*	21.2±4.1*
Kidney weight (g) Right	1.0±0	3.3±0.3**	0.9±0	1.0±0.1	3.3±0.3**	2.8±0.2*
Kidney weight (g) Left	1.0±0	3.5±0.3**	0.9±0	1.0±0.1	3.5±0.2**	3.1±0.3*

Values are Mean±SD (n = 5 rats), CG: Control group, IRDG: Induced renal damage group, SEG: Solid extract group, SAEG: Solid and aqueous extract group, PG1: Prevention group 1, PG2: Prevention group 2. *p<0.05, **p<0.01 compared to corresponding data in CG (Control Group)

Table 2: Effect on rat body and kidney weight of *A. schlechtendalii* Kunth root treatment, with and without adenine administration

Groups	Initial weight (g)	Final weight (g)	Difference (%)	Kidney weight (%)
CG	210±2	284±7	34.9±7	0.71±0.00
SEG	208±2	280±2	34.3±3	0.66±0.02
SAEG	221±6	293±21	33.4±11	0.73±0.13
IRDG	214±5	162±9	-24.2±6	4.20±0.58**
PG1	211±4	161±8	-23.4±11	4.20±0.47**
PG2	221±5	144±7	-34.6±6	4.10±0.47*

Values are Mean±SD (n = 5 rats), Kidney weight was expressed as percentage of final weight, CG: Control group, IRDG: Induced renal damage group, SEG: Solid extract group, SAEG: Solid and aqueous extract group, PG1: Prevention group 1, PG2: Prevention group 2. *p<0.05, **p<0.01 compared to corresponding data in CG (Control Group)

Table 3: Biochemical measurements in rats treated with *A. schlechtendalii* Kunth, with or without adenine administration

Parameters	CG	IRDG	SEG	SAEG	PG1	PG2
Creatinine (mg dL^{-1})	0.5±0.1	3.3±0.6**	0.5±0.1	0.4±0.1	2.8±0.5**	2.8±0.7**
BUN (mg dL^{-1})	18±3.0	272±81**	19±1.0	23±3.0	211±18**	262±105**
24 h Urine protein (mg/day)	0.5±0.2	7.7±2.6*	0.4±0.3	0.7±0.8	8.6±1.9**	7.5±1.9*
Creatinine clearance (mL min^{-1})	0.9±0.3	0.07±0.03**	0.8±0.3	1.3±0.2	0.06±0.02**	0.07±0.03**

Values are Mean±SD (n = 5 rats), CG: Control group, IRDG: Induced renal damage group, SEG: Solid extract group, SAEG: Solid and aqueous extract group, PG1: Prevention group 1, PG2: Prevention group 2. *p<0.05, **p<0.01 compared to corresponding data in CG (Control Group)

Kunth and with or without adenine, are shown in Table 3. In contrast to the SEG and SEAG experimental groups, mean serum creatinine levels reached highly significant increase (p<0.01) in the IRDG, PG1 and PG2 groups compared to the control group. Serum urea showed the same pattern or trend as creatinine reaching very significant values (p<0.01) for the IRDG, PG1 and PG2 groups compared to the CG group. The 24 h urine protein concentration increased significantly (p<0.05) in the IRDG and PG2 groups and very significantly (p<0.01) in the PG1 group in relation to the CG group, but not for the SEG and SEAG groups. Compared to CG, creatinine clearance levels were not significantly different in the SEG and SEAG groups, whereas levels decreased significantly (p<0.01) compared to CG group in the IRDG, PG1 and PG2 groups.

DISCUSSION

As far as could be ascertained, this is the second study dealing with *A. schlechtendalii* Kunth phytochemical or ethnopharmacological issues. In this particular study, the effect of the administration of solid and aqueous extracts of *A. schlechtendalii* Kunth on adenine-induced renal damage for 4 weeks revealed that the IRDG, PG1 and PG2 groups experienced a significant body loss of 24.3, 23.7 and 34.8%, respectively, directly related to the ingestion of the toxic substance (adenine) contained in the diet. In addition, these groups consumed significantly more fluid (55.1, 26.4 and 25.8%, respectively) and produced significantly greater urine volume (3.4, 2.7 and 2.8 fold, respectively) compared to the control group, the IRDG group being the most outstanding. The mean kidney weight was greater with significantly increases (3.1 and 3.3 fold for the right and left kidney, respectively), compared to the control group. This renal dysfunction, or weight gain, shows that the induced renal damage model develops nephrotoxicity due to a functional hypertrophy caused by the toxic substance. This alteration has been reported and well documented in previous studies by Ali *et al.*[7,20].

On the other hand, in addition to kidney enlargement, the induced renal damage revealed the excessive accumulation of uremic toxins (azoemias). Serum creatinine levels attained significantly higher levels of 6.6 fold for the IRDG group and 5.6 fold for prevention groups 1 and 2 (PG1 and PG2). Blood urea nitrogen (BUN) levels were 15.1, 11.7 and 14.5 times higher and 24 h proteins were15.4, 17.2 and 15 fold higher for the IRDG, PG1 and PG2 groups,

respectively compared to the control group. In contrast, creatinine clearance levels decreased significantly, 12.8 fold for the IRDG and PG2 groups and 15 fold for the PG1 group, relative to CG. The described findings are characteristic of chronic renal pathology in which there is functional and structural hypertrophy, an increase in serum azoates, kidney weight and 24 h urine volume. Compatible results have been reported by Yokozawa[16], Ali *et al.*[20], Okada *et al.*[21] and Ali *et al.*[22]. Adenine-induced chronic renal failure has been reported as a condition whose progression increases proportionally with longer periods of toxic administration[23]. A comparison of two studies dealing with extracts with similar bioactive components resulted in a better response in the case of 14 days, as opposed to 38 days, adenine-feeding time[24], a period in which according to the authors the kidneys were too damaged. As has been mentioned, the present study lasted 30 days.

Under the conditions used in the present study (administration in the established time of *A. schlechtendalii* Kunth root extract at concentrations of 125 mg kg^{-1} of weight or 1.8 mg mL^{-1} in PG1 and PG2 groups, respectively), testing for a possible nephroprotective action of these groups against adenine induced damage, it can be considered from the statistical point of view that this capacity was not observed in the extracts. However, analyzing the averages attained, the serum creatinine and BUN in the PG1 and PG2 groups are comparatively lower than those in the IRDG group. This leads to a possible scenario for confirmation or not of nephroprotection of the extracts, if changes are made in experimentation. Within the possible changes, the increase in the extract dose and/or time of treatment may be considered.In the case of extract dose and based on an adenine-induced chronic renal failure model, there are studies using different plants but with similar bioactive components where a dose of 13 g kg^{-1} body weight extract administration favoured nephroprotective action, as opposed to 50 mg kg^{-1} body weight[23,24]. An increase in *A. schlechtendalii* Kunth extract dosage is justified for two reasons, the first is the LC50 which reveals non-toxicity and the second is the observation that the responses obtained with the administration of only the solid extract and the diet without adenine (SEG group) or solid and aqueous extract and diet, also without adenine (SEAG group) were statistically equivalent to the control group. The latter partly demonstrates that *A. schlechtendalii* Kunth root extract used as a traditional remedy for the treatment of renal diseases may have beneficial effects on health, possibly due to the presence of antioxidant agents of the flavonoid type and polyphenols as has been reported in some *Anthurium* species[13,25]. These bioactive compounds could be responsible for preventing glomerular inflammatory lesions and renal oxidative stress, conditions that are involved in the pathogenesis of chronic kidney disease. In studies conducted by the group of Ali *et al.*[7] using gum arabic (acacia gum), it has been suggested that its nephroprotective effect, shown in CKF models induced by adenine, is based on its anti-inflammatory and anti-oxidant action.

Among other possible mechanisms, blocking both the angiotensin receptor and the inhibition of the angiotensin-converting enzyme would prevent renal oxidative damage indicating a certain role for angiotensin II, avoiding renal tubule cell hypertrophy and vasoconstriction[26,27]. Another associated mechanism could be the inhibition of inflammatory mediators via NF-kB, reducing both pro-inflammatory (IL-1β, TNF-α, MCP-1 and MCP-2) and anti-inflammatory molecules (TGF-β e IL-10) in the proximal tubule cells[28]. To the best of our knowledge, this is the first study to report results on the effect of aqueous extracts from *A. schlechtendalii* Kunth root in relation to the nephroprotective and remission capacity on the severity of adenine-induced renal damage in a murine model. It is necessary to continue the studies on the subject to define whether or not this capacity exists against the model of adenine induced nephrotoxicity, with the appropriate changes in the conditions of experimentation.

From the beginnings of mankind, plants have been considered as our allies. More than 90% of the drugs used in the non-industrialized world are natural products and more than 60% of medicines used in Western medicine originate from plants and microbes[29]. In Mexico, since the pre-Hispanic period, several species of the *Araceae* family have been used for medicinal, food, magical-religious and ornamental purposes[30]. However, the chemical and biological activity studies of some species are practically null, including that of the genus *A. schlechtendalii* Kunth. Little is known about this plant, about the different uses and applications it has had in traditional Mexican medicine. In order to strengthen the knowledge of this species, which up to that time remained unrecorded in Western medicine and patent databases, as well as in ethnobotanic and ethno pharmacological studies, firstly the toxicity evaluation of the aqueous extract of this plant was carried out. According to a preliminary toxicity test study with *Artemia salina* to determine the lethal concentration (LC50) through PROBIT transformation, the extract from *A. schlechtendalii* Kunth was shown to be non-toxic.

Renal insufficiency is a health problem in Mexico and in particular the state of Veracruz has occupied the first

place in new cases of chronic kidney disease (CKD) with 600 cases/million inhabitants. Due to the importance of the problem, there is an interest in finding alternatives for prevention, for therapeutic treatments by nephroprotective agents or remission of kidney damage through natural resources. The rat models are an important tool to investigate the development of CKD since anatomically and physiologically they are analogous with humans. The effects on renal and extra-renal damage of natural products have been studied in rat models inducing chronic renal failure by the administration of adenine[7,20,31,32].

CONCLUSION

In order to accrue scientific knowledge that can support or reject medico-ethnobotanical uses or claims of *A. schlechtendalii* Kunth, particularly those linked with the renal or urinary system, this pioneer study was performed, using adenine-induced renal damage as a model. Under the conditions used (dose and administration time), testing for possible nephroprotective action of the plant extract against adenine induced damage, from the statistical point of view, it can be considered that this capacity was not observed. However the need to continue and expand the research to clarify the effectiveness of *A. schlechtendalii* Kunth root in the prevention, mitigation or remission of kidney damage has become evident by the results achieved.

SIGNIFICANCE STATEMENT

The specific finding of this study is that under the conditions used in the preclinical experiment (with rats), *Anthurium schlechtendalii* Kunth extract did not show nephroprotective or renal damage remission capacity in a murine model where the renal damage was induced by oral administration of adenine. Further research needs to be carried out, covering phytochemical characterization and preclinical studies.

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