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Original Article

Caryota urens and *Hyophorbe lagenicaulis* as Nutraceutical by Managing Commercially Available Drug Induced Nephrotoxicity

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ABSTRACT

Background: *Caryota urens* flowers and *Hyophorbe lagenicaulis* leaves have huge beneficial properties, medicinal uses and rich phyto-pharmacological constituents. Nutraceutical potentiality of the selected plants on the basis of phytochemicals present in the aerial parts of *Caryota urens* and *Hyophorbe lagenicaulis* were taken as the background of the study. **Aim:** The present study investigates the nephroprotective potentiality of *Caryota urens* flowers and *Hyophorbe lagenicaulis* leaves against cisplatin and gentamycin induced nephrotoxicity. **Materials and Methods:** The extract of *Caryota urens* flowers and *Hyophorbe lagenicaulis* leaves were screened for preliminary phytochemical analysis. The *in vitro* antioxidant activity of *Caryota urens* flower extract (CUFE) and *Hyophorbe lagenicaulis* leaves extract (HLLE) was performed by DPPH and H_2O_2 radical scavenging activity. *In vivo* acute oral toxicity test was performed by following OECD guideline 420. The screening models for cisplatin and gentamycin induced nephrotoxicity by using albino Wistar rats were also carried out. **Results:** In *in vitro* antioxidant studies CUFE and HLLE (*p<0.01 and **p<0.001) for both standard and test drugs. It also act as potent nutraceuticals in cisplatin and gentamycin induced nephrotoxicity (**p<0.001). No major side effects were seen in any of the experimental animal during acute oral toxicity. **Conclusion:** CUFE and HLLE (1:1) have nutritionally rich source of dietary food supplements and due to this they are also helpful in managing the commercial drugs induced nephrotoxicity.

Keywords: Nutraceuticals, Phytochemical, Cisplatin, Gentamycin, Nephrotoxicity.

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INTRODUCTION

Nutraceuticals are dietary components naturally found in foods and believed to have a health benefit, including protecting and treating from many chronic diseases. Nutraceutical provides a better immune system.[1] An especially increasing nutritional interest in promoting healthiness. Current therapies have increased the life span of many peoples and these medicines are helpful in managing several diseases. For health care benefits completely understands the mechanism of action of major nutraceuticals food supplements and their possible efficacy in anti-aging and to improve RBC level, VLDL level, and with other health care benefits.[2] Discoveries gave us prompts to continue for useful food advancement having nutraceutical potential.[3] The possible mechanisms of their activity, evidence for potential health promoting activity, antioxidants and these phytochemicals in nutrition as substitutes for synthetic antibiotic activity promoters has also been addressed.[4,5] *Caryota urens* (family: Arecaceae) is widely known as the fish tail palm. The palm tree as a whole is native to Sri Lanka, India, Myanmar, and Malaysia, where it fills up fields and jungle clearings.[6] It is said to have originated in Cambodia. *Urens* is Latin for "stinging," and refers to the compounds found in *Caryota urens* fruit. Solitary fishtail palm, kitul palm, toddy palm, wine palm, sago palm, and jaggery palm are some of the common names in English.[7,8] The promising cancer prevention by *Caryota urens* and α-glucosidase restraint these herbal extracts are supposed to most likely because of the presence of bioactive phyto-pharmaceuticals present in them which acts as a potent nutraceutical elements.[9,10] *Hyophorbe lagenicaulis* (family *Arecaceae*) commonly known as bottle palm or palmistegargoulette, is a species of flowering plant. It is native to Round Island, Mauritius.[11,12] Inspite of effective role of *Caryota urens* and *Hyophorbe lagenicaulis* in folk traditional medicines, till date not appropriate scientific evidences are available on their biological activities and phytochemical distribution.[13,14] Both the selected plants are nutritionally rich therapeutic values and contains a combination of flavonoids, carotenoids, phenolics, phytoestrogenes and saturated fatty acids and sugars like sucrose,

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glucose, and fructose, and further new sap has shown potential for refreshments.[6,15]

Micronutrients are one of the major groups of nutrients our body needs. It contains essential minerals, biotin, fibers rich elements, macronutrients, prebiotic nutrients, and antioxidant vitamins or other essential elements that improve our health conditions.[5] It may be consumed as a dietary supplement or as a functional food unit which is a derivative of many isolated herbal plants with many medicinal properties.[16] These nutraceutical-based products play an essential role in human health.[17] The majority of the peoples are consuming all these herbal based nutraceutical products, which has safety and therapeutic effects. In the recent study of certain areas, such as raw material has uniformity and find the ability of good source of dietary and have the potential effect of these nutraceuticals.[18]

However, detailed analysis of health promoting bioactive compounds and antioxidants are present, especially in Himalayan wild edible flowers or leaves. The research on encompasses the main sources of these chemicals present in the herbal plant *Caryota urens* L. flowers and *Hyophorbe lagenicaulis* leaves.[19,20] Bioactive compounds and antioxidant potential of the richest source of total phenolics; for flavonoids; for ascorbic acid and for beta-carotene. Phenolic compounds, i.e. gallic acid varied among species.[21] Antioxidant activity showed the significant relation with total phenolics, flavonoids and phenolic compounds.[22,23] Keeping in mind all this background the current research work was aimed to perform the *in vitro* antioxidant and *in vivo* nephroprotective activity of *Caryota urens* and *Hyophorbe lagenicaulis* by cisplatin and gentamycin induced nephrotoxicity animal models using experimental animals.

MATERIALS AND METHODS

Collection and Authentication

The flowers of *Caryota urens* and leaves of *Hyophorbe lagenicaulis* were collected from NIET (Pharmacy Institute), Knowledge Park-II, Greater Noida in November 2019. It was authenticated by Dr. Anjula Pandey (Taxonomist), National Bureau Plant Genetic Resources (NBPGR), Pusa grounds, New Delhi. A voucher (specimen no: NHCP/NBPGR/2020-23) is protected in the herbarium segment by the ordered branch of NBPGR, New Delhi.

Extraction of plant materials

The aerial parts of both plant materials of *Caryota urens* and *Hyophorbe lagenicaulis* were shaded dried. Each one of the dried powdered samples was extracted with ethanol solvents upto 96 hr. The dried flower and leaf (150g) of *Caryota urens* and *Hyophorbe lagenicaulis* were extracted independently with ethanol (500ml) using the soxhlet apparatus. The liquid extracts were concentrated by using hot water bath set at 60°C then kept in a hot water bath to get more solid extract. The dry extract was then stored at 4°C until used.

Phytochemical analysis of the aerial part of Caryota urens flowers extract and Hyophorbe lagenicaulis leaves extract

A wide range of phytochemical components present in the extract of *Caryota urens* flowers and *Hyophorbe lagenicaulis* leaves. They were screened by preliminary phytochemical screening methods.[24] The phytochemical test was conducted by using the different chemical tests in ethanolic solvents to identify the different active phytochemical compounds such as organic compound contains an alkaloid, flavonoid, phenol, oxalic acid and inorganic mixtures, etc. distinctive essential metabolites were found in flowers of *Caryota urens* and leaves of *Hyophorbe lagenicaulis* with high concentration. Protein was present in less concentration in herbal plant extract of *Caryota urens* and *Hyophorbe lagenicaulis*.[25]

In vitro Antioxidant Activity Study

Antioxidant activity of both the extracts, *Caryota urens* flowers (CUFE) and *Hyophorbe lagenicaulis* leaves (HLLE) were determined by following the two methods; DPPH free radical scavenging activity and hydrogen peroxide free radical scavenging activity.[26,27]

DPPH free radical scavenging activity

Estimation of the free radical scavenging activity of CUFE and HLLE (1:1) ratio was done by DPPH free radical scavenging activity. The absorbance of ethanol preparation of 2,2-diphenyl1-1-picryl-hydroxyl (DPPH) was carried by UV spectrophotometer.

% inhibition = Absorbance of the control - Absorbance of the test/Absorbance of Control x 100.

Hydrogen peroxide scavenging activity

The free radical scavenging activity of CUFE and HLLE in the hydrogen peroxide (H_2O_2) model was also identified. The arrangement of H_2O_2 (40mm) was set up in phosphate buffer pH 7.4 and the concentrated solution was identified by observing the abs at 560nm using a UV-spectrophotometer.

% scavenged hydrogen peroxide = 1- Absorbance (standard)/ Absorbance (control) x100.

In vivo Pharmacological Studies

Oral acute toxicity study of CUFE and HLLE (1:1) according to OECD guidelines 420

Group I: Test drug (CUFE and HLLE) 5mg/kg, was suspended in 1% CMC w/v, P.O

Table 1: Antioxidant activity of standard drugα-Tocopherol (Vitamin E) as % inhibition of DPPH free radical scavenging.

Sl. No.	Drug Concentration (µg/ml)	α-Tocopherol (Absorbance) 295nm % inhibition
1.	10 µg/ml	0.039 nm
2.	20 µg/ml	0.044 nm
3.	40 µg/ml	0.052 nm
4.	60 µg/ml	0.064 nm
5.	80 µg/ml	0.073 nm

The effect of antioxidant activity (Table 1) of standard drug α-tocopherol (Vitamin-E) was showed the % inhibition of DPPH free radical scavenging activity at different concentrations.

Group II: Test drug (CUFE and HLLE) 50mg/kg, was suspended in 1% CMC w/v, P.O

Group III: Test drug (CUFE and HLLE) 300mg/kg, was suspended in 1% CMC w/v, P.O

Group IV: Test drug (CUFE and HLLE) 2000mg/kg, was suspended in 1% CMC w/v, P.O

Albino Wistar rats were separated into 4 groups (Group I, Group II, Group III, and IV) of *n*=6 animals of both sex (3 Males and 3 Females) each. Test medication of CUFE and HLLE (1:1) at different given doses of 5mg/kg, 50mg/kg, 300mg/kg, 2000 mg/kg body weight was suspended in carboxymethyl cellulose (CMC) and administration orally in the wistar rats.

Cisplatin induced nephrotoxicity

In cisplatin induced nephrotoxicity, induction of kidney damage was done by experimentally induced single dose of cisplatin. The animal groups of Albino Wistar rats were divided into 3 groups. Group 1- Negative control group, Group 2- Standard Group of α-tocopherol (150mg/kg) (I.P), Group 3 Received extract of (CUFE and HLLE) (1:1) with single-dose 100mg/kg suspended in 1% CMC w/v and administered oralroute + Cisplatin (20mg/kg) IV route. After administration of the test drug CUFE and HLLE (1:1) suspension, animals were observed daily upto 21 days. Any toxic signs in the experimental animals were observed carefully. Then the animals were sacrificed as per the guidelines and kidney further sent for the histopathological findings.[28,29]

Gentamycin induced nephrotoxicity

In the gentamycin induced nephrotoxicity, the Albino Wistar rats were separated into 3 groups (n-6). Group 1- Negative control group, Group 2- Standard Group- α-tocopherol 150mg/kg (I.P route), Group 3- Received extract of (CUFE and HLLE) (1:1)with single-dose 100mg/kg suspended in 1% carboxymethyl cellulose (CMC) w/v and administered oral route + Gentamycin (80mg/kg) I.P route. After administration of the test drug CUFE and HLLE (1:1) suspension, animals were observed daily for upto 21 days. Any toxic signs in the animals were observed. Then the animals were sacrificed and observed for any major nephrotoxicity signs.[30,31]

Histopathological Study

At the end of the 21st day, food was withheld from the Albino Wistar rats, and they were fasted overnight but the animals had easy access to water. Under strong ether anaesthesia, the animals were killed and slaughtered through cervical dislocation. Surgically, the kidney was removed. After, following that, the isolated kidneys were immersed in 10% formalin for 1 hr (diluted to 10% with normal wine) to avoid shrinking of the organ utilized for histological investigations. Blood free kidney was taken out and stored in the containers separately filled with formalin (10% v/v). It was incubated at 37°C under aseptic conditions for histopathological evaluation under the microscope.[32,33]

RESULTS AND DISCUSSION

Phytochemical analysis of the aerial part of *Caryota urens* flowers extract (CUFE) and *Hyophorbe lagenicaulis* leaves extract (HLLE)

The plants *Caryota urens* and *Hyophorbe lagenicaulis* have large variety of phytoconstituents present such as alkaloids, flavonoids, phenols, oxalic acid, organic compounds and inorganic mixtures, etc. Distinctive essential metabolites were found with high concentration in their extracts. The presence of terpenoids, oxalic acid, phenols and flavonoids in CUFE and HLLE have shown strong antioxidants properties.[23,34] Terpenoids have antioxidants as well as anti-cancer properties and promote the plant growth regulators by glutathione s-transferase. Oxalic acid also have antioxidants properties, they act as primary chelator of calcium. It is used as a nutraceutical for health benefits with healthy weight

Table 2: Effect of CUFE and HLLE (1:1) in DPPH free radical scavenging activity.

Sl. No.	Extract	Concentration (µg/ml)	Inhibition %
1.	CUFE and HLLE (1:1)	10µg/ml	13.15±1.010
2.	CUFE and HLLE (1:1)	20µg/ml	21.16±1.714
3.	CUFE and HLLE (1:1)	40 µg/ml	41.37±1.589*
4.	α-tocopherol	40µg/ml	52.72±1.926*

Values were estimated as mean ± SD of each group. The effect of CUFE and HLLE (1:1) showed the % inhibition of free radical scavenging activity was found to be 41.37%* as compared to the reference standard drug α-tocopherol 52.72%*. The p-value was found to be *$p<0.01$ for both CUFE and HLLE.

Table 3: Effect of CUFE and HLLE (1:1) in hydrogen peroxide scavenging method.

Sl. No.	Drug Concentration (µg/ml)	CUFE and HLLE (1:1) (%)	α-Tocopherol (%)
1.	0.0625	15.79±0.008	11.11±0.016
2.	0.125	33.35±0.012	15.61±0.007
3.	0.25	41.62±0.007	19.25±0.005
4.	0.5	59.68±0.019*	27.41±0.004*
5.	1	64.72±0.03**	38.12±0.02**

gains property. Protein was present in less concentration in CUFE as compared to HLLE.[19]

In vitro Study of Antioxidant Activity

DPPH free radical scavenging activity

In *in vitro* antioxidant activity, free radical scavenging activity of CUFE and HLLE (1:1) ratio was performed by DPPH free radical scavenging method. The absorbance of ethanol preparation of 2, 2-diphenyl1-1-picryl-hydroxyl (DPPH) was carried by UV-spectrophotometer.[16] The DPPH free radical scavenging activity was estimated by α-tocopherol as standard drug. Various concentration of the CUFE and HLLE (1:1) with α-tocopherol was prepared to check the free radical scavenging activity with the initial concentration 40 µg/ml. Absorbance was estimated at 295nm after 30 min by using a UV spectrophotometer. The % inhibition of free radicals was calculated with reference standard. The free radical scavenging ability of CUFE and HLLE (1:1) was shown. The results were tabulated in Table 2. The effect of anti-oxidant were showed as % inhibition of DPPH free radical activity at different concentrations of test and standard drugs.

The % inhibition of free radical scavenging activity was increased as the concentration of CUFE and HLLE (1:1) rises, at 40µg/ml concentration the % inhibition was found to be 41.37% as compared to the standard drug α-tocopherol which was 52.72%.

Hydrogen peroxide scavenging activity

Values were estimated as mean ± SD of each group. The effect of CUFE and HLLE (1:1) showed good scavenging activity compared with the reference standard drug α-tocopherol. At 0.5µg/ml of the % inhibition was found to be 59.68 and 27.41% respectively. At 1µg/ml of the % inhibition was found to be 64.72 and 38.12% respectively. The *p*-value was found to be **p*<0.01 and ***p*<0.001 for both standard and test drugs.

The antioxidant effect of CUFE and HLLE (1:1) was also evaluated by using Hydrogen peroxide scavenging method (Table 3). Sample were prepared in ethanol solvent at 5 different concentrations (0.0625, 0.125, 0.25, 0.5 and 1µg/ml) of CUFE and HLLE (1:1) and reference standard drug α-tocopherol respectively. The absorbance was detected for both test and standard drug by UV spectrophotometer at 295nm. The % inhibition of test drug and the reference standard was calculated. The effect of CUFE and HLLE (1:1) showed good H_2O_2scavenging activity compared with the reference standard drug α-tocopherol. At 0.5µg/ml of the % inhibition was found to be 59.68 and 27.41% respectively and at a dose of 1µg/ml of the % inhibition was found to be 64.72 and 38.12% respectively. The *p*-values was found to be **p*<0.01 and ***p*<0.001 for both standard and test drugs.

Statistical Analysis

It was estimated that the CUFE and HLLE (1:1) suspension contains a considerable amount of antioxidant compounds with high anti-oxidative value and free radical scavenging activities and all experimental measurements were calculated as a normal of three examinations ± SD. The investigations were determined by the student t-test and p-values were calculated by single direction ANOVA. The**p*<0.01 and ***p*<0.001 were viewed as critical point.

In vivo Pharmacological Studies

Determination of oral acute toxicity (according to OECD guidelines 420)

To study the oral acute toxicity of CUFE and HLLE (1:1) suspension by using OECD 420 guideline Table 4, no any major adverse reaction or mortality in experimental animal was observed. The dose levels of CUFE and HLLE (1:1) suspension were 5 mg/kg, 50 mg/kg, 300 mg/kg, and 2000 mg/kg during the entire period of experimentation. There were no clinical signs of toxicity or abnormal behaviours on any of the treated experimental animals were observed.

Cisplatin Induced Nephrotoxicity Model

Test of hematological parameters of cisplatin induced nephrotoxicity

The effect of various hematological parameters in cisplatin induced nephrotoxicity was estimated in experimental rats at the end of 21 days of drug treatment. Estimation of Hb, RBC, WBC, MCHC, MCH, and MCH levels were increased, the blood glucose level was normalized and there was a decrease in Cr, BUN and VLDL levels were observed in CUFE and HLLE treated rats as shown in Table 5.

The findings of hematological parameters showed that the test drugs CUFE and HLLE (1:1) are responsible for the better health effects as compared to the control group. Reduction

Table 4: Oral acute toxicity test (according to OECD guidelines 420).

Sl. No.	Group no.	0 Day (g)	1 Day (g)	2 Day (g)	Total Body weight (g)
1	Group I- CUFE and HLLE (1:1) Suspended 5mg/kg	160.73 ± 3.57	163.91 ± 2.13	172.97 ± 2.90	25.14 ± 1.15 ^{NS}
2	Group II- CUFE and HLLE (1:1) Suspended 50mg/kg	164.47 ± 4.10	171.38 ± 5.16*	189.70 ± 5.94*	25.96 ± 2.76*
3	Group III- CUFE and HLLE (1:1) Suspended 300mg/kg	170.37 ± 5.10	181.46 ± 6.36**	195.70 ± 6.94**	26.59 ± 4.26**
4	Group IV- CUFE and HLLE (1:1) Suspended 2000mg/kg	175.47 ± 5.70	189.97 ± 6.59***	194.47 ± 7.61***	27.09 ± 5.39***

CUFE (*Caryota urens* flowers extract) and HLLE (*Hyophorbe lagenicaulis* leaves extract). The mean values were estimated mean as ± SEM of 6 rats in each group. The *p*-value was found to be *p<0.05, **p<0.01 and ***p<0.001, NS: non-significant at different concentrations of test drugs.

Table 5: Effect of blood profile in cisplatin induced nephrotoxicity.

Sl. No.	Hematological parameters nephrotoxicity	Group I [Negative control +cisplatin]	Group II [CUFE and HLLE (1:1) suspension +cisplatin]	Group II [α-tocopherol +cisplatin]
1	HB (g/dl)	11.14 ± 1.41	13.55 ± 1.62**	12.96 ± 1.65*
2	RBC (m/mm^3)	7.92 ± 0.34	8.52 ± 0.34**	8.12 ± 0.56*
3	WBC(m/mm^3)	8.21 ± 1.08	9.33 ± 0.62*	9.13 ± 0.90**
5	MCH(pg)	15.35 ± 1.55	15.43 ± 1.67**	16.35 ± 1.81*
6	MCHC %	31.28 ± 1.82	33.38 ± 1.62**	30.88 ± 1.22*
7	Total Cholesterol (mg/dl)	95.14 ± 5.81	97.27 ± 4.91**	105.27 ± 4.61*
8	TG (mg/dl)	92.07 ± 11.60	95.07 ± 11.60**	103 ± 1.87*
9	Glucose(mg/dl)	97.85 ± 5.95	98.19 ± 4.85**	106.15 ± 5.55*
10	Creatinine(mg/dl)	0.52 ± 0.06	0.53 ± 0.05**	0.55 ± 1.03*
11	Urea (mg/dl)	36.78 ± 1.49	33.98 ± 1.58**	38.83 ± 1.77*

The effect of CUFE and HLLE (1:1) suspension was compared with that of the control group and the standard group treated animals. All the values were expressed in the mean ±SEM of six rats in each group. For a given portion, Non-significant (NS) and significant value presented at *p<0.01 and **p<0.001.

in the serum of Cr, BUN, and total cholesterol level or VLDL level in cisplatin-treated rats were also showed to improve the health conditions of the treated rats so, the test drugs CUFE and HLLE (1:1) are considered as the potent herbal nutraceutical as they improve the haematological profile as well as acts as a nephroprotective agent in the treated animals group.

Gentamycin Induced Nephrotoxicity Model

Test of hematological parameters of gentamycin induced nephrotoxicity

The effect of various hematological parameters in gentamycin induced nephrotoxicity was estimated in experimental rats at the end of 21 days of drug treatment. Estimation of Hb, RBC, WBC, MCHC, MCH were done. MCH levels were increased as compared to control groups, the blood glucose level was normalized and there was a significant decrease in Cr, BUN and VLDL (total cholesterol level) were observed in CUFE and HLLE treated rats as shown in the Table 6.

Histopathological Study

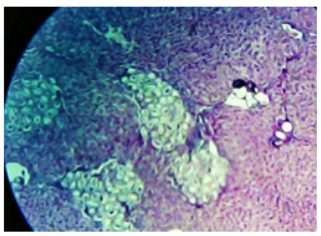
Cisplatin induced nephrotoxicity

Histopathological studies of organ (kidney) was performed and concerned images were depicted in Figure 1. After the 21 days of the treatment time frame, the histopathological observations from the experimental rat's kidney, sections showed Figure 1 (A) Microscopic section of kidney of negative control rats showed sporadic cells and stromal cell damage. In glomeruli, mesangial cellularity was increased. In tubules, a residue of destroyed cells, a single layer, and cuboidal cells appeared and focal lympho plasmacytic infiltrate was observed. Figure 1 (B) Nephrotoxicity induced animal treated with CUFE and HLLE (1:1) with single-dose 100mg/kg suspended in 1% (CMC) +

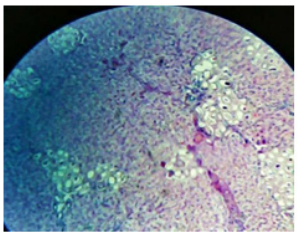
Table 6: Effect of blood profile of gentamycin induced nephrotoxicity study.

Sl. No.	Hematological parameters	Group I[Negative control + gentamycin]	Group II[CUFE and HLLE (1:1) suspension+ gentamycin]	Group II[α-tocopherol+ gentamycin]
1	HB (g/dl)	10.14 ± 1.71	12.45 ± 1.65*	13.76 ± 1.36**
2	RBC (m/mm^3)	6.92 ± 0.34	7.82 ± 0.34**	7.22 ± 0.86*
3	WBC(m/mm^3)	7.21 ± 1.08	8.09 ± 0.89*	8.83 ± 0.20**
5	MCH(pg)	14.15 ± 1.50	15.43 ± 1.57*	16.35 ± 1.71**
6	MCHC %	31.82 ± 1.28	32.84 ± 1.26*	33.18 ± 1.82**
7	Total Cholesterol (mg/dl)	96.54 ± 5.56	99.77 ± 6.91**	103.49 ± 4.61*
8	TG (mg/dl)	93.07 ± 11.10	98.01 ± 10.60**	108.22 ± 1.88*
9	Glucose(mg/dl)	96.85 ± 4.95	99.19 ± 4.85**	105.55 ± 5.55*
10	Creatinine (mg/dl)	0.64 ± 0.06	0.51 ± 0.05**	0.59 ± 1.01*
11	Urea (mg/dl)	36.74 ± 1.49	37.79 ± 1.28**	38.83 ± 1.27*

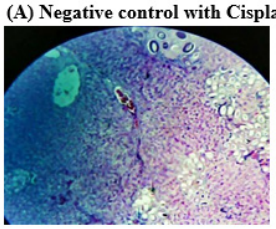
The effect of CUFE and HLLE (1:1) suspension was compared with that of the control group and the standard group treated animals. All the values were expressed in mean ±SEM of six rats in each group. For a given portion, Non-significant (NS) and significant at value presented at *p<0.01 and **p< 0.001.



(A) Negative control with Cisplatin,

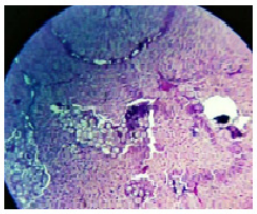


B) CUFE & HLLE with Cisplatin

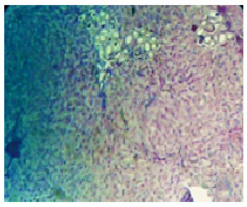


(C) α-Tocopherol with Cisplatin

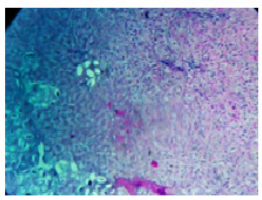
Figure 1: Histopathology of kidney: Cisplatin-induced nephrotoxicity.



(A) Negative control with Gentamycin,



B) CUFE & HLLE with Gentamycin and



C) α-Tocopherol with Gentamycin

Figure 2: Histopathology of kidney: Gentamycin-induced nephrotoxicity.

Cisplatin (20mg/kg) showed prominent recovery in glomeruli architecture and significantly decreased in the infiltration of lymphocytes, plasma cells in the stroma, and glomeruli. Figure 1 (C) Nephrotoxicity induced animal treated with α-tocopherol (150mg/kg)+Cisplatin (20mg/kg) showed prominent recovery as same in test group from cisplatin-induced changes in the smallest cells of the kidney (nephron). It indicated α-tocopherol was able to restore normal histological architecture of kidney.

Gentamycin induced nephrotoxicity

After 21 days of the treatment time frame, the histopathological observations from the experimental rats kidney, were showed Figure 2 (A) Microscopic section of kidney negative control rats showed that the single layer renal sporadic cells and cell disarrangements. In glomeruli, mesangial cellularity was increased. In tubules, in a residue of destroyed cells, a single layer, cuboidal cells appeared and focal lymphoplasmacytic infiltrate was observed. Figure 2 (B) Nephrotoxicity induced animal treated with CUFE and HLLE (1:1) 100mg/kg suspended in 1% (CMC) + gentamycin (80mg/kg) showed prominent recovery in glomeruli architecture and significantly decreased the infiltration of lymphocytes, plasma cells in the stroma and glomeruli. It also a mild increase in mesangial cellularity. Figure 2 (C) Nephrotoxicity induced animal treated with α-tocopherol (150mg/kg) + gentamycin (80mg/kg) showed prominent significance with gentle assurance from initiated changes in the stroma cells of the kidney (nephrons). It indicated α-tocopherol was able to restore normal histological architecture of kidney.

The intensity of cisplatin and gentamycin induced nephrotoxicity essentially causes tubules interstitial injuries and decreases body

weight were recorded. Cisplatin causes toxicity in the renal tubules, mainly in the fragment of the external medulla and mitochondrial expansion in the kidney nephrons. The reports of the intensity of cisplatin and gentamycin induced pathological damage in the kidney and its prevention by CUFE and HLLE (1:1) suspension was observed. In both cisplatin and gentamycin induced nephrotoxicity models, the CUFE and HLLE (1:1) suspension was significantly effective. CUFE and HLLE (1:1) was found to be more potent in cisplatin induced nephrotoxicity after 21 days of test drug administration as compared to the gentamycin induced nephrotoxicity. This protective effect is might be due to the presence of rich amount of antioxidants present in both the plants which works synergistically when given in combination. Based on the above findings, it was concluded that the impact of CUFE and HLLE against cisplatin and gentamycin induced nephrotoxicity in Wistar rats was observed to be beneficial. Thus CUFE and HLLE are acting as potent nutraceutical by preventing vital organ damage (kidney) due to the commercially available synthetic drugs like cisplatin and gentamycin.

CONCLUSION

Present investigation has clearly showed that the *Caryota urens* flowers extract and *Hyophorbe lagenicaulis* leaves extract (CUFE and HLLE) (1:1) suspension have great bioactive components and a nutritionally rich source of food suppliment. The preliminary phytoconstituent testing was determined the presence of alkaloids, carbohydrates, amino acids, proteins, and flavonoids, in the CUFE and HLLE both. The phytoconstituents present in CUFE and HLLE like phenols and flavonoids assumed to acts as an essential part by keeping shielding oxidative stress from free radicals. These essentials elements bioactive molecules are utilized to treat gastric ulcers, snake chomps, headaches, hair growth and rheumatic swellings. *Caryota urens* and *Hyophorbe lagenicaulis* both plants are considered multipurpose and have various therapeutic efficacies in all the vital organs (multiorgan). It was the first time that the extract obtained from the aerial parts of *Caryota urens* and *Hyophorbe lagenicaulis* administered orally in the suspension form for the evaluation of nutraceutical supplementation that showed potent antioxidant and prevention from cisplatin and gentamycin induced nephrotoxicity in experimental animals.

The present research work was concluded that *Caryota urens* and *Hyophorbe lagenicaulis* having potent antioxidants and nephroprotective properties along with presence of essential components required for healthy weight gain. So both of the plants can be considered as a good nutraceutical for the management nephrotoxicity occurred because of the commercially available synthetic drugs.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

DPPH: 2, 2-diphenyl1-1-picryl-hydroxyl; **H_2O_2:** Hydrogen peroxide; **RBC:** Red blood cell; **VLDL:** Very low density lipoprotein; **Hb:** Hemoglobin; **Cr:** Creatinine; **BUN:** Blood urea nitrogen; **WBC:** White blood cell; **MCHC:** Mean corpuscular hemoglobin concentration; **MCH:** Mean corpuscular haemoglobin; **UV:** Ultraviolet; **OECD:** Organization of economic corporation development; **PO:** Per oral; **CMC:** Carboxymethyl cellulose; **v/v:** Volume/Volume; **SD:** Standard deviation; **ANOVA:** Analysis of variance; **CUFE:** *Caryota urens* flowers extract; **HLLE:** *Hyophorbe lagenicaulis* leaves extract.

SUMMARY

Nutraceuticals (nutritional supplements) are often used to treat both core symptoms and comorbidities, however some have yet to be fully tested in case of organ related various toxicities. Correction of micronutrient deficiencies caused by a poor diet, as well as support for metabolic processes such as redox regulation, mitochondrial dysfunction, and melatonin generation, are all possible biological mechanisms of nutraceuticals.

Kidney dysfuctioning can be caused by continuous exposure of environmental toxins, drugs, alcohol abuse, as well as over the counter drug usages.

The aim of the present study was to determine the action of nephroprotective activity of *Caryota urens* and *Hyophorbe lagenicaulis* by using two established commercially available drugs Cisplatin and Gentamycin induced nephrotoxicity in albino wistar rats.

The results obtained are significant nephroprotective effects along with improving vital functioning and body weights of experimental animals showed the efficacies of *Caryota urens* and *Hyophorbe lagenicaulis* as potential nutraceutical by managing nephrotoxicity.

The effects showed by CUFE and HLLE are might be due to the potential opposed nephrotoxicity by the treatment with bioactive constituents present in both the plants and their strong antioxidant nature.

In this present research work study, the nephroprotective activity was observed that showed the CUFE and HLLE (1:1)

has a prominent defensive action against both the standard drugs cisplatin and gentamycin. The combination of *Caryota urens* flower extract and *Hyophorbe lagenicaulis* leaves extract has revealed the capability to improve the normal functioning of the kidney not only this they also enhance the body weight and haematological paramenter acting as a potent nutraceutical. From the above fundamental examination results, it very well may be reasoned that the *Caryota urens* flower and *Hyophorbe lagenicaulis* leaves are demonstrated to be one of the herbal remedies for drug induced nephrotoxicity.

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