

An **INNOVATIVE** Approach for  
MANAGEMENT OF POOR KIDNEY FUNCTIONS

# NEERI<sup>®</sup> KFT

**ACTS AS NEPHROPROTECTIVE**  
**EXERTS ANTI-OXIDANT ACTION**  
**ACTS AS IMMUNOMODULATOR**

## A Natural Kidney Function Toner

A unique formulation developed  
by extensive research work for

# PRIMARY KIDNEY CARE

in patients with impaired  
Kidney Functions.

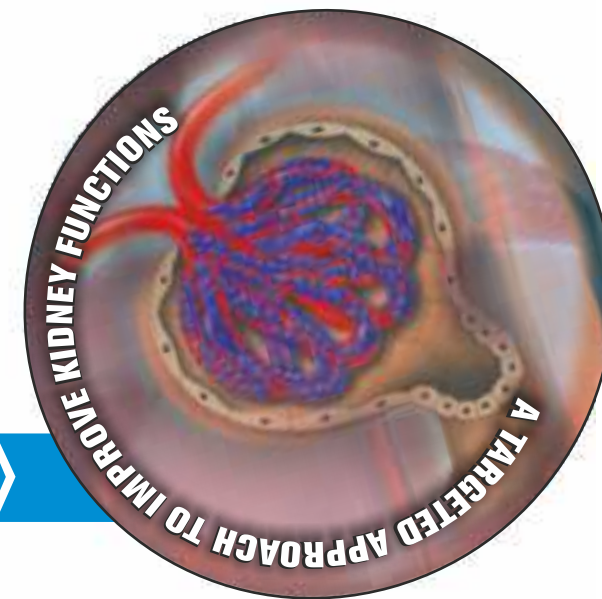




# NEERI<sup>®</sup> KFT

**A Natural Kidney Function Toner**

Providing  
**PRIMARY  
KIDNEY  
CARE**



## **Reduces elevated Blood Urea & Serum Creatinine Significantly**

Protects nephrons, decreases the elevated biochemical markers such as blood urea & serum creatinine - **Punernava** & **Varuna**



## **Improves the functional capacity of kidneys**

Helps maintain the cellular integrity and architecture of kidneys, prevent renal injuries. Also helps improve haemopoiesis - **Sigru** & **Sariva**



## **Protects against various Nephrotoxins**

Detoxifies the effects of Nephrotoxic agents. Significantly reduces the deposition of 2,8-dihydroxyadenine content - **Ravend Chini**



## **Checks serum electrolyte imbalance & maintains GFR**

Restores electrolytic homeostasis by improving activity of  $\text{Na}^+$ - $\text{K}^+$ -ATPase - **Kasni**



## **Helps Protect from Diabetes induced Nephron Damage**

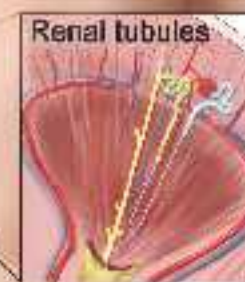
Exerts potent aldose reductase inhibitory activity, checks diabetes induced oxidative stress- **Makoi** & **Punernava**



**Improves Impaired Kidney Functions**

**Acts as Nephroprotective**

**Acts as Nephrocorrective**



## **Acting as Anti-oxidant**

Neeri KFT provides a rich concentration of Anti-oxidant phytoconstituents and very high dose of Anti-oxidants even have been suggested to reduce frequency of renal dialysis significantly - **Sigru**



## **Acting as Immunomodulator**

Neeri KFT stimulates defence system by modulating several immunological parameters like TLC, DLC, NBT, DTH, IgG, IgM etc - **Shirish**



## **Protects Kidneys by renal vasodilation**

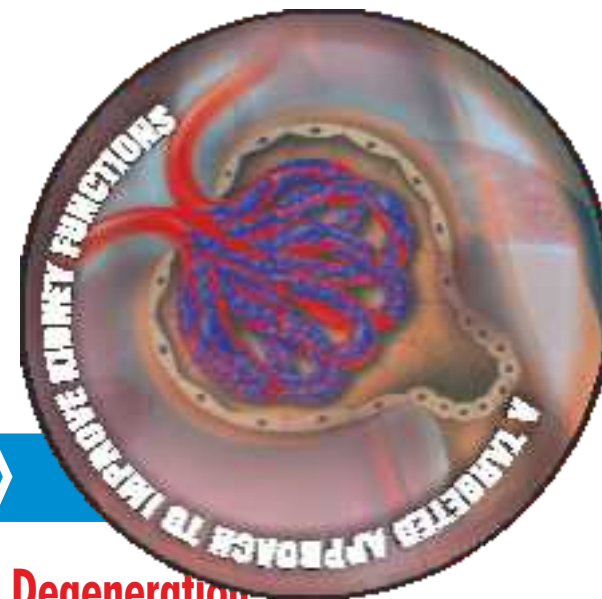
Exhibits Alpha-adrenoceptor activity, inhibits Angiotensin converting enzyme thereby, reducing renal hypertension - **Papaya** & **Coriander**





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## Reduces increased Blood urea & Serum creatinine

### Protects Nephrons, checking tubular necrosis and cell degeneration

The study was designed to investigate the effects of pre-treatment of aqueous extract of **Boerhaavia diffusa** (Punernava) root (200 – 400 mg/kg/day) in repeated dose acetaminophen induced nephropathic experimental subjects for 14 days.

Administration of **B. diffusa** induced marked improvement of renal functions, characterized by a significant decrease in blood urea nitrogen (BUN), serum creatinine ( $p < 0.01$ ) and protected the renal cells as evident from decreased level of kidney malondialdehyde (MDA),

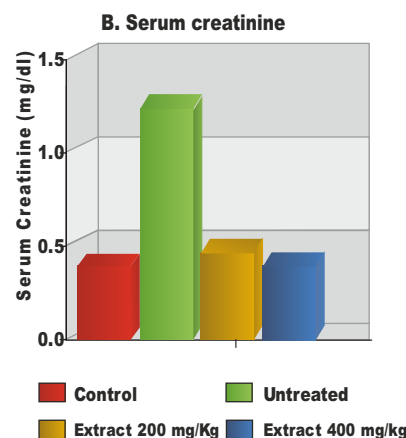
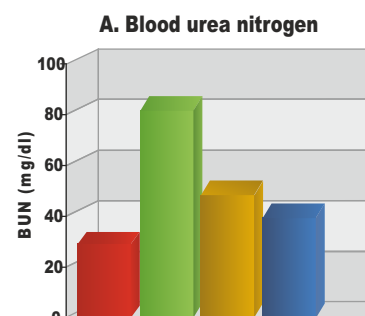
protein thiol ( $p < 0.01$ ) along with restoration of super oxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) activities and increased glutathione (GSH) levels ( $p < 0.01$ ). Thus pretreatment with **B. diffusa** extract protected against these changes.

(Pharmacology on line 2: 698-706, 2011)

**Boerhaavia diffusa** (Punernava) reversed the histopathological changes caused by acetaminophen i.e. Structural damages to kidneys like tubular necrosis, degeneration of epithelial cells, glomerular damage and congestion



Effect of *B. diffusa* aqueous extract on renal function



Effect of *B. diffusa* aqueous extract treatment on renal enzyme and other antioxidant marker in rat kidney homogenate analysis

Antioxidant Marker /Enzyme	Normal (Normal saline)	Control (normal saline+acetaminophen)	Treated (200 mg/kg extract)	Treated (400 mg/kg extract)
Malondialdehyde (µM/mg protein)	43.24±1.8	98.35±5.1 <sup>a</sup>	65.38±2.2 <sup>b</sup>	54.70±3.5 <sup>b</sup>
Catalase (µM H <sub>2</sub> O <sub>2</sub> decomposed/min)	38.2±1.2	23.5±1.6 <sup>a</sup>	32.6±1.5 <sup>b</sup>	35.4±0.9 <sup>b</sup>
Super Oxide Dismutase (U/mg protien)	9.64±0.2	3.82±0.9 <sup>a</sup>	7.15±0.6 <sup>b</sup>	7.98±0.5 <sup>b</sup>
Reduced Glutathione (nM/mg protien)	28.45±0.7	10.80±1.3 <sup>a</sup>	24.40±0.9 <sup>b</sup>	25.90±0.4 <sup>b</sup>
Glutathione Peroxidase (U/mg protien)	16.75±0.8	9.46±1.3 <sup>a</sup>	13.54±0.2 <sup>b</sup>	14.70±0.3 <sup>b</sup>
Total Protien Content (mg/dl)	58±2.5	215± 7.8 <sup>a</sup>	80±3.8 <sup>b</sup>	63± 4.1 <sup>b</sup>

Values are expressed in mean ± SEM (n=6)

<sup>a</sup> p<0.001 compared with normal group; <sup>b</sup> p<0.01 compared with control group

### Reverses Cisplatin-induced Nephron Degeneration

The extract of **Crataeva nurvala** (Varuna), when administered at two dose levels, i.e., 250 and 500 mg/kg body weight, **significantly reduced the increase in blood urea and serum creatinine and brought about a marked recovery in kidneys as evidenced microscopically. In the present work, extract of C. nurvala was found to increase the glutathione level and catalase activity and to decrease the concentration of TBARS in the kidney cortex.**

Hence, the possible mechanism of nephroprotection by this plant may be attributed to its antioxidant and free radical scavenging properties. (Pharmaceutical biology 42 (7),559-564, 2004)

**Crataeva nurvala** (Varun)

possesses marked nephroprotective activity and has a promising role to play in treatment of acute renal injury induced by nephrotoxins.

#### Effect of extract of *Crataeva nurvala* stem bark on Cisplatin induced renal damage

Groups no.	% Change in body weight	Blood urea nitrogen (mg/ dL)	Serum creatinine (mg/dL)
1 Normal Control	12.54±2.46	38.79±3.5	0.59±0.04
2 Treatment Control	13.8±3.17	39.5±3.86	0.56±0.016
3 Toxic Control	-17.5±1.3 <sup>a</sup>	79.74±3.15 <sup>a</sup>	1.57±0.028 <sup>a</sup>
4 Treatment Group I	-3.18±2.34 <sup>b</sup>	56.61±4.37 <sup>b</sup>	0.95±0.016 <sup>b</sup>
5 Treatment Group II	4.47±1.85 <sup>b</sup>	43.85±3.18 <sup>b</sup>	0.74±0.024 <sup>b</sup>

#### Effect of extract of *Crataeva nurvala* stem bark on biochemical variables indicative of oxidative stress in Cisplatin induced renal damage

Groups no.	Glutathione (µg/mg protein)	TBARS (mM/100 g tissue)	Catalase (µg of H <sub>2</sub> O <sub>2</sub> /min. mg protein)
1 Normal Control	4.39 ± 0.25	1.40 ± 0.09	358.39± 18.37
2 Treatment Control	4.42 ± 0.3	1.45 ± 0.13	366.63± 21.18
3 Toxic Control	1.16 ± 0.2 <sup>a</sup>	2.89 ± 0.15 <sup>a</sup>	198.14 ± 16.69 <sup>a</sup>
4 Treatment Group I	2.29 ± 0.26	1.92 ± 0.09 <sup>b</sup>	246.42 ± 25.86
5 Treatment Group II	3.35 ± 0.2 <sup>b</sup>	1.5 ± 0.05 <sup>b</sup>	310.96 ± 21.63 <sup>b</sup>

Values are mean ± S.E.M.

<sup>a</sup> P<0.05 vs Control (Group 1).

<sup>b</sup> p< 0.05 vs Cisplatin 16 th day ( Group 3)

One way ANOVA followed by post hoc sheffe's test.

1. Normal saline treated

2. Normal saline+ *C. nurvala* 500 mg/kg treated

3. Cisplatin treated

4. Cisplatin+ *C. nurvala* 250 mg/kg treated

5. Cisplatin+ *C. nurvala* 500 mg/kg treated





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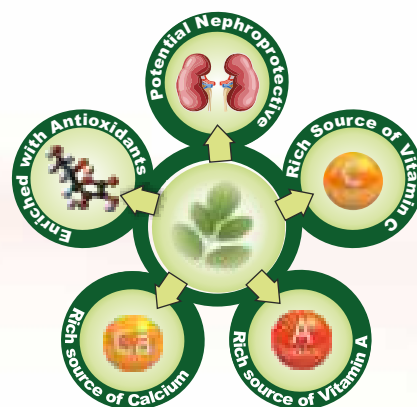
Restores the cellular integrity of kidneys

## Repairs & Improves Regenerative capacity of Kidneys

The nephroprotective effect of extract of *Moringa oleifera* (Sigru) (MO) leaves (150 and 300 mg/kg) was evaluated against gentamicin-induced (80 mg/kg) renal injury. Serum urea and creatinine levels were evaluated as the markers of renal nephrotoxicity. Treatment with different doses of MO reduced the levels of raised serum urea and creatinine in dose dependent manner. At high dose (300 mg/kg body wt.), MO restored the renal function after daily administration during 10 days; suggesting that the contents of MO not only protected the integrity of kidney but, at the same time increased its

regenerative and reparative capacity.

Although the present investigation suggests that the antioxidant activity may be the main mechanism for the nephro-protection by MO, other mechanisms, including a sympatholytic effect, a modulation of nitric oxide synthesis, and an inactivation of renine-angiotensin system, cannot be ruled out.



Effect of aqueous extract of *Moringa oleifera* leaves (MO) on serum urea in rabbits treated with gentamicin sulfate (GM)

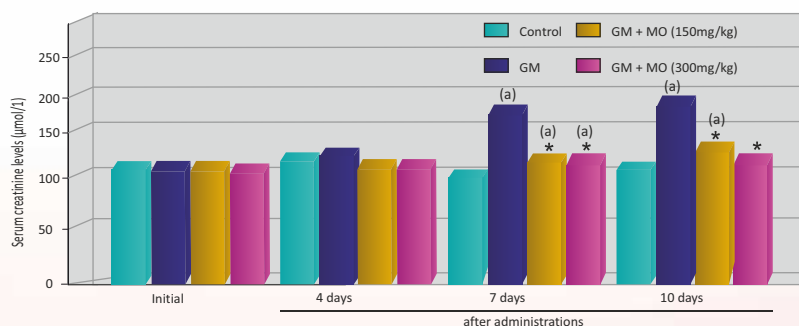
Groups	Treatment	Serum urea(mmol/l)			
		Before experiment	Days following administrations		
			4 days	7 days	10 days
Control	Vehicle	8.8±2.5	7.8±1.6	8.1±2.0	8.5±1.4
GM	80 mg/kg	8.2±1.0	9.1±1.8**	13.3±1.1**	17.1±1.8**
GM+MO	80mg/kg+150mg/kg	7.7±2.0	8.8±1.6	11.2±1.0*	15.4±2.0*
GM+MO	80ma/kg+300ma/kg	8.3±1.7	9.0±1.4	10.1±2.1*	11.5±1.5*

Values are mean± S.D (n=6 animals).

\*p<0.01 (Bonferroni's test) significant different from Gentamicin group (GM).

\*\*p<0.01 (Bonferroni's test) significant different from Control group.

Effect of aqueous-ethanolic extract of *Moringa oleifera* leaves (MO) on serum creatinine levels in rabbits treated with gentamicin sulfate (GM). Values are mean ± S.D., n = 6 animals. \*p < 0.01 (Bonferroni's test) significantly different from Gentamicin group. \*p < 0.01 (Bonferroni's test) significantly different from control group.

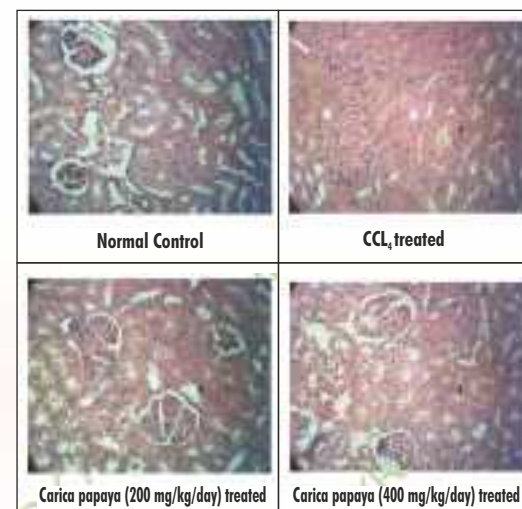


(Experimental & Toxicologic pathology 65, 335-339, 2013)

## Restores Renal histological architecture

In the present study on *Carica papaya* (Papita) (CPE), it was observed that treatment with CCl<sub>4</sub> induced a significant elevation in the levels of serum uric acid, urea and creatinine within 72 hours of exposure to it. These biochemical alterations were corroborated by the histological findings of glomerular and tubulo-interstitial necrosis in the untreated model control group. However, daily pretreatment with CPE for 7 days conferred nephroprotection on the CCl<sub>4</sub> renal injured exp. subjects in a dose-dependent fashion. Again, the histological findings of almost normal renal histological architecture corroborate the protection conferred by the extract within the stipulated time interval.

(Biology & Med. 1(1) 11-19, 2009)



## Ameliorates Nephrotoxicity, preventing acute renal failure

Administration of cisplatin shows significant increase in blood creatinine and serum urea concentrations as compared to normal control, which clearly indicates the intrinsic acute renal failure. The present study has shown that the drug *Hemidesmus indicus* (Sariva) extract in the experimental dosage significantly prevent the increase of cisplatin-induced serum creatinine and urea concentrations.

Effect of *Hemidesmus indicus*/Acorus calamus extracts on S. creatinine and blood urea levels in mice treated with cisplatin (\*P<0.001 when compared with cisplatin alone treated group).

Treatment Groups	Blood Urea (mg/dL)	S. Creatinine (mg/dL)
Control	28.084±0.47*	0.46±0.03*
Cisplatin	41.3±2.86	1.1±0.02
Cisplatin+ <i>H.indicus</i> (250 mg/kg bw)	34.54±0.37*	0.76±0.09*
Cisplatin+ <i>H.indicus</i> (500 mg/kg bw)	29.92±2.5*	0.56±0.06*
Cisplatin + <i>A. Calamus</i> (250 mg/kg bw)	30.12±0.96*	0.61±0.06*

(Pharmaceutical biology 48(3) 290-295, 2010)

“  
***Moringa oleifera***  
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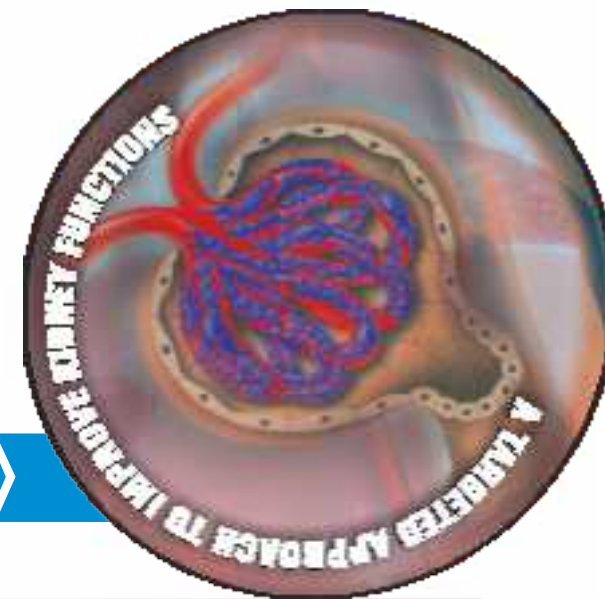
“  
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## Providing PRIMARY KIDNEY CARE

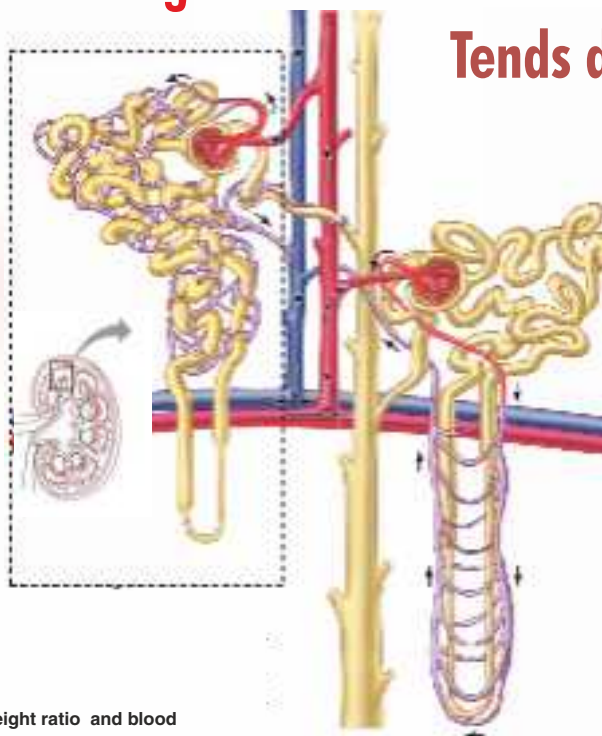


Improves the functional capacity of kidneys

### Improves Haemopoiesis, reverses Nephron Damage

Gentamicin in the dose of 90 mg/kg body weight of experimental subjects, was selected, which was injected i.m. for 6 days. In this group of experimental subjects (gentamicin control, gentamicin natural recovery and gentamicin plant recovery), there was a fall in body weight. The progressive rise in BUN with gentamicin administration indicated a decrease in the functional capacity of the kidneys because of acute renal failure. Raised levels of creatinine substantiated these findings.

*Hemidesmus indicus* (Sariva) prevented the fall in bodyweight of experimental subjects, which was seen in other groups that received gentamicin. The levels of BUN and creatinine showed a rise after 6 days, which was also seen in the plant treated group, but this was less than that observed in the group receiving gentamicin. These parameters indicated preservation of functional capacity. The attenuation of damage was confirmed on histopathology. Normal architecture was preserved.



Effect of gentamicin and root powder of *Hemidesmus indicus* (Sariva) on organ to bodyweight ratio and blood biochemical parameters in male and female experimental subjects

Test	Normal control	Gentamycin control	Gentamycin recovery	Gentamycin & Hemidesmus
<b>Male subjects</b>				
Kidney / bodyweight ratio				
Rt	0.003±0.0006	0.003±0.0002	0.003±0.0003	0.003±0.0002
Lt	0.003±0.0006	0.003±0.0004	0.0035±0.000	0.0034±0.000
Haemoglobin	16.3±0.47	13.3±1.90	15.8±1.55	17.0±1.60*
Serum creatinine	0.6±0.13	1.0±0.16	0.73±0.10	0.69±0.10*
BUN	16.4±2.30	21.1±2.84	18.1±2.40	18±1.6*
TC	86.8±5.06	98.8±4.58	117.1±11.63	110±20.2
<b>Female subjects</b>				
Kidney / bodyweight ratio				
Rt	0.003±0.0004	0.002±0.0003	0.0042±0.000	0.003±0.0001
Lt	0.003±0.0004	0.002±0.0003	0.004±0.0006	0.003±0.0002
Haemoglobin	14.2±0.70	12.8±1.21	16.6±0.82	17.1±0.74*
Serum creatinine	0.7±0.16	1.7±0.26	0.97±0.11	0.8±0.2*
BUN	18.5±1.48	21.5±4.81	17.1±0.70	17±1.17*
TC	135.8±11.4	135±12.82	134.5±20.8	108.1±7.30

All the values are expressed as mean ± SD, where n=6 Differences, which are significant, are marked as: \*P<0.5. BUN , blood urea nitrogen; LT, left ; Rt, right ; TC, total cholesterol

(Nephrology, 9, 142-152, 2004)

### Tends detoxify the effects of Nephrotoxic agents

*Solanum nigrum* (Makoi) fruit extract (SNFet) detoxifies the toxic effects of acetaldehyde and that it is also involved in regeneration processes.

This protective effect is mainly due to its free radical scavenging activity.

The below table shows the effect of SNFet on renal functional markers. The levels of urea, uric acid and creatinine were significantly higher in ethanol-administred rats whereas treatment with SNFet and silymarin significantly

decreased the levels to near normal values. *Solanum nigrum* (Makoi) contains phytochemicals such as alkaloids, flavonoids, terpenoids, glycosides, saponins, tannins, phenols, thiols, resins and anthroquinones. Pretreatment with aqueous extract of *S. nigrum* prevents the biochemical changes maintaining their values to near normal, which suggest that *S. nigrum* has nephroprotective activity.

*Solanum nigrum* possesses phytochemical constituents i.e. alkaloids, flavonoids, which prevent the biochemical changes maintaini

Effect of SNFet on renal function markers in the serum of control and ethanol treated rats

Groups	Urea (mg/ dL)	Uric acid (mg/dL)	Creatinine (mg/dL)
Control	25.38±1.69 <sup>ad</sup>	1.30±0.06 <sup>a</sup>	0.86±0.06 <sup>a</sup>
Ethanol	45.26±2.96 <sup>b</sup>	2.63±0.35 <sup>b</sup>	1.88±0.07 <sup>b</sup>
Ethanol + SNFet (250mg/kg b. Wt)	30.51±2.13 <sup>c</sup>	2.01±0.16 <sup>c</sup>	0.99±0.08 <sup>c</sup>
Ethanol + silymarin (250 mg/kg b. Wt)	27.86±2.01 <sup>d</sup>	1.93±0.13 <sup>c</sup>	0.89±0.06 <sup>d</sup>
Control + SNFet	23.65±1.19 <sup>a</sup>	1.39±0.08 <sup>a</sup>	0.80±0.01 <sup>d</sup>
Control+ silymarin	25.74±1.72 <sup>ad</sup>	1.35±0.07 <sup>a</sup>	0.67±0.03 <sup>c</sup>

Values are expressed as mean ± SD, n=6.

Values not sharing a common superscript (a,b,c,d) differ significantly at p<0.05.

(J.biochem Tech , 3(4), 339-343, 2012)

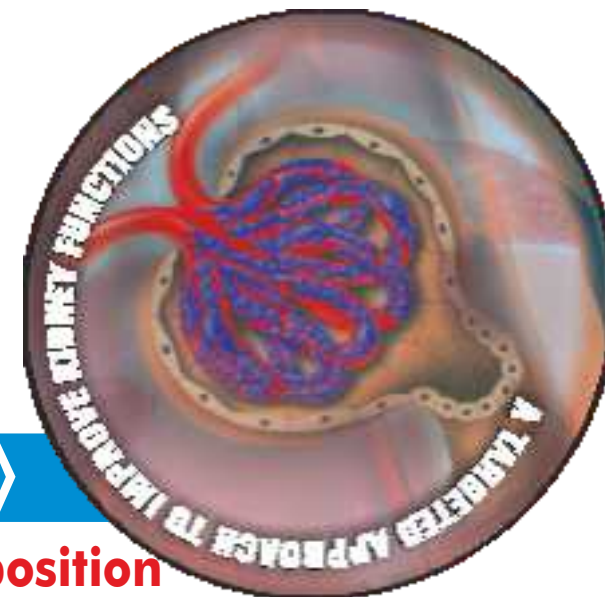






# NEERI® KFT

## Providing PRIMARY KIDNEY CARE



Nephroprotective effect on kidneys at proximal tubule (S1, S2, S3) »

### Effectively Protects against Nephrotoxins including heavy metals

The nephroprotective effects of extract of *Rheum emodi* (Revand chini) were investigated on cadmium chloride, mercuric chloride, potassium dichromate and gentamicin-induced nephrotoxicity in experimental subjects and normal experimental subjects by monitoring the levels of urea nitrogen and creatinine in serum.

The present investigations provide evidences that water soluble (WS) fraction has nephroprotective effect on all the proximal tubule segments (S<sub>1</sub>, S<sub>2</sub> and S<sub>3</sub>).

Cadmium chloride treatment caused nephrotoxicity as evidenced by marked elevation in blood urea (360%) and serum creatinine (157%) compared to control animals. Co-administration of Rheum extract with cadmium chloride (s.c.) inhibited the rise in blood urea (100%) and serum creatinine (135.6%).

### Significantly reduces the deposition of 2, 8-dihydroxyadenine content

The effect of the extract from *Rheum emodi* (Revand chini) was examined in experimental subjects with chronic renal failure induced by an adenine diet. On the treatment with Rhubarb extract, the level of urea nitrogen and creatinine in the serum showed a significant decrease, indicating an improvement of renal function. The urea concentrations in the kidneys were also decreased after the treatment. In addition the administration of the rhubarb extract to rats markedly decreased the kidney weight and 2,8- dihydroxyadenine content in the kidneys.

Effect of Rhubarb extract on urea nitrogen and creatinine in serum

Feeding period (d)	Group	Urea-N (mg/100ml)	Creatinine (mg/100ml)
6	Control	28.3±1.0 (100)	1.15±0.01 (100)
	Rhubarb extract	24.8±1.3 <sup>a)</sup> (88)	1.01±0.02 <sup>a)</sup> (88)
12	Control	31.3±1.7 (100)	1.33±0.04 (100)
	Rhubarb extract	31.6±1.3 (101)	1.16±0.03 <sup>b)</sup> (87)
18	Control	30.9±2.3 (100)	1.45±0.04 (100)
	Rhubarb extract	24.9±1.0 <sup>a)</sup> (81)	1.19±0.04 <sup>a)</sup> (82)
24	Control	59.5±4.5 (100)	1.70±0.06 (100)
	Rhubarb extract	38.7±4.5 <sup>a)</sup> (65)	1.40±0.06 <sup>b)</sup> (82)

Values are means± S.E. of experimental subjects  
Figures in parentheses are percentages of the control value.  
a) Significantly different from the control value, P<0.05 b) p<0.01 c) p<0.001

Effect of Rhubarb extract on urea concentration in the Liver and Kidney

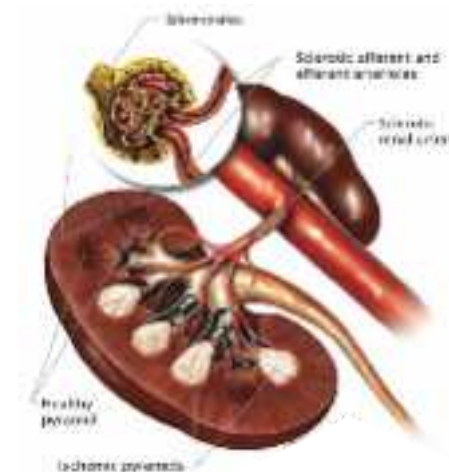
Feeding period (d)	Group	Liver Urea (mg/g tissue)	Kidney urea (mg/g tissue)
6	Control	0.40±0.02 (100)	0.87±0.05 (100)
	Rhubarb extract	0.35±0.02 <sup>a)</sup> (88)	0.69±0.04 <sup>a)</sup> (79)
12	Control	0.34±0.02 (100)	0.44±0.03 (100)
	Rhubarb extract	0.38±0.01 (112)	0.46±0.02 (105)
18	Control	0.40±0.02 (100)	0.54±0.03 (100)
	Rhubarb extract	0.34±0.01 <sup>a)</sup> (85)	0.44±0.01 <sup>b)</sup> (81)
24	Control	0.76±0.05 (100)	0.86±0.02 (100)
	Rhubarb extract	0.48±0.05 <sup>a)</sup> (63)	0.65±0.06 <sup>b)</sup> (76)

Values are means± S.E. of experimental subjects  
Figures in parentheses are percentages of the control value.  
a) Significantly different from the control value, P<0.05 b) p<0.01

Effect of Rhubarb Extract on 2,8 Dihydroxyadenine content in the Kidneys

Feeding period (d)	Group	2,8 Dihydroxyadenine (mg/kidneys)
6	Control	191 (100)
	Rhubarb extract	147(77)
12	Control	433 (100)
	Rhubarb extract	396(91)
18	Control	513 (100)
	Rhubarb extract	403 (79)
24	Control	690(100)
	Rhubarb extract	494(72)

Six rats were used in each group. Figures in parentheses are percentages of the control value.  
(Chem. Pharm. Bull 31(8) 2762-2768, 1983)



*Rheum emodi* (Revand Chini) has Nephroprotective effect on all segments (S1, S2 & S3) of proximal tubules by preventing rise in blood urea and serum creatinine



Study also confirmed that potassium dichromate at 20 mg/kg produces significant nephrotoxicity as evidenced by increase in blood urea (648%) and serum creatinine (360%). In contrast, the levels of BUN and serum creatinine were reduced by 39.2 and 43.3%, respectively in Experimental subjects fed with Rheum extract.

Experimental subjects which received mercuric chloride alone showed a significant increase in the levels of BUN (660%) and serum creatinine (432%). Experimental subjects of this model, which received Rheum extract, showed a significant prevention in the rise of serum markers like BUN (82.6%) and creatinine (68.4%).

Administration of gentamicin at 100 mg/kg for 5 days caused renal dysfunction in experimental subjects as evidenced by increase in blood urea (184%) and serum creatinine (471.6%) compared with control. Co-administration of Rheum extract with gentamicin (s.c.) prevented the rise in blood urea (62.6%) and serum creatinine (58.6%). From these experimental studies conducted with renotoxic metal agents (Cd, Cr, Hg) it may be concluded that WS fraction of *Rheum emodi* has a protective effect on all the segments (S1, S2 and S3) of proximal tubule. (J. Ethnopharmacol, 96, 121-125, 2005)





# NEERI® KFT

## Providing PRIMARY KIDNEY CARE



Normalises renal architecture and reduces frequency of renal dialysis

### Heals renal injuries, restoring renal architecture

***Boerhavia diffusa* (Punernava)** extract (BDE) was given to nephrolithiasis treated experimental subjects. Histological analysis depicted that BDE treatment inhibited renal cell damage. Renal histology of control animals showed no crystal deposits with

normal glomeruli and tubular architecture. Whereas animals exposed to ethylene glycol (EG) only showed shrinkage of glomeruli and severe tubular damage. Flat epithelial lining and glomerular capsule was also broken at few instances. Numerous crystal depositions were

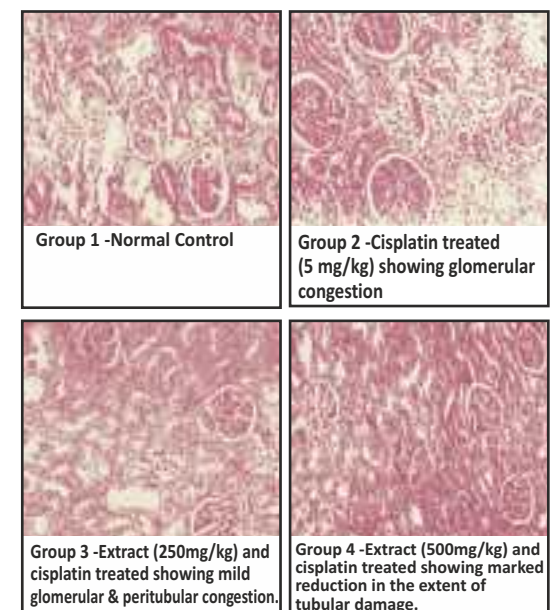
seen in renal tubule lumen and interstitial sites. Grossly, kidneys of untreated hyperoxaluric animal were damaged severely. However, simultaneous treatment with BDE reduced these renal injuries and normalized the renal architecture in dose-dependent manner.

### Reverses nephrotoxicity, checking tubular necrosis

This investigation demonstrates that cisplatin-induced renal injury was evidenced by elevated biochemical markers, such as blood urea and serum creatinine, as well as by the histopathological features of acute tubular necrosis.

The extract of *Crataeva nurvala* (Varuna), when administered at two dose levels, i.e., 250 and 500 mg/kg body weight, significantly reduced the increase in blood urea and serum creatinine and brought about a marked recovery in kidneys as evidenced microscopically.

Kidney sections



Histopathological analysis of hyperoxaluria-induced renal damage and crystal depositions.

Observational parameter	Control	Untreated	Treated (BDE 100 mg/kg)	Treated (BDE 200 mg/kg)
Tubular degeneration	□	+++	+	+
Tubular necrosis	□	+++	+	□
Tubular desquamation	□	+++	++	+
Tubular congestion	□	+++	+	+
Glomerular congestion	□	+++	++	□
Glomerular damage	□	+++	++	□
Interstitial edema	□	+++	□	□
Crystal deposits	□	+++	++	+
Gross damage to renal architecture	Normal	Severe	Moderate	Mild

Scores are based on average observations of renal damage observed in minimum 6 different fields per slide.  
+ mild, ++ moderate, +++ severe damage and □ normal; Similarly for crystal deposits, + rare, ++ few, +++ numerous and □ nil.

(Pharmaceutical biology 49(12), 1224-1233, 2011)



### Effect of extract of *Crataeva nurvala* stem bark on histological features of Cisplatin induced renal damage

Histological features	Group 1	Group 2	Group 3	Group 4
Glomerular congestion	-	++	+	-
Tubular casts	-	++	-	-
Peritubular congestion	-	++	+	-
Epithelial desquamation	-	++	-	-
Blood vessel congestion	-	++	-	-
Interstitial edema	-	++	-	-
Inflammatory cells	-	++	+	-

-normal; + mild; ++ severe

(Pharmaceutical biology 42 (7),559-564, 2004)





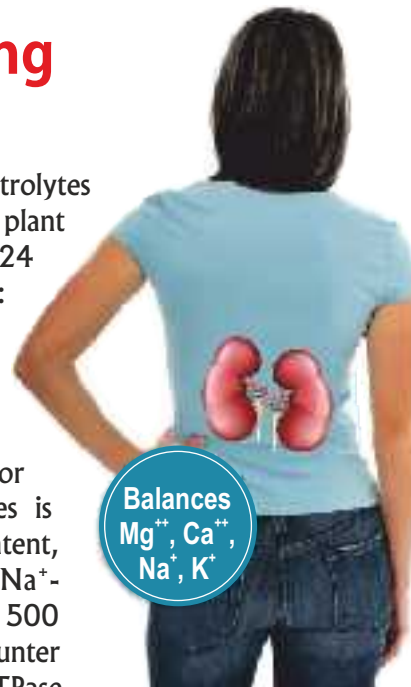
# NEERI<sup>®</sup> KFT

## Providing PRIMARY KIDNEY CARE

Helps restore serum electrolyte balance

### Checks disturbances, restoring Na<sup>+</sup> -K<sup>+</sup> -ATPase activity

Cisplatin is known by its toxicity by disturbing electrolytes homeostasis. Thus we aimed to find out the role of herbal plant *Cichorium intybus* on Cisplatin – induced toxicity. 24 experimental subjects were randomly divided into 4 groups: Group I is termed as untreated control; Group II is Cisplatin control and received 3 mg/ kg b.w.; i.p.; Group III received *C. intybus* ethanolic extract at a dose of 500 mg/kg b.w. orally for 10 consecutive days and Group IV is Cisplatin + *C. intybus* pretreated group. *C. intybus* is given 30 minutes prior to Cisplatin. Cisplatin – induced electrolytes disturbances is indicated by increase Intra - erythrocyte sodium content, decreased plasma magnesium, calcium and Intra-erythrocyte Na<sup>+</sup>-K<sup>+</sup>-ATPase which implicates the renal toxicity. At a dose of 500 mg/kg b.w. of *C. Intybus* pretreatment showed partial counter action on the electrolytes imbalances and Na<sup>+</sup> -K<sup>+</sup> -ATPase activity.

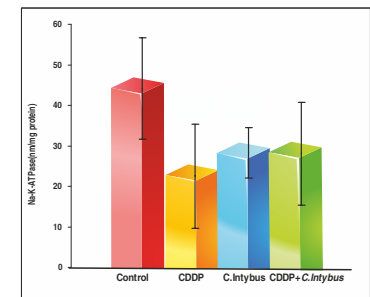


### Reverses the toxin induced elemental alteration in serum

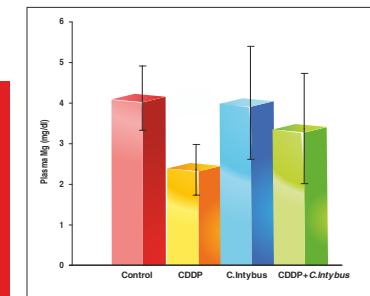
Toxicity induced by Cisplatin treatment is due to the disturbances in the electrolytes homeostasis which finally reduced the activity of Na<sup>+</sup>-K<sup>+</sup> -ATPase activity and leading to cell death. The study suggests that electrolytes imbalance particularly increase Intraerythrocyte sodium content, decreased plasma magnesium, calcium and Intra-erythrocyte Na<sup>+</sup>-K<sup>+</sup> -ATPase may implicate the nephrotoxicity. Treatment with extract of *C. intybus* protected the ion homeostasis altered by Cisplatin administration. Increased doses and time duration of herbal polyphenolic extract could function to reverse the toxic effect.



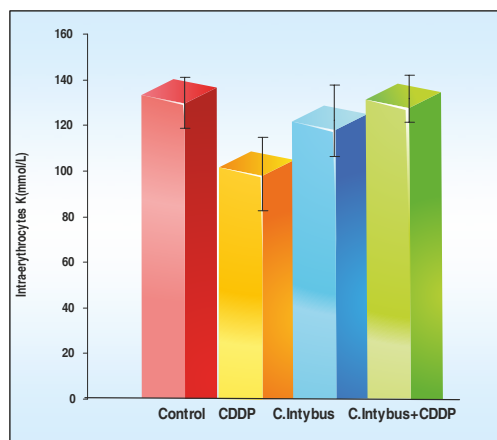
“ Treatment with extract of *Cichorium Intybus* (Kasni) protected the ion homeostasis altered by Cisplatin administration. Its Increased doses and time duration could function to reverse the toxic effect. ”



Intra-erythrocytes Na<sup>+</sup>-K<sup>+</sup>-ATPase level in Control, Cisplatin, *C. intybus* and CDDP + *C. intybus* - pretreated exp. subjects.

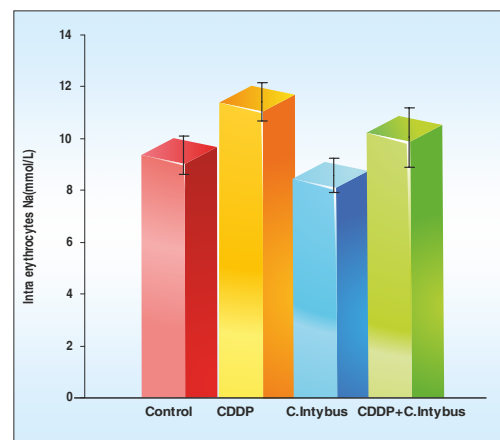


Plasma Mg<sup>++</sup> level in Control, Cisplatin, *C. intybus* and CDDP + *C. intybus* - pretreated exp. subjects.

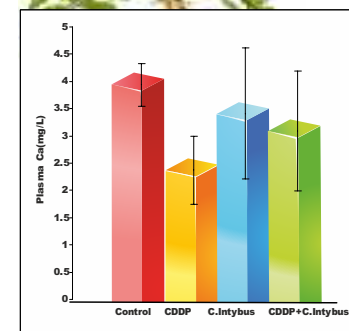


Intra-erythrocytes K<sup>+</sup> level in Control, Cisplatin, *C. intybus* and CDDP + *C. intybus* - pretreated exp. subjects.

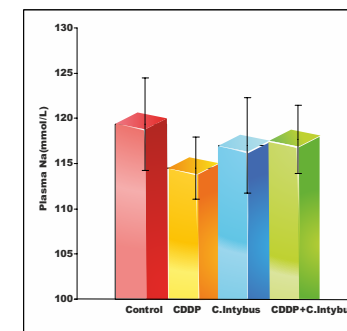
(Pak.J.Pharm. Sci. 25(4) , 857-862, 2012)



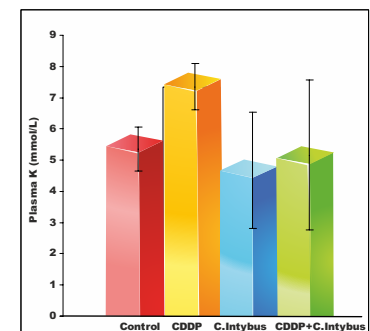
Intra-erythrocytes Na<sup>+</sup> level in Control, Cisplatin, *C. intybus* and CDDP + *C. intybus* - pretreated exp. subjects.



Plasma Ca<sup>++</sup> level in Control, Cisplatin, *C. intybus* and CDDP + *C. intybus* - pretreated rats.



Plasma Na<sup>+</sup> level in Control, Cisplatin, *C. intybus* and CDDP + *C. intybus* - pretreated exp. subjects.



Plasma K<sup>+</sup> level in Control, Cisplatin, *C. intybus* and CDDP + *C. intybus* - pretreated exp. subjects.

(Pak.J.Pharm. Sci. 25(4) , 857-862, 2012)





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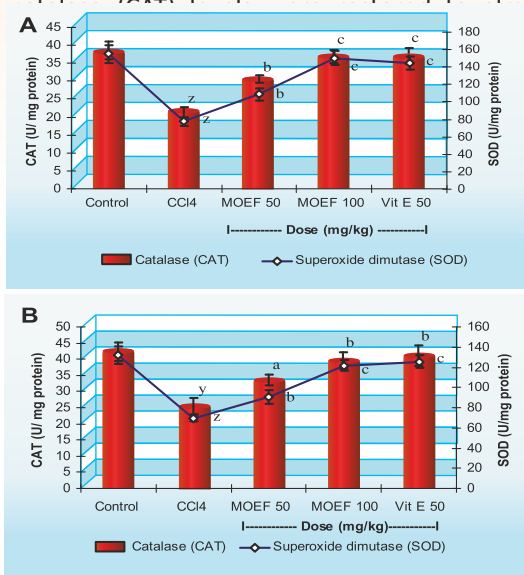
Tones hepato-renal functions, exerting anti-oxidant

## Potent protection against oxidative DNA damage

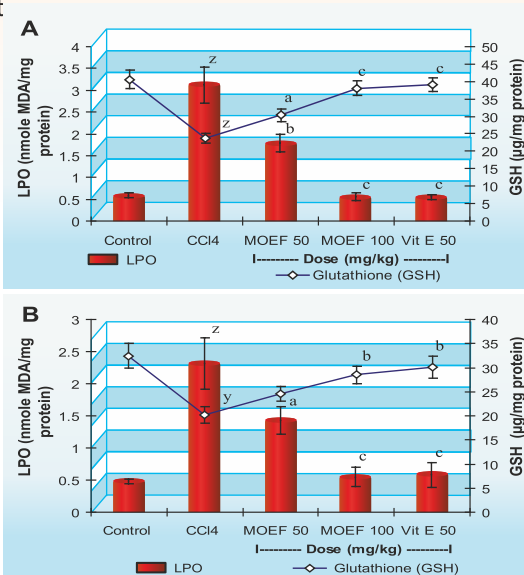
On the basis of in vitro antioxidant properties polyphenolic fraction of *Moringa oleifera* (Sigru) (MOEF) was chosen as the potent fraction and used for the DNA nicking and in vivo antioxidant properties. MOEF shows concentration dependent protection of oxidative DNA damage induced by HO<sup>•</sup> and also found to inhibit the toxicity produced by CCl<sub>4</sub> administration as seen from the decreased lipid

per oxides (LPO) and increased glutathione (GSH) levels. Among the antioxidant enzymes superoxide dismutase (SOD) and

normal levels compared to CCl<sub>4</sub> intoxicated experimental subjects. The HPLC analysis indicated the presence of phenolic acids (gallic, chlorogenic, ellagic and ferulic acid) and flavonoids (kaempferol, quercetin and rutin). Thus, it may be concluded that the MOEF possess high phenolic content and potent antioxidant properties, which may be mediated through direct trapping of the free radicals and also through metal chelation. The co-treatment of MOEF effectively protected the decline of antioxidant activity. The level of MDA was lowered in the MOEF treated animals in a dose-dependent manner. This is due to enhanced antioxidant status in the liver as well as in the kidney.



Effects of MOEF on level of antioxidant enzymes CAT (U/mg protein) and SOD (U/mg protein) in liver (A) and kidney (B) of CCl<sub>4</sub> intoxicated rats. Values are mean ± SEM for six rats; P: y < 0.01 and z < 0.001 compared to respective control group; P: a < 0.05, b < 0.01 and c < 0.001 compared to respective CCl<sub>4</sub> treated group. (Food & chemical toxicology 47, 2196-2201, 2009)



Effects of MOEF on level of LPO (nmole MDA/mg protein) and glutathione (μg/mg protein) in liver (A) and kidney (B) of CCl<sub>4</sub> intoxicated rats. Values are mean ± SEM for six rats; P: y < 0.01 and z < 0.001 compared to respective control group; P: a < 0.05, b < 0.01 and c < 0.001 compared to respective CCl<sub>4</sub> treated group.

## Effects on Renal Oxidative Stress and Enzymes of Antioxidant Defense System

*Moringa oleifera* (Sigru) seeds are reported to contain an exceptionally high content of methionine and cysteine amino acids. Beside sulphhydryl containing amino acids, *M. oleifera* has also been reported to possess numerous antioxidants like vitamin C, β-carotene, α- and γ-tocopherol, β-sitosterol, vitamin A, and phenolic compounds such as quercetin and kaempferol, flavonoides, anthocyanins. Studies reported a potent antioxidant activity of *Moringa oleifera* seed powder along with moderate chelating property against arsenic. *Moringa oleifera*, due to its antioxidant nature, could restore impaired pro-oxidant/antioxidant balance and thus accelerating clinical/ biochemical recoveries.

*Moringa oleifera* (Sigru) contains exceptionally high content of Methionine and Cysteine, which restore impaired antioxidant balance & accelerates clinical/biochemical recoveries.

Effect of MIADMSA, *Moringa oleifera* either alone or in combination on biochemical variables suggestive of renal oxidative stress in arsenic-exposed mice

	Normal animals	As, 100 ppm	MIADMSA	<i>M. oleifera</i>	MIADMSA + <i>M. oleifera</i>
SOD	3.10 ± 0.14	2.51 ± 0.04	3.69 ± 0.20	3.81 ± 0.15	3.33 ± 0.13
Catalase	6.86 ± 0.27	4.74 ± 0.34	5.45 ± 0.64	4.39 ± 0.66	6.64 ± 0.69
GPx	1.66 ± 0.03	0.97 ± 0.05	1.06 ± 0.14	1.28 ± 0.07	1.65 ± 0.18
TBARS	2.60 ± 0.07	4.37 ± 0.19	4.36 ± 0.55	3.72 ± 0.47	3.93 ± 0.46
GSH	1.75 ± 0.05	1.63 ± 0.08	1.71 ± 0.11	1.63 ± 0.23	1.93 ± 0.12
GSSG	0.21 ± 0.01	0.24 ± 0.01	0.20 ± 0.00	0.23 ± 0.02	0.23 ± 0.02
GSH:GSSG	8.06 ± 0.27	6.93 ± 0.10	8.18 ± 0.29	7.05 ± 0.36	8.5 ± 0.13

SOD, superoxide dismutase as units/min/mg protein; catalase as μmoles of H<sub>2</sub>O<sub>2</sub> consumed/min/mg protein; GPx, glutathione peroxidase as μg of GSH consumed/min/mg protein; TBARS, thiobarbituric acid reactive substances as μg/g of tissue; GSH, reduced glutathione as mg/gm tissue; GSSG, oxidized glutathione as mg/gm tissue. Values are mean ± SE; n = 5.

Effect of MIADMSA, *Moringa oleifera* either alone or in combination on arsenic and essential metal concentration in blood, liver, kidney, and brain

Element	Tissues	Normal	As	MIADMSA	<i>M. Oleifera</i>	MIADMSA+ <i>M. Oleifera</i>
As	Blood	0.05 ± 0.0	0.5 ± 0.01	0.25 ± 0.0	0.27 ± 0.0	0.1 ± 0.0
	Liver	0.07 ± 0.01	1.6 ± 0.01	1.1 ± 0.01	1.3 ± 0.02	1.2 ± 0.1
	Kidney	0.06 ± 0.0	1.5 ± 0.01	1.0 ± 0.01	1.4 ± 0.02	1.1 ± 0.2
	Brain	0.1 ± 0.0	1.8 ± 0.2	0.9 ± 0.1	1.45 ± 0.3	0.6 ± 0.1
Cu	Blood	3.1 ± 0.2	2.9 ± 0.2	0.6 ± 0.1	3.7 ± 0.2	2.3 ± 0.2
	Liver	5.8 ± 0.2	6.0 ± 0.05	3.9 ± 0.3	6.3 ± 0.3	6.31 ± 0.1
	Kidney	12.0 ± 1.0	7.5 ± 0.5	8.2 ± 0.2	12.3 ± 3.1	10.3 ± 0.3
	Brain	9.0 ± 0.2	7.9 ± 0.3	6.9 ± 0.1	8.2 ± 0.3	7.4 ± 0.2
Zn	Blood	4.0 ± 0.7	8.0 ± 0.7	5.0 ± 0.9	5.3 ± 0.3	5.4 ± 0.3
	Liver	35.0 ± 0.9	35.1 ± 0.8	33.0 ± 1.0	40.1 ± 5.0	38.1 ± 2.0
	Kidney	49.2 ± 4.2	24.3 ± 1.9	30.0 ± 1.0	42.3 ± 4.0	39.0 ± 1.8
	Brain	38.7 ± 1.3	33.1 ± 1.2	22.0 ± 1.3	40.3 ± 1.8	30.5 ± 0.9
Fe	Blood	180.0 ± 40.9	60.2 ± 20.2	48.1 ± 10.0	110.0 ± 10.0	55.0 ± 20.1
	Liver	90.3 ± 10.7	120.0 ± 10.9	140.5 ± 10.5	110.3 ± 20.3	145.1 ± 10.2
	Kidney	152.1 ± 10.2	140.0 ± 20.1	148.0 ± 10.8	245.3 ± 50.2	151.7 ± 2.9
	Brain	130.5 ± 10.3	131.1 ± 20.2	89.1 ± 10.7	155.5 ± 20.7	147.0 ± 10.3

As, Arsenic as ng/ml blood; liver, kidney as μg/g and brain as ng/g wet tissue; Cu, Copper as μg/ml blood; liver, kidney and brain as μg/gm wet tissue; Zn, Zinc as μg/ml blood; liver, kidney, and brain as μg/gm wet tissue; Fe, Iron as μg/ml blood; liver, kidney, and brain as μg/gm wet tissue. Values are mean ± SE; n = 5.

MIADMSA: Monoisomyl 2, 3-dimercaptosuccinic acid-a thiol chelator

(Toxicology Mechanisms and methods, 19, 169-182, 2009)

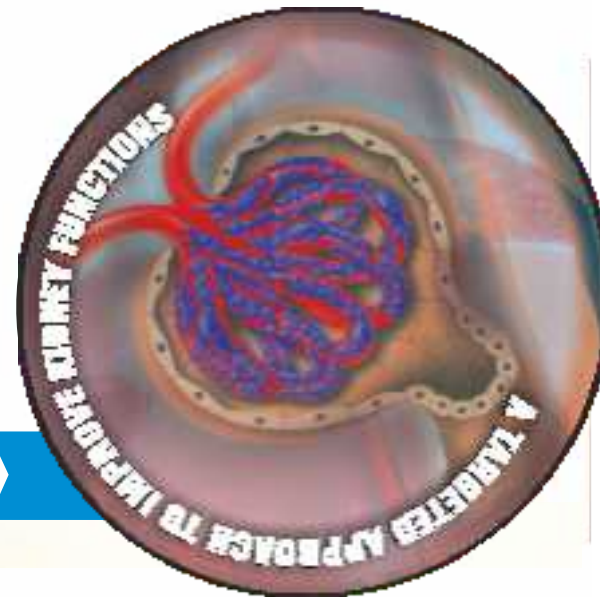




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Tones cellulo protection mechanism acting as an immunomodulator

## Proliferation of stem cells of Bone marrow

The immunomodulatory activity of **Nelumbo nucifera (Kamal kakri) rhizome (NNRE) and seed (NNSE) extract** was evaluated using various *in vivo* models including the total and differential leukocyte count (TLC and DLC), nitroblue-tetrazolium reduction (NBT) test, neutrophil adhesion test, phagocytic response and delayed type hypersensitivity (DTH) reaction. Sheep red blood cells (SRBC) were used to immunize the animals. Rhizome extract and Seed extract at the doses of 100 and 300 mg/kg were administrated. The TLC and lymphocyte count increased significantly but the

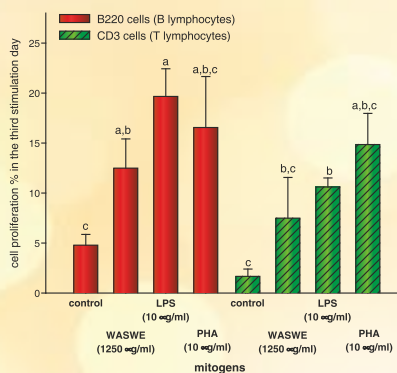
neutrophil count was decreased for rhizome extract and seed extract treated groups compared to the control. A dose-dependent potentiation of DTH reaction induced by SRBC was observed from the extracts. This result provides primary evidence that extracts of rhizome and seeds of **Nelumbo nucifera altered the total and differential WBCs count**, potentiated the effect on DTH response and phagocytosis. Thus the extracts showed stimulation of defense system by modulating the immunological parameters.

Total and differential count of leucocytes in NNRE and NNSE treated animals.						
Group	Total count (TLC)	Differential count (DLC)				
		Neutrophil	Eosinophil	Basophil	Monocyte	Lymphocyte
Control	4528.33±11.37	43.66±0.80	0.83±0.16	1.66±0.21	1.4±0.42	51.66±2.15
NNRE 100 mg/kg	5528.33±15.58 <sup>a</sup>	40.33±2.04	1.83±0.16 <sup>c</sup>	0.66±0.21 <sup>c</sup>	0.83±0.16	37.66±0.95
NNRE 300 mg/kg	5686.66±7.60 <sup>a</sup>	36.83±1.79	1.66±0.21	0.72±0.19	0.60±0.24	56.83±2.10
NNSE 100 mg/kg	5423.33±10.54 <sup>a</sup>	41.83±0.94	0.66±0.21	0.50±0.22 <sup>b</sup>	1.21±0.32	59.16±0.60 <sup>b</sup>
NNSE 300 mg/kg	5573.33±15.84 <sup>a</sup>	37.33±2.92	1.33±0.21	0.66±0.21 <sup>c</sup>	1.44±0.42	58.83±0.47 <sup>c</sup>
DMS 2 mg/kg	5826.66±12.56 <sup>a</sup>	32.83±1.07 <sup>b</sup>	2.33±0.33 <sup>a</sup>	0.83±0.16 <sup>c</sup>	0.80±0.37	59.66±0.49 <sup>b</sup>

Values are expressed as mean±SEM; one-way analysis of variance, ANOVA followed by Tukey-Kramer Multiple Comparisons Test (n=6), values are compared with control animals. <sup>a</sup>P<0.001; <sup>b</sup>P<0.01; <sup>c</sup>P<0.05; NNRE =Nelumbo nuciferorhizome extract; NNSE=Nelumbo nucifera seed extract; DMS= dexamethasone.

(J. Ethano Pharmacol. 128, 490-494, 2010)

Immuno-stimulatory effect of wild **Amaranthus spinosus (Chaulai) water extract (WASWE)** on spleen cells from female BALB/c mice was studied and it was found that it



LPS : a B cell mitogen  
PHA : a T cell mitogen

significantly stimulated splenocyte proliferation. However, isolated B lymphocytes, but not T lymphocytes, could be stimulated by A. spinosus extract in a dose response manner. After sequentially purifying the extract, a novel immuno-stimulating protein (GF1) with a molecular weight of 313 kDa was obtained. The immuno-stimulating activity of the purified protein (GF1) was 309 times higher than that of the extract. These results indicate that A. spinosus extract does indeed exhibit immuno-stimulating activity via direct stimulating B lymphocyte activation *in vitro*

(International Immunopharmacology, 5, 711-722, 2005)

**Amaranthus spinosus (Chaulai) shows immunomodulatory effect on splenocytes, beta-lymphocytes**

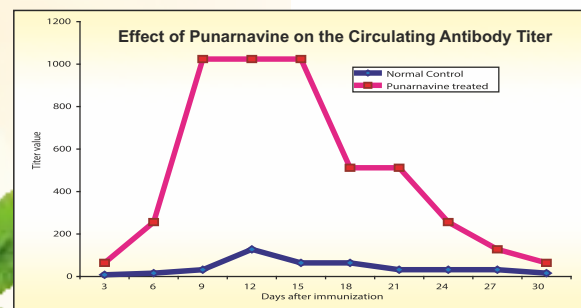
## Punarnavine increased the total WBC count

The effect of Punarnavine on the immune system was studied. Administration of Punarnavine (40 mg/kg body weight) was found to enhance the total WBC count on 6th day. Bone marrow cellularity and number of α-esterase positive cells were also increased by the administration of Punarnavine. Treatment of Punarnavine along with the antigen, sheep red blood cells (SRBC), produced an enhancement in the circulating antibody titer and the number of plaque forming cells (PFC) in the spleen. Maximum number of PFC was obtained on the 6th day. Punarnavine also showed enhanced proliferation of splenocytes, thymocytes and bone marrow cells both in the presence and absence of specific mitogens *in vitro* and *in vivo*. More over

administration of Punarnavine significantly reduced the Lipopolysaccharides (LPS) induced elevated levels of proinflammatory cytokines such as TNF-α, IL-1β, and IL-6 in mice. These results indicate the immunomodulatory activity of Punarnavine.

Administration of Punarnavine increased the total WBC count in Balb/c mice. In the animals treated with Punarnavine the maximum WBC count was 15078.75±334.7 cells/mm<sup>3</sup> obtained on 6th day. Prior to the Punarnavine treatment the total WBC count was only 6952.5±274.7 cells/mm<sup>3</sup>. The untreated control animals maintained the normal total WBC count during the experimental time.

(Immunopharmacology & Immunotoxicology, 31(3), 377-387, 2009)



Effect of Punarnavine on proliferation of bone marrow cells *in vivo*.

	Rate of proliferation (CPM) Counts per minute				
	without mitogens	Con A	PHA	PWM	LPS
Bone marrow (untreated control)	1164 ± 46	1597 ± 49	3201 ± 38	2099 ± 47	3304 ± 76
Punarnavine treated	3340 ± 113*	3674 ± 58*	5081 ± 29*	4199 ± 64*	5679 ± 33*

PHA = phytohemagglutinin, CON A = concanavalin A, PWM = Poke Weed Mitogen, LPS = lipopolysaccharide. Treated animals received Punarnavine (40 mg/kg body weight, i.p) for 5 consecutive days. Bone marrow cells were cultured in the presence and absence of various mitogens and rate of proliferation was checked by <sup>3</sup>H-thymidine incorporation assay. The statistical analysis was done by using Dunnett's multiple comparison test. \*p < 0.001 compared with specific mitogen control.

Effect of Punarnavine on splenocytes proliferation *in vitro*.

	Rate of proliferation (CPM) Counts per minute Punarnavine			
	Control	1 µg/ml	5 µg/ml	10 µg/ml
Spleen				
Without mitogens	1701 ± 20	4001 ± 63*	4072 ± 46*	4295 ± 45*
+Con A	4790 ± 76	5564 ± 76*	5650 ± 56*	6006 ± 179*
+PHA	3738 ± 56	4796 ± 55*	5061 ± 47*	5097 ± 57*
+LPS	4065 ± 49	5973 ± 40*	6252 ± 58*	6506 ± 42*
+PWM	4027 ± 93	5116 ± 21*	5366 ± 27*	5453 ± 38*

PHA = phytohemagglutinin, CON A = concanavalin A, PWM = Poke Weed Mitogen, LPS = lipopolysaccharide. Spleen cells were cultured in the presence and absence of various mitogens and rate of proliferation was checked by <sup>3</sup>H-thymidine incorporation assay. The statistical analysis was done by using Dunnett's multiple comparison test. \*p < 0.001 compared with specific mitogen control.





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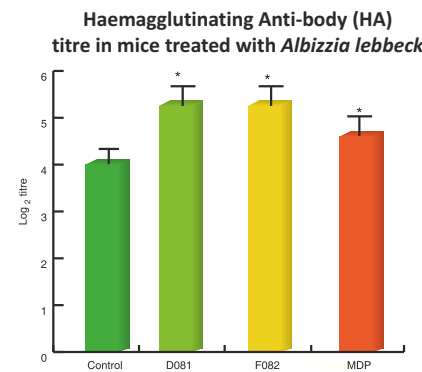


Promotes toxin elimination by effective diuresis, maintaining GFR

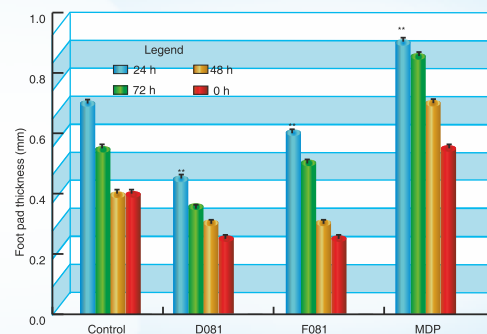
## Antigen Specific Immune Response

The immunomodulatory effect of the bark of **Albizia lebbbeck** (Sirisha) was evaluated by studying humoral and cell mediated immune responses. The hot aqueous extract (D081) and its butanolic fraction (F082) were administered once daily for one week in mice, immunised previously with sheep red blood cells (SRBC). At the dose levels tested (6.25, 12.5 and 25 mg/kg, p.o.), A. Lebbbeck treated mice developed higher serum antibody titres compared to the vehicle treated group and the effect was comparable to the standard drug muramyl dipeptide(MDP). Delayed type hypersensitivity response was suppressed in SRBC immunised mice treated with A. lebbbeck extract. The macrophage migration index remained unaltered in both strains of mice. These results are discussed in the light of possible immunopotentiating effects of A. Lebbbeck. (Pharmaceutical biology, 38(3), 161-166, 2000)

Develops  
higher serum  
antibody  
titres



## Delayed Type Hypersensitivity (DTH) Response



Effect of A. lebbbeck (25 mg/kg, p.o., x 7 days) on delayed type hypersensitivity response in BALB/c mice immunised with SRBC (n=5, mean±S.D.) \*\* P< 0.01.

The mean DTH response to SRBC was suppressed by both the hot aqueous extract (D081) and the butanol fraction (F081) of *A. lebbbeck* (Sirisha) 24 h after the injection of SRBC in the foot pad of BALB/c mice. Maximum suppression was observed with 25 mg/kg given orally. Similar results were also obtained with albino mice at 24 h, significant in comparison to the control group. In contrast, the standard drug muramyl dipeptide showed an immunostimulating response, as evident by enhanced swelling at 24 h. The extract as well as the fraction were equipotent in their effects in both BALB/c and albino mice.

(Pharmaceutical biology, 38(3), 161-166, 2000)

## Induces Dose-dependent Diuresis, Natriuresis, Kaliuresis, Chloride Excretion and Maintains GFR.

The aqueous extract of *coriander seed* was administered by continuous intravenous infusion (120 min) at two doses (40 and 100 mg/kg) to anesthetized wistar experimental subjects. Furosemide (10 mg/kg), a standard diuretic was used as the reference drug. Excretion of water and electrolytes (sodium, potassium and chloride) in urine was measured, and glomerular filtration rate (equal to creatinine clearance) was determined. The crude aqueous extract of coriander seeds increased diuresis, excretion of electrolytes, and glomerular filtration rate in a dose-dependent way; furosemide was more potent as a diuretic and saluretic.

Continuous infusion of the crude aqueous extract of *Coriandrum sativum* induced a significant dose-dependent increase in diuresis, natriuresis, kaliuresis, chloride excretion and GFR.

Effect of infusion of an aqueous extract of *Coriandrum sativum* seeds or furosemide on plasma levels of creatinine, urinary excretion of creatinine and creatinine clearance (glomerular filtration rate) in anesthetized experimental subjects

Experimental group/dose	Control period	Experimental period	% Change <sup>a</sup>
Plasma levels of creatinine (μmol/L)			
Saline	53.0±1.2	51.0±1.5	-3
Plant extract (40 mg/kg)	49.0±1.4	39.0±2.0	-22
Plant extract (100 mg/kg)	44.0±1.8	38.0±2.3	-14
Furosemide (10 mg/kg)	50.0±3.5	48.0±1.3	-4
Urinary excretion of creatinine (mmol/L)			
Saline	9.90±0.24	7.76±0.48	-22
Plant extract (40 mg/kg)	8.04±0.27	6.25±0.32	-22
Plant extract (100 mg/kg)	8.86±0.36	4.01±0.59*	-55
Furosemide (10 mg/kg)	12.32±0.86	3.98±0.21*	-68
Glomerular filtration rate = creatinine clearance (mL/min)			
Saline	1.74±0.20	1.87±0.27	+6
Plant extract (40 mg/kg)	2.06±0.18	4.78±0.40*	+132
Plant extract (100 mg/kg)	1.90±0.32	5.13±0.50*	+170
Furosemide (10 mg/kg)	1.80±0.20	7.50±0.33*	+317

The values for the four control and four measurement periods were averaged.

Data are expressed as mean±S.E.M. for six rats in each group.

<sup>a</sup> Experimental minus control value.

\*p < 0.05.

**EXTRACT OF CORIANDER SEEDS INCREASED DIURESIS, EXCRETION OF ELECTROLYTES, AND GLOMERULAR FILTRATION RATE IN A DOSE-DEPENDENT WAY**

Effect of intravenous infusion of an aqueous extract of *Coriandrum sativum* seeds or furosemide on diuresis and urinary excretion of sodium and potassium in anesthetized experimental subjects; absolute increase in urinary excretion of water and electrolytes caused by the plant extract or furosemide on a per milligram dose basis.

Experimental group/dose	Water (urine) <sup>a</sup>	Sodium <sup>a</sup>	Potassium <sup>a</sup>	Chloride <sup>a</sup>	Sodium/potassium ratio
Plant extract (40 mg/kg)	0.43	0.33	0.028	0.75	11.8
Plant extract (100 mg/kg)	0.39	0.42	0.017	0.39	24.7
Furosemide (10 mg/kg)	8.32	4.32	0.310	4.87	13.9
Furosemide (10 mg/kg)/plant extract (100 mg/kg) potency ratio	21.3	10.3	18.2	12.5	-

<sup>a</sup> Absolute increase in urinary excretion of water (μL/min mg) and electrolytes (μmol/min mg) over control values caused by the administration of the plant extract or furosemide, adjusted for dose.

(J. Ethano Pharmacol. 115, 89-95, 2008)





# NEERI® KFT

Protects the kidney by renal vasodilation

Providing  
**PRIMARY  
KIDNEY  
CARE**

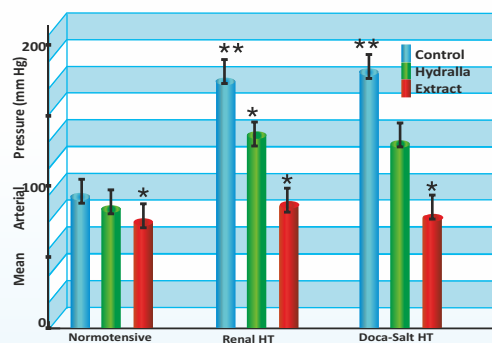


## Exhibits $\alpha$ -Adrenoceptor activity producing vascular tone relaxation

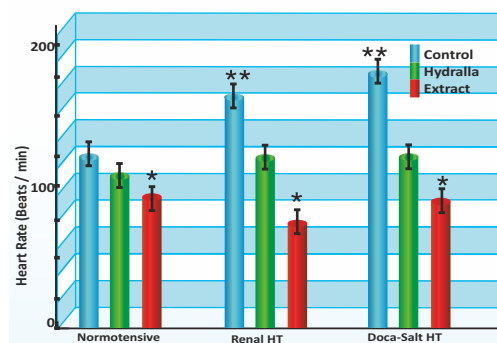
A crude ethanol extract was prepared from the **unripened fruit of *Carica papaya***. Experimental subjects were randomly divided into three batches (15 per batch)—renal, DOCA-salt hypertensives and normotensives. Each batch was further divided into three groups—the untreated, hydralazine and extract treated groups. The mean arterial blood pressure (MAP) and the heart rate were measured in all groups. From the results, the basal (control) MAP were  $93.8 \pm 4.5$ ,  $175.2 \pm 5.1$  and  $181.3 \pm 6.2$  mmHg in the normotensive, renal and DOCA-salt hypertensives, respectively.

*Carica papaya* (Papita) contains antihypertensive agent(s) which exhibits mainly  $\alpha$ -adrenoceptor activity

Both hydralazine (200  $\mu$ g/100 g i.v) and extract (20 mg/kg.i.v) produced a significant depression of MAP in all groups (\*p < 0.01 vs controls), but the extract produced about 28% more depression of MAP than hydralazine in the hypertensive groups. In vitro studies using isolated rabbit arterial (aorta, renal and vertebral) strips showed that the extract (10  $\mu$ g/mL) produced relaxation of vascular muscle tone which was, however, attenuated by phentolamine (0.5–1.5  $\mu$ g/mL). **It is concluded that the fruit juice of *C. papaya* probably contains antihypertensive agent(s) which exhibits mainly  $\alpha$ -adrenoceptor activity.**



Effect of *C. papaya* fruit extract on the mean arterial blood pressure (MAP) of normotensive, renal hypertensive (renal HT) and DOCA-salt hypertensive (DOCA-salt HT) exp. subjects. Hydralazine (Hydralazine; 200  $\mu$ g/100 g i.v.; and the extract (20 mg/kg. i.v.;) were administered to each group of animals. Given are the mean values  $\pm$  SEM n = 5, \*\*p < 0.01 vs normotensive controls, \*p < 0.01 vs group controls.



Effect of *C. papaya* fruit extract on the heart rate of normotensive, renal hypertensive (renal HT) and DOCA-salt hypertensive (DOCA-salt HT) exp. subjects. Hydralazine (Hydralazine; 200  $\mu$ g/100 g i.v.; and the extract (20 mg/kg. i.v.;) were administered to each group of animals. Given are the mean values  $\pm$  SEM n = 5, \*\*p < 0.01 vs normotensive controls, \*p < 0.01 vs group controls.

The present results show clearly that *C. papaya* fruit extract markedly depressed the blood pressure and heart rate in mineralocorticoid salt and in renal hypertensive experimental subjects when compared with that in the normotensive controls. The extract appeared to be more potent than hydralazine, a well known antihypertensive (vasodilating) agent.

(Phytother. Res. 14, 235–239, 2000)

## Inhibits angiotensin-1 converting enzyme, reducing renal hypertension

Angiotensin I-converting enzyme (ACE) is known to catalyze the conversion of angiotensin-I to angiotensin-II, which is the biologically active peptide elevating blood pressure, thereby being implicated in the pathogenic process of hypertension. Therefore, ACE inhibitory substances are expected to reduce the blood pressure in hypertensive patients.

Effects of extract obtained from ***Nelumbo nucifera* (Lotus flower & Rhizome)** on ACE activity were examined in-vitro to search for potentially effective substances against hypertension. The extracts of both plant parts caused their inhibitory effects on ACE activity, similar in their properties and different in their potencies. Thus, the aqueous extracts prepared from lotus is suggested to contain novel substances inhibiting ACE activity, thereby reducing blood pressure by inhibiting the production of active hypertensive peptide. (Pharmacology 3(2), 309–318, 2012)

## Coriander fruit exhibits blood pressure lowering and diuretic activities.

Coriander crude extract (Cs.Cr) was evaluated through in vitro and in vivo techniques. Cs.Cr caused atropine sensitive stimulatory effect in isolated guinea-pig ileum (0.1–10 mg/ml). In rabbit jejunum preparations, Cs.Cr evoked a similar contractile response but in the presence of atropine, it exhibited relaxation against both spontaneous and high  $K^{(+)}$  (80 mM)-induced contractions as well as shifted the  $Ca^{(2+)}$  concentration-response curves to right, similar to that caused by verapamil. Cs.Cr (1–30 mg/ml) caused fall in arterial blood pressure of anesthetized animals, partially blocked by atropine. Cs.Cr produced vasodilatation against phenylephrine and  $K^{(+)}$  (80mM)-induced contractions in rabbit aorta and cardio-depressant effect in guinea-pig atria. Cs.Cr produced diuresis in rats at 1–10mg/kg. Bio-assay-directed fractionation revealed the separation of spasmogenic and spasmolytic components in the aqueous and organic fractions respectively. Coriander fruit exhibits gut stimulatory, inhibitory and hypotensive effects mediating possibly through cholinergic,  $Ca^{(2+)}$  antagonist and the combination of these mechanisms respectively.



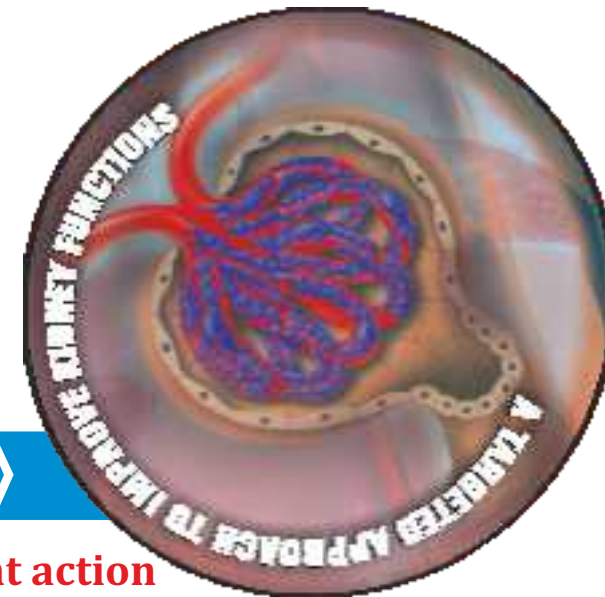
(J. Adv. Pharm. Health Res., 1(3), 28–48, 2011)





# NEERI<sup>®</sup> KFT

## Providing PRIMARY KIDNEY CARE



Shows significant nephroprotective activity

**Nephroprotective activity of Neeri KFT (denoted as NS-RF) was studied in lead acetate induced nephrotoxicity in experimental subjects. The prevention of nephrotoxicity in the group pre-treated with Neeri KFT for 5 days followed by co-treatment with lead acetate for 6 weeks, as assessed with biochemical markers of serum and urine, antioxidant activity and histopathological studies were found to be highly significant as compared to lead acetate induced nephrotoxic subjects -**

### Prevents alterations in biochemical parameters in serum

Neeri KFT co-treated group showed highly significant nephroprotective activity with prevention of elevation in serum creatinine, blood urea and reduction in serum proteins and serum albumin as compared to lead acetate treated group, maintaining their values within near normal range and quite superior to that with standard antioxidant, vitamin E, treated group

#### Effect of NS-RF on Serum biochemistry

Groups	Creatinine (mg/dl)	Urea (mg/dl)	Total Protein (g/dl)	Albumin (g/dl)
Normal	0.58±0.06***	28±1.03***	6.70±0.27***	5.0±0.28***
Lead acetate (8mg/kg)	1.70±0.09	51±1.39	4.18±0.12	2.10±0.11
Vitamin E (100mg/kg)	1.03±0.17**	45±1.06**	4.74±0.19	3.04±0.25*
NS-RF (3280mg/kg)	0.75±0.13***	29±0.96***	5.92±0.14***	4.30±0.20***

Values are expressed as mean±SEM. (n=5). \*indicates significance at P<0.05, \*\*indicates significance at P<0.01 and \*\*\* indicates significance at P<0.001 as compared to lead acetate treated group, using one way ANOVA followed by Dunnett's multiple comparison test.



### Prevents alterations in biochemical parameters in urine

Neeri KFT co-treated group showed highly significant nephroprotective activity with prevention of elevation of urinary protein, urinary glucose and reduction of urinary creatinine as compared to lead acetate treated group.

#### Effect of NS-RF on Urine biochemistry

Groups	Protein (g/dl)	Creatinine (mg/dl)	Glucose (mg/dl)
Normal	0.08±0.01***	15.34±0.40***	0.20±0.045***
Lead acetate (8mg/kg)	2.25±0.17	9.14±0.15	18.30±0.52
Vitamin E (100mg/kg)	1.77±0.04**	9.98±0.15	15.34±0.41*
NS-RF (3280mg/kg)	0.23±0.01***	13.70±0.30***	7.40±0.57***

Results are expressed as mean±SEM. (n=5). \*indicates significance at P<0.05, \*\*indicates significance at P<0.01 and \*\*\* indicates significance at P<0.001 as compared to lead acetate treated group, using one way ANOVA followed by Dunnett's multiple comparison test.



### Provides pronounced antioxidant action

Lead causes nephrotoxicity via several mechanisms and oxidative stress is one which has been suggested to play a significant role. It is reported that oxidative stress may induce the injury of proximal convoluted tubule of nephron. The antioxidants level were significantly decreased and TBARS content increased in lead nephrotoxicity, suggesting an increased oxidative stress and lipid peroxidation.

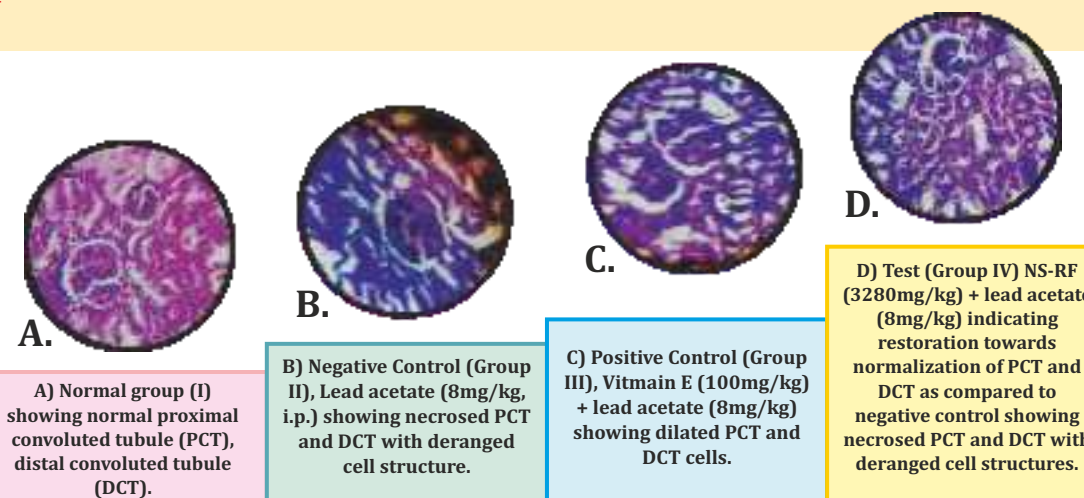
Effect of NS-RF on anti-oxidant profile (based on TBARS assay)

Groups	Lipid peroxidation (Absorbance at 532nm)
(I) Normal	0.002±0.003***
(II) Lead acetate (8mg/kg)	0.338±0.0173
(III) Vitamin E (100mg/kg)	0.188±0.044***
(IV) NS-RF (3280mg/kg)	0.098±0.0143***

Results are expressed as mean±SEM. (n=5). \*indicates significance at P<0.05, \*\*indicates significance at P<0.01 and \*\*\* indicates significance at P<0.001 as compared to lead acetate treated group, using one way ANOVA followed by Dunnett's multiple comparison test. Neeri KFT treated group significantly reverted the increased TBARS and hence lipid peroxidation levels towards normal.

### Prevents alterations in histopathological picture

The kidney sections of normal group showed normal tubular brush border, intact glomerulus and Bowman's capsule while the kidneys of lead acetate treated group showed the deranged and necrosed tubular cells. However, the kidney of NS-RF treated group showed normalized tubular cells.



A) Normal group (I) showing normal proximal convoluted tubule (PCT), distal convoluted tubule (DCT).

B) Negative Control (Group II), Lead acetate (8mg/kg, i.p.) showing necrosed PCT and DCT with deranged cell structure.

C) Positive Control (Group III), Vitamin E (100mg/kg) + lead acetate (8mg/kg) showing dilated PCT and DCT cells.

D) Test (Group IV) NS-RF (3280mg/kg) + lead acetate (8mg/kg) indicating restoration towards normalization of PCT and DCT as compared to negative control showing necrosed PCT and DCT with deranged cell structures.

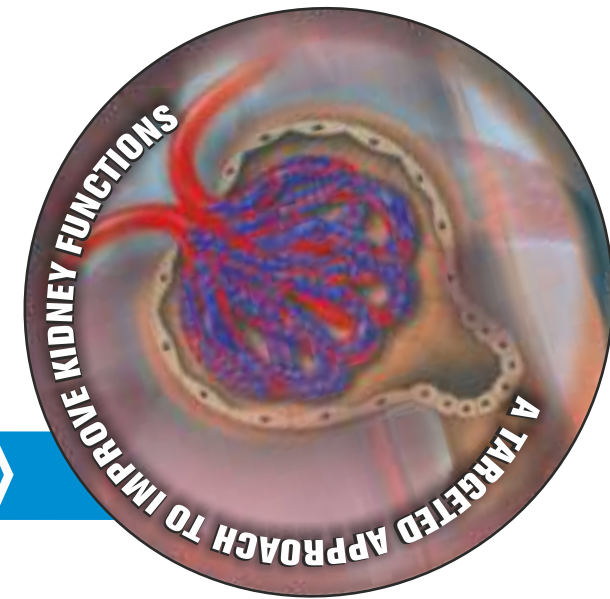
**The present study suggests that NS-RF has a very comprehensive protective effect against lead acetate induced nephrotoxicity.**





# NEERI® KFT

Providing  
**PRIMARY  
KIDNEY  
CARE**



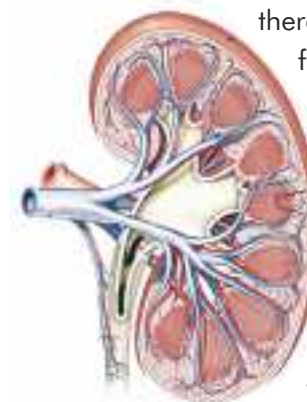
**PUNERNAVA – identified as nephroprotective**

**TO PREVENT RENAL INJURY**

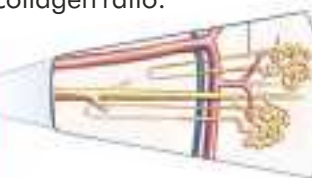
**Kidneys functional capacity...**

Study on mercuric chloride induced kidney necrosis, with *Boerhaavia diffusa* (Punernava) showed rapid disappearance of pallor and return towards normalcy. Histological findings revealed lesser connective tissue infiltration, and an early clearance of necrotic debris, as compared to control. In induced glomerulonephritis and infection with *Staphylococcus aureus*, increase in collagen content was found to be less in punernava treated group than the untreated control...

**Stimulates regeneration...**



thereby, these studies are suggestive of significant improvement in functional status of kidney due to maintenance of parenchyma: collagen ratio.



Experimental & pharmacological studies show antiinflammatory & antibacterial

effects of *Boerhaavia diffusa*

(Punernava), and also being a diuretic this drug keeps the nephrons flushed which is again beneficial for regeneration of tubular cells.

(Advances in Ayurvedic Medicine; RH Singh, K N Udupa, 2005)

**CLINICAL STUDIES WITH PUNERNAVA  
IN NEPHRITIS, NEPHROTIC SYNDROME,  
OTHER KIDNEY DISORDERS.**

Clinical study with *Boerhaavia diffusa* (PUNERNAVA) in patients suffering from various Kidney disorders like nephritis, nephrotic syndrome revealed significant improvement, quite comparable with modern drug therapy.

TYPE OF THERAPY	Total No. of patients	No. of patients relieved	No. of patients improved	No. of patients unchanged
Patients on Punernava therapy	14	4	9	0
Patients on modern drugs (Corticosteroids, Anti hypertensive Diuretic, Antibiotics...)	12	2	4	4

(Advances in Ayurvedic Medicine; RH Singh, K N Udupa, 2005)

**ANTIOXIDANT STATUS IN POLYCYSTIC  
ENDSTAGED RENAL DISEASED PATIENTS  
AND ANTIHEMOLYTIC EFFECT OF  
*Boerhaavia diffusa***

A clinical study with *Boerhaavia diffusa* (Punernava) revealed a significant antihemolytic activity on erythrocytes of the end stage renal disease (ESRD) patients. Shortening of life-span of erythrocytes, due to an increase in oxidative stress, is considered to be one of the major risk factors in these patients. ( Indian Journal of Biochemistry and Biophysics Vol.46(3) [June 2009])

**Punernava in  
Neeri KFT  
provides  
longterm  
Nephroprotection  
to promote  
its  
functions and  
Stimulate  
Regeneration**

**PUNERNAVA**

*Boerhaavia diffusa*







# NEERI® KFT

## Frequently Asked Questions - FAQs

## Providing PRIMARY KIDNEY CARE»



### What is NEERI KFT ?

Neeri KFT is the scientifically developed combination of selected, high quality, nephroprotective herbs and has been specially designed for primary kidney care while protecting, maintaining and even help improve kidney functions.

*Boerhaavia diffusa* & *Moringa oleifera* protect nephrons against potentially nephrotoxic drug molecules like acetaminophen, gentamicin etc. thereby, preventing elevation of serum creatinine and blood urea.

In cases of renal infections *Boerhavvia diffusa* protect the kidneys while significantly preventing change in parenchyma: collagen ratio.

The highly promising component herbs, acting synergistically, studied on modern parameters, have been found to provide pronounced nephroprotective activities very comprehensively through multiple mechanisms against various factors deleterious for kidneys viz. pollutants, toxic metals, potentially nephrotoxic drug molecules or due to diabetes, hypertension, renal stones, urinary infections.

*Boerhaavia diffusa*, *Crataeva nurvala*, *Moringa oleifera*, *Carica papaya*, *Hemidesmus indicus* help significantly prevent deterioration of kidney function parameters like serum biochemistry (serum creatinine, blood urea, serum uric acid, serum proteins, serum albumin) and urinary biochemistry (creatinine, proteinuria, glycosuria), urine output and also histopathological picture (cellular integrity, architecture) due to nephrotoxins through various mechanisms, including that with very high antioxidant activity.

*Rheum emodi*, *Moringa oleifera* selectively chelate nephrotoxic metals like cadmium, mercury, chromium, arsenic to help detoxify safely.

*Solanum nigrum*, *Rheum emodi* protect against ethanol and adenine induced nephrotoxicity.

In cases of renal infections *Boerhavvia diffusa* protect the kidneys while significantly preventing change in parenchyma: collagen ratio. *Carica papaya*, *Boerhavvia diffusa* provide antihypertensive action while *Coriandrum sativum* provide diuretic activity in edematous conditions to the benefit of patients with kidney diseases in the patient friendly way without any untoward effect. Overall Neeri KFT tends to check degenerative alterations in kidneys & helps prevent deterioration in kidneys health.

Phytocomponents like *Coriandrum sativum* in Neeri KFT induce dose dependent diuresis, natriuresis, kaliuresis, chloride excretion and maintains GFR. An experimental study showed that aqueous extract of coriander seeds increased glomerular filtration rate in a dose dependent manner.

The formulation has been designed to maintain a normal eGFR of the patients without creating any electrolyte disturbances.

### How NEERI KFT helps to maintain eGFR?

### How is NEERI KFT important for patients with kidney diseases?

*Crataeva nurvala* and *Carica papaya* protect kidneys against nephrotoxic chemicals like cisplatin, carbon tetrachloride.

The formulation has been designed to maintain a normal eGFR of the patients without creating any electrolyte disturbances.

### Have there been studies with NEERI KFT, establishing its efficacy and safety ?

Treatment with Neeri KFT showed that even the frequency of dialysis could be reduced in some patients .

Experimental studies were conducted with Neeri KFT (Indo American Journal of Pharmaceutical Research, 2015; communicated). The studies revealed that Neeri KFT significantly protected experimental subjects from lead acetate induced nephrotoxicity. Neeri KFT co-treated group showed -

- Reduced serum creatinine, blood urea and increased serum protein and serum albumin.
- Decreased urinary protein and glucose while increased urinary creatinine.
- Pronounced antioxidant activity, inhibiting lipid peroxidation with reduced TBARS level. Anti-oxidant activity has been found to be quite superior to that with standard antioxidant, vitamin E.
- Near normalization of PCT (proximal convoluted tubule) and DCT (distal convoluted tubule) against necrosed PCT and DCT and deranged cell structures in lead acetate treated group.

Clinical study with Neeri KFT, with or without modern medicines depending upon severity of kidney diseases, continued for the study period of 6 months, showed that even the frequency of dialysis could be reduced in some patients while it could be just maintained at the existing level in patients on the verge to have higher frequency of dialysis. Elevated level of serum creatinine and blood urea declined and hemoglobin level increased significantly. (Gupta et al 2015)

Neeri KFT prevented deranged cell structures in lead acetate treated group

### In a number of cases, a very high dose of Anti-oxidants have been found to reduce the frequency of dialysis.

Very high dose of antioxidants have been found to be highly useful in various kidney diseases as they have been found to provide nephroprotective activity and improve kidney function parameters and in a number of cases, even reduce the frequency of dialysis. However, in deteriorating kidney conditions, many of the antioxidants may not be advisable to be taken. The component herbs of Neeri KFT, which have been described in ancient texts and established by modern studies for their nephroprotective activities, provide safe, very high antioxidant activity, preventing lipid peroxidation. The experimental studies revealed antioxidant activities to be much higher as compared to standard

oxidant, vitamin E. Moreover, besides, preventing lipid peroxidation they have been found to restore body's own antioxidant system viz. catalase, super oxide dismutase, reduced glutathione peroxidase level in kidneys so as to improve the function of kidneys significantly while protecting the kidneys from various nephrotoxins and hence oxidative stress.

### What is the importance of antioxidant activity with NEERI KFT?





# NEERI® KFT

## Providing PRIMARY KIDNEY CARE



### Frequently Asked Questions - FAQs

Neeri KFT restores body's own anti-oxidant systems to protect kidneys from possible nephrotoxins.



The kidneys have a marked capacity of regeneration. In pathological conditions, the kidneys regenerate only in states where there is only cellular damage and renal architecture & the supporting structures are not distorted and there is an adequate increase in physiological demand on the kidney due to massive disease. Kidneys with focal or slowly progressing disease, involving the disruption of basement membrane, do not show regenerative repair and lead to progressive connective tissue ingrowth and replacement fibrosis.

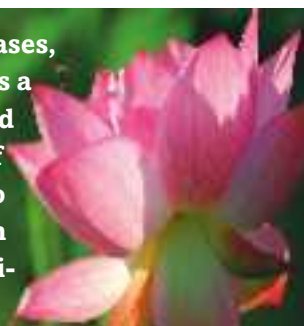
The phytoconstituents from herbal ingredients in Neeri KFT have diuretic, anti-inflammatory, antibacterial, cardiotonic, antioxidant, nephroprotective activities acting effectively & gently against possible nephrotoxins. By virtue of such properties, Neeri KFT protects kidneys from deterioration and effects on early recovery of the kidney from different diseases and facilitates regenerative repair. **Neeri KFT may be recommended in the management of number of renal conditions. All mild to moderate cases of nephritis and nephrotic syndrome may be managed with Neeri KFT and all those patients who are treated with modern corticosteroids, diuretics etc. after controlling initial crisis may be shifted to Neeri KFT for long term maintenance for effective and safe management.** Moreover, studies substantiate the ancient concept of Mutral (Diuretic), Shothahara (Anti-inflammatory and anti-oedema) effect with Rasayana (rejuvenative) and Punerjanaan (regenerative) effects attributed to these nephroprotective constituents.

Does NEERI KFT help in regenerative repair of kidneys ?

Neeri KFT protects kidneys not only from deterioration but also helps in repair in state where there is cellular damage in the kidneys

How would NEERI KFT be useful in patients with hypertension ?

In hypertensive patients with kidney diseases, Neeri KFT may well be safely co-prescribed as a nephroprotective along with recommended anti-hypertensive drugs. The ingredients of Neeri KFT like *Nelumbo nucifera* (Kamal) also supports anti-hypertensive mechanism thereby, acting synergistically with Anti-hypertensive molecules.



Can NEERI KFT prevent patient's kidney function from getting worse?

Yes, Neeri KFT has been specially developed to serve this purpose. It not only preserves the kidney functions but also prevents further damage to the kidney cells by providing an antioxidant shield imparting nephroprotection. Phytoconstituents in NEERI KFT maintain patient's eGFR, lowers S.creatinine, Blood urea and also controls Proteinuria significantly.

It not only preserves the kidney functions but also prevents further damage to the kidney cells

Neeri KFT blocks the effects of TGF-beta on the kidneys, thereby controlling inflammation in the kidneys

There have been several reports/evidences suggesting the inflammatory changes in the kidneys due to Hypertension, diabetes, obesity, lupus and Rheumatoid arthritis. **Curcuma longa in NEERI KFT has been shown to have a strong anti-inflammatory effect on the kidneys.** It also blocks the effects of TGF-beta on the kidneys. Various other components of the formulation provide potent anti-inflammatory action synergistically on kidneys.



What is the role of NEERI KFT in chronic inflammation of various aetiologies affecting the kidneys?

Is NEERI KFT safe for diabetic patients?

Neeri KFT sugar free has been specially developed for diabetic and other calorie conscious patients. Neeri KFT Sugar free contains sucralose which is a good option as a sweetening agent and diabetic fit sugar substitute.



***Hemidesmus indicus and Boerhaavia diffusa stimulate erythropoiesis and body mass while increasing serum protein and helping reduce proteinuria,*** the activities very much required in kidney patients. Neeri KFT treated group showed highly significant nephroprotective activity with prevention of elevation of urinary protein, urinary glucose and reduction of urinary creatinine.

Will NEERI KFT help improve general health in patients with kidney diseases?



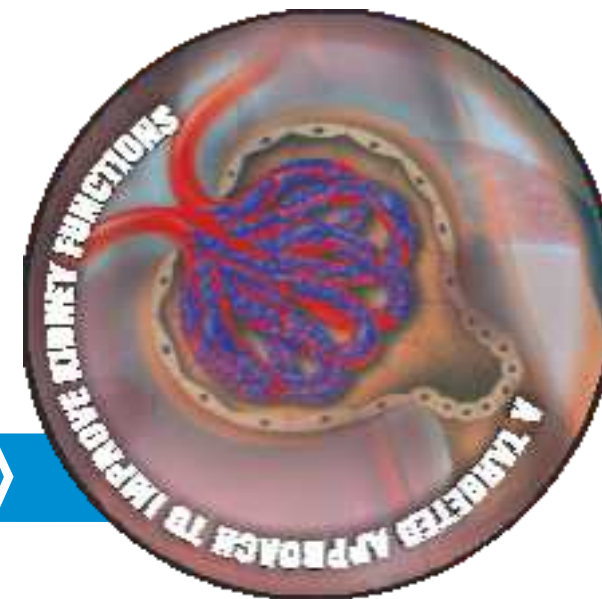


# NEERI<sup>®</sup> KFT

Syrup  
Sugar  
Free

Providing

## PRIMARY KIDNEY CARE



### A Natural Kidney Function Toner

**For primary kidney care in conditions of**

**Nephritis**

**Nephropathy**

**Impaired GFR**

**Poor Renal Functions**

**Anasarca**

**Oedema &  
Other urinary disorders**

### ADDITIONAL BENEFITS

- ★ Helps prevent nephro-degeneration.
- ★ Improves overall health & vital parameters.
- ★ A **Nephroprotective adjuvant** to Life saving, but... Nephrotoxic drugs like:-

**NSAID's (Ibuprofen, Diclofenac)**

**Antibiotics (Gentamicin)**

**Anti-cancer Agents like (Cisplatin)**

**Anti-rheumatic drugs (Methotrexate)**

#### DOSAGE

**ADULTS (MEN AND WOMEN):**  
3 teaspoonful 3 times daily

**CHILDREN (3-6 YEARS):**  
1/2 teaspoonful 2 times daily

**CHILDREN (7-12 YEARS):**  
1 teaspoonful 2 times daily or as directed by the Physician.



One teaspoonful  
= approx. 5 ml



Available in the pack of 450 ml. and 200 ml.