

**Table S1:** Composition of NEERI KFT and their ethnopharmacological claim for kidney/urinary, urolithiatic disorder via immunomodulation and anti-inflammatory by API, UPI, Unani texts, and reports of current evidences.

Sr.No	Common name	Botanical name and source	Concentration (mg)	Traditional claim		
				API	UPI	Current Evidences
1.	Punernava	<i>Boerhavia diffusa</i> L., root	1000	Mutrala (Diuretic), Vatakantaka/sothahara (Anti-inflammation) API, Part-I, Vol-I, V & IX, 140, 211 & 103		(Mishra et al., 2014), (Singh et al., 2020)
2.	Kasni	<i>Cichorium intybus</i> L., stem	600	-	Mudir-e-Baul (Diuretic) UPI, Part-I Vol-VI 96	(Bahmani et al., 2015)
3.	Makoya	<i>Solanum nigrum</i> L., fruit	500	Prameha (Urinary disorder/ increased frequency and turbidity of urine) API, Part-I, Vol-II, 68	Muhallil-e-auram (Anti-inflammatory) UPI, Part-I, Vol-VI, 93	(Azarkish et al., 2017)

4.	Giloe	<i>Tinospora cordifolia</i> (Willd.) Miers, stem	500	Prameha (Urinary disorder/ increased frequency and turbidity of urine) API, Part-I, Vol-I, 41	Mudirr-e-Baul (Diuretic) UPI, Part-I, Vol-I, 31	(Singh and Chaudhuri, 2017)
5.	Kamal fool	<i>Nelumbo nucifera</i> Gaertn., flower	400	Mutra virajaniya (Urinary depigmenter) API, Part-I, Vol-II, 70		(Sharma et al., 2020)
6.	Palash	<i>Butea monosperma</i> (Lam.) Taub., flower	300	Mutrakrcchra (Dysuria) and Prameha (Urinary disorder/ increased frequency and turbidity of urine) API, Part-I, Vol-V, 162	Mudirr-e-Baul (Diuretic) UPI, Part-I Vol-II, 83	(Singh et al., 2020)
7.	Gokshru	<i>Tribulus terrestris</i> L., fruit	300	Mutrakrcchra (Dysuria) API, Part-I, Vol-1, 40	Mudirr-e-Baul (Diuretic), Mufattit-e-Hasat (anti-lithotriptic) UPI, Part-I Vol-I, 53	(Kaushik et al., 2019)

8.	Sirisa	<i>Albizia lebbbeck</i> (L.) Benth., stem	200	-		(Ahmed et al., 2014)
9.	Lal chandan	<i>Pterocarpus</i> <i>santalinus</i> L.f., stem	200	-	Bol-ud- dam(Heamaturia) Tanqueehul Mufradat (Tanqueehul mufradat, Pg-169)	(Bulle et al., 2016)
10.	Haridra	<i>Curcuma longa</i> L., rhizome	200	Prameha (Urinary disorder/ increased frequency and turbidity of urine) API, Part-I, Vol-I, 61	Muhallil-e-Auram (Anti- inflammatory) Tanqueehul Mufradat (Tanqueehul mufradat, Pg-108)	(Ghosh et al., 2014)
11.	Ushira/Khas	<i>Vetiveria</i> <i>zizanioides</i> (L.) Nash, stem	150	Mutrakrechra (Dysuria) API, Part-I, Vol-III, 221		
12.	Aanantmool	<i>Hemidesmus</i> <i>indicus</i> (L.) R. Br. ex Schult., stem	150	Raktavikara (Blood detoxification) API, Part-I, Vol-I, 107		(Sandeep and Krishnan Nair, 2010)

13.	Dhania	<i>Coriandrum sativum</i> L., fruit	100	Mutrala (Diuretic) API, Part-I, Vol-I, 31	Muhallil-e-waram (Anti-inflammatory) UPI, Part I, Vol-I, 57	(Lakhera et al., 2015)
14.	Sigru	<i>Moringa oleifera</i> Lam., seed	100	Mutrasarkara (Normalization of glucose in urine), API, Part-I, Vol-IV, 111		(Akinrinde et al., 2020)
15.	Varun	<i>Crataeva nurvala</i> Buch. Ham. stem	100	Raktavikara (Disorders of blood) API, Part-I, Vol-VI, 87		(Sharma et al., 2020)
16.	Chaulai	<i>Amaranthus spinosus</i> L. seed	100	-		(Amuthan et al., 2012)
17.	Revand chini	<i>Rheum emodi</i> Wall., rhizome	100	-	Mudirr-e-Baul(Diuretic) UPI, Part-I, Vol-II, 92	(Alam et al., 2005)

18.	Kakri Beej	<i>Cucumis utilissimus/melo</i> Roxb., seeds	100	Mutrakrechra (Dysuria) API, Part-I, Vol-II, 39	Mudirr-e-Baul (Diuretic) UPI, Part-I, Vol-IV, 64	(Saleem et al., 2019)
19.	Papita Jad	<i>Carica papaya</i> L., root	50	Mutraroga (Urinary diseases), API, Part-I, Vol-VI, 89		(Naggayi et al., 2015)

## References

- Ahmed, D., Kumar, V., Verma, A., Gupta, P.S., Kumar, H., Dhingra, V., Mishra, V., Sharma, M., 2014. Antidiabetic, renal/hepatic/pancreas/cardiac protective and antioxidant potential of methanol/dichloromethane extract of Albizzia Lebbeck Benth. stem bark (ALEx) on streptozotocin induced diabetic rats. BMC Complement. Altern. Med. 14, 243.  
<https://doi.org/10.1186/1472-6882-14-243>
- Akinrinde, A.S., Oduwale, O., Akinrinmade, F.J., Bolaji-Alabi, F.B., 2020. Nephroprotective effect of methanol extract of moringa oleifera leaves on acute kidney injury induced by ischemia-reperfusion in rats. Afr. Health Sci. 20, 1382–1396.
- Alam, M.M.A., Javed, K., Jafri, M.A., 2005. Effect of Rheum emodi (Revand Hindi) on renal functions in rats. J. Ethnopharmacol. 96, 121-125.
- Amuthan, A., Chogtu, B., Bairy, K.L., Sudhakar, Prakash, M., 2012. Evaluation of diuretic activity of Amaranthus spinosus Linn. aqueous extract in Wistar rats. J. Ethnopharmacol. 140, 424-427.

- Azarkish, F., Hashemi, K., Talebi, A., Kamalinejad, M., Soltani, N., Pouladian, N., 2017. Effect of the administration of *Solanum nigrum* fruit on prevention of diabetic nephropathy in streptozotocin-induced diabetic rats. *Pharmacognosy Res.* [https://doi.org/10.4103/pr.pr\\_47\\_17](https://doi.org/10.4103/pr.pr_47_17)
- Bahmani, M., Shahinfard, N., Rafieian-Kopaei, M., Saki, K., Shahsavari, S., Taherikalani, M., Ghafourian, S., Baharvand-Ahmadi, B., 2015. Chicory: A review on ethnobotanical effects of *Cichorium intybus* L. *J. Chem. Pharm. Sci.* ISSN:0974-2115
- Bulle, S., Reddy, V.D., Hebbani, A.V., Padmavathi, P., Challa, C., Puvvada, P.K., Repalle, E., Nayakanti, D., Aluganti Narasimhulu, C., Nallanchakravarthula, V., 2016. Nephro-protective action of *P. santalinus* against alcohol-induced biochemical alterations and oxidative damage in rats. *Biomed. Pharmacother.* 84, 740-746.
- Ghosh, S.S., Gehr, T.W.B., Ghosh, S., 2014. Curcumin and chronic kidney disease (CKD): Major mode of action through stimulating endogenous intestinal alkaline phosphatase. *Molecules.* 19, 20139-20156.
- Kaushik, J., Tandon, S., Bhardwaj, R., Kaur, T., Singla, S.K., Kumar, J., Tandon, C., 2019. Delving into the Antiuro lithiatic Potential of *Tribulus terrestris* Extract Through –In Vivo Efficacy and Preclinical Safety Investigations in Wistar Rats. *Sci. Rep.* 9, 1-3.
- Lakhera, A., Ganeshpurkar, A., Bansal, D., Dubey, N., 2015. Chemopreventive role of *Coriandrum sativum* against gentamicin-induced renal histopathological damage in rats. *Interdiscip. Toxicol.* 8, 99-102.
- Mishra, S., Aeri, V., Gaur, P.K., Jachak, S.M., 2014. Phytochemical, therapeutic, and ethnopharmacological overview for a traditionally important herb: *Boerhavia diffusa* linn. *Biomed Res. Int.* 2014, 808302.
- Naggayi, M., Mukiibi, N., Iliya, E., 2015. The protective effects of aqueous extract of carica papaya seeds in paracetamol induced nephrotoxicity in male wistar rats. *Afr. Health Sci.* 15, 598-605.
- Saleem, M., Javed, F., Asif, M., Baig, M.K., Arif, M., 2019. HPLC analysis and in vivo renoprotective evaluation of hydroalcoholic extract of cucumis melo seeds in gentamicin-induced renal damage. *Med.* 55, 107.
- Sandeep, D., Krishnan Nair, C.K., 2010. Amelioration of cisplatin-induced nephrotoxicity by extracts of *Hemidesmus indicus* and *Acorus calamus*. *Pharm. Biol.* 48, 290-295.

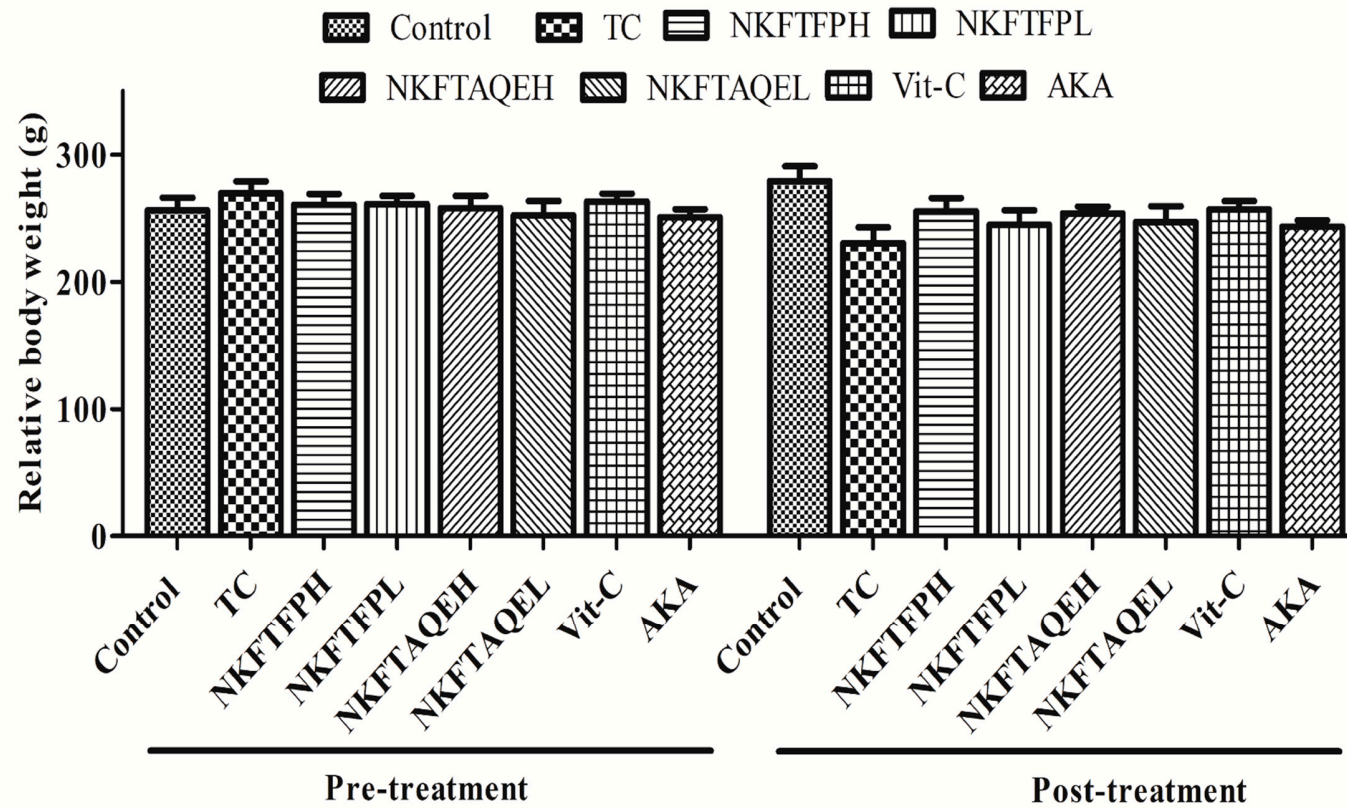
- Sharma, S., Baboota, S., Amin, S., Mir, S.R., 2020. Ameliorative effect of a standardized polyherbal combination in methotrexate-induced nephrotoxicity in the rat. *Pharm. Biol.* 58, 184-199.
- Singh, B., Singh, Bikarma, Kishor, A., Singh, S., Bhat, M.N., Surmal, O., Musarella, C.M., 2020. Exploring plant-based ethnomedicine and quantitative ethnopharmacology: Medicinal plants utilized by the population of Jasrota Hill in Western Himalaya. *Sustain.* 12, 7526.
- Singh, D., Chaudhuri, P.K., 2017. Chemistry and pharmacology of *Tinospora cordifolia*, in: *Natural Product Communications*. 12, 1934578X1701200240.

**Table S2:** Potential genes showing interaction with metabolites of NEERI KFT.

<b>Sr. no.</b>	<b>gene name</b>	<b>protein name</b>	<b>uniport id</b>
1.	Casp7	Caspase-7	P55210
2.	CASP3	Caspase-3	P42574
3.	BCL2	Bcl-2-related protein A1	Q16548
4.	BAAT	Bile acid-CoA:amino acid N-acyltransferase	Q14032
5.	CDH11	Cadherin-11	P55287
6.	UGT1A7	UDP-glucuronosyltransferase 1A7	Q9HAW7
7.	TP53	Cellular tumor antigen p53	P04637
8.	CHUK	Inhibitor of nuclear factor kappa-B kinase subunit alpha	O15111
9.	MAPK3	Mitogen-activated protein kinase 3	P27361
10.	UGT1A3	UDP-glucuronosyltransferase 1A3	P35503
11.	MMP2	72 kDa type IV collagenase	P08253
12.	GATA3	Trans-acting T-cell-specific transcription factor GATA-3	P23771



13.	MAPK1	Mitogen-activated protein kinase 1	P28482
14.	MMP3	Stromelysin-1	P08254
15.	HNF4A	Hepatocyte nuclear factor 4-alpha	P41235
16.	MMP9	Matrix metalloproteinase-9	P14780
17.	SOD1	Superoxide dismutase [Cu-Zn]	P00441
18.	AGTR1	Type-1 angiotensin II receptor	P30556
19.	ACE2	Angiotensin-converting enzyme 2	Q9BYF1
20.	PRKCA	Protein kinase C alpha type	P17252
21.	IL6	Interleukin-6 receptor subunit alpha	P08887
22.	JUN	Transcription factor Jun	P05412



**Figure S1:** Assessment of pre-treatment and post-treatment relative body weight. The statistical representation were made as Mean  $\pm$  SD (n=6) using One-way ANOVA followed by Tukey test. The comparisons were made to control and toxic, toxic to drug-treated groups. The significance level was observed at  $p < 0.05$ .