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REVIEW ARTICLE

A REVIEW OF PHARMACOLOGICAL ACTION OF *VISHAGHNA DRAVYAS* FROM *CHARAKOKT MAHAKASHAY* IN DRUG-INDUCED NEPHROTOXICITY W.S.R. TO *GARAVISHAJANYA SHOTHA*

MANASI SUBHASH BRID[1] ASHWIN VITHALRAO NIKAM[2] UDAY VENKATRAO PAWADE[3]

ABSTRACT:

Kidney being a major organ of excretion, is susceptible to the damage caused due to variety of toxins such as xenobiotics, drugs, environmental toxins etc. Nephrotoxicity is impairment of renal function which occurs due to adverse effects of these toxins on kidney. Oxidative stress is implicated as one of the mechanisms of drug induced nephrotoxicity. Drug induced nephrotoxicity (DIN) can be correlated with the concept of *gara visha* in *Ayurveda*. *Shotha* is one of the important manifestations found in *gara visha* as well as drug induced nephrotoxicity. *Vishaghna dravyas* from *Charakokt Mahakashays* possess *shothaghna, raktashodhak*, *tridoshashamak* and *mutral* properties. Also, these *dravyas* have been reported for antioxidant and nephroprotective potential. Hence, these *vishaghna dravyas* from *Charakokt Mahakashays* can be useful in *garavishajanya shotha* as well as drug induced nephrotoxicity. This review article is an attempt to discuss the role of *vishaghna dravyas* as antioxidant and *gara vishaghna* in oxidative stress induced nephrotoxicity with special reference to *garavishajanya shotha*.

KEY WORDS: Drug-Induced Nephrotoxicity, Oxidative Stress, Antioxidants, *Garavishajanya Shotha, Vishaghna Dravyas, Charakokt Mahakashay.*

[1]PG Scholar, [2]HOD & Professor, [3]Associate Professor, Dept. of Agadtantra, Shri Ayurved Mahavidyalaya, Nagpur, INDIA

Corresponding Email id: manasibrid@gmail.com Access this article online: www.jahm.in

1. INTRODUCTION:

Humans are routinely exposed to variety of toxins which includes industrial chemicals, environmental pollutants, pesticides, medications etc. Kidney being a primary excretory organ, bears most of the damage caused due to these toxins. Nephrotoxicity can be defined as adverse effects of substances on renal function[1]. Nowadays the incidences of drug induced nephrotoxicity are increasing rapidly. Easy accessibility & availability of drugs, therapeutic misadventures, use of multi-drug regimen for treating diseases, irrational use of self-medications, indiscriminate use of over the counter drugs (OTC) and lack of proper knowledge and awareness are some of the factors responsible for growing incidences of drug induced toxicities. Commonly drug induced nephrotoxicity manifests as Acute Tubular Necrosis (ATN) and Acute Interstitial nephritis (AIN). Oxidative stress plays major role in induction of ATN while AIN arises due to immunologic inflammatory response to toxicants or drugs. Clinically drug induced nephrotoxicity manifests as acute renal failure and oedema is important manifestation of it.

Ayurveda has classified *visha* as *Akritrim* (natural) and *Kritrim visha* (artificial)[2]. *Gara visha* is a form of *kritrim visha* which when administered exerts adverse effects on body. *Shotha* is one of the important manifestations of *gara visha*[3]. *Ayurveda*, the traditional and oldest system of medicine is based on holistic approach for treatment of diseases, primarily relying on medicinal plants. *Acharya Charaka* has classified medicinal plants as per their pharmacological actions into 50 groups known as *Panchashat Mahakashay*, each containing 10 herbs. This review article is an attempt to screen *vishaghna dravyas* from the *Panchashat Mahakashay* and to understand their probable mode of actions in drug induced nephrotoxicity with special reference to *garavishajanya shotha*.

2. REVIEW OF LITERATURE:

2.1 *Garavishajanya Shotha* with special reference to Drug Induced Nephrotoxicity-

Gara visha is a form of *kritrim visha* (artificial poison) which when administered shows acute or chronic effects on the body or produces various disorders[4]. Incompatible drug formulations and less potent *vishayogas* are also included under *gara visha*[5]. The person afflicted by *gara visha* develops symptoms like *Pandu, Krushata, Ajeerna, Shwayathu* etc[6]. *Shwayathu* i.e. *Shotha* is one of the important manifestations of *gara visha*. In *Ayurveda*, *Shotha* is described as separate *vyadhi* (disease) as well as *lakshana* and *updrava* of certain diseases like *pandu*, *vrikkaroga*[7] [8]. *Ayurveda* classifies *Shotha* as *vataj, pittaj and kaphaj*, based on the predominance of *dosha*. *Shotha* is also

classified as *nij* and *agantuj*[9]. *Gara visha* and *ama* are factors responsible for causation of *nij Shotha*[10]. The etiopathogenesis of *Garavishajanya Shotha* is described in figure 1[11] [12].

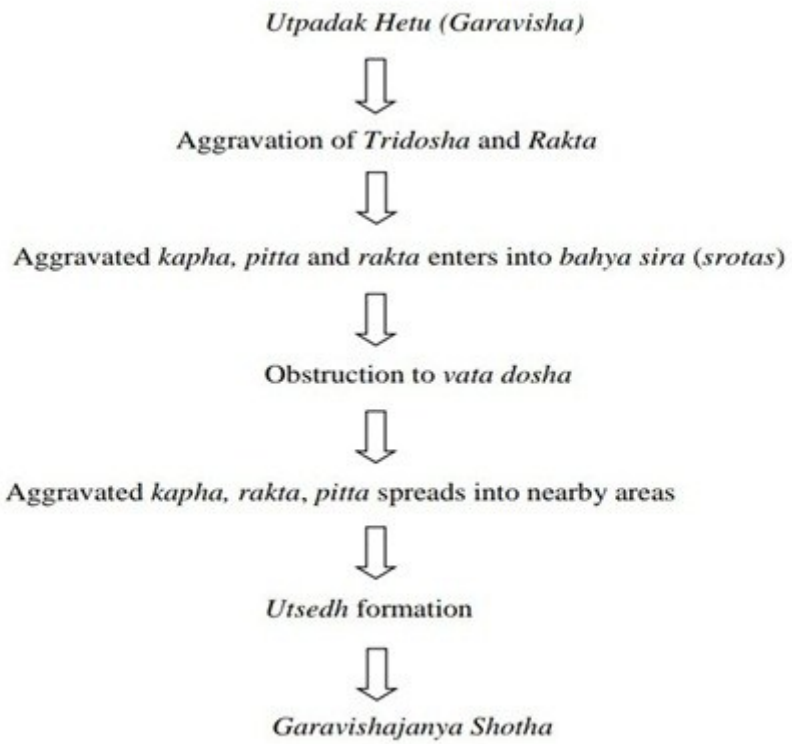

Figure 1: Etiopathogenesis of *Garavishajanya Shotha*

Nephrotoxicity is characterized by impairment of renal function. In *Ayurveda*, the references *about vrikka* i.e. kidney are miniature and there is no direct reference of involvement of *vrikka* in urine formation. As per *Ayurveda*, urine formation takes place in *pakwashaya* during the process of *saar- kitta vibhajan* during *tritiya avastha paak*, under the influence of *saman vayu*[13] [14]. P*akwashaya* is a primary site of *vata dosha* especially *apan vayu* and it is responsible for elimination of urine[15]. Aggravation of *apan vayu* and obstruction to its normal course leads to impairment of process of elimination of urine. Hence in *garavishajanya shotha* in relation to *vrikka, apan vayu* can be considered as one of the pathophysiological factors responsible. In short etiopathogenesis of *garavishajanya shotha* in *vrikka* is as follows:

1. *Hetu - Gara visha*
2. Factors responsible for *Samprapti*:
    a) *Dosha - Vata Pradhan Tridosha Predominantly Apan, Saman and Vyan Vayu*
    b) *Dushya – Rasa, Rakta*
    c) *Vyadhi Adhishthana – Vrikka*

3. Type of *Srotodushti- Sanga*

2.2 Drug induced nephrotoxicity-

Kidney performs number of essential functions such as excretion of waste products through urine, maintenance of electrolyte and acid- base balance, control of volume status, hemopoietic and endocrine function[16]. Being a major organ of excretion kidney is regularly exposed to high concentration of both endogenous & exogenous toxicants. Nephrotoxicity occurs when kidney specific detoxification and excretion do not work properly due to damage or destruction of kidney function by exogenous or endogenous toxins[17]. In nephrotoxicity tubulo-interstitial compartment of kidney gets affected & manifests as either Acute Tubular Injury (ATI) or Acute Interstitial Nephritis (AIN). Drug induced nephrotoxicity constitute an important cause of Acute Renal Failure (ARF) & Chronic Renal Failure (CRF) in present days clinically. It manifests as oliguria, fluid retention, oedema, proteinuria, fatigue, shortness of breath, nausea, hypertension etc[18]. Incidences of drug induced nephrotoxicity are increasing day by day. Number of drugs have been reported for their nephrotoxic potential. Table 1 summarizes the drugs imparting adverse effect on kidney.

Table 1- List of nephrotoxic drugs [19]

Sr. No.	Drug Class	Examples	Pathophysiological manifestations
1	Analgesics	NSAIDs	AIN, CIN, Glomerulonephritis
2	Antidepressants or Mood stabilizers	Amitriptyline, Doxepin,	Rhabdomyolysis
		Fluoxetine, Lithium	CIN, Interstitial nephritis, Glomerulonephritis, Rhabdomyolysis
3	Antihistamines	Diphenhydramine	Rhabdomyolysis
4	Antimicrobials	Acyclovir	AIN, Crystal nephropathy
		Aminoglycosides	Tubular Cell Toxicity
		Amphotericin B	Tubular Cell Toxicity
		Beta lactams	AIN
		Foscarnet	Crystal nephropathy, TCT
		Ganciclovir	Crystal nephropathy
		Pentamidine	Tubular Cell Toxicity
		Quinolones	AIN, Crystal nephropathy (Ciprofloxacin)
		Rifampicin	AIN
		Sulphonamide	AIN
		Vancomycin	AIN
5	Antiretrovirals	Indinavir	AIN, Crystal nephropathy

		Adefovir, Cidofovir	Tubular Cell Toxicity
6	Benzodiazepines	-	Rhabdomyolysis
7	Calcineurin inhibitors	Cyclosporine	Altered intraglomerular haemodynamic, CIN, Thrombotic microangiopathy
		Tacrolimus	Altered intraglomerular haemodynamic
8	Cardiovascular Agents	ACE I, ARBs	Altered intraglomerular haemodynamic
		Clopidogrel, Ticlopidine	Thrombotic microangiopathy
		Statins	Rhabdomyolysis
9	Chemotherapeutics	Cisplatin	CIN, Tubular Cell Toxicity
		Interferon- alfa	Glomerulonephritis
		Methotrexate	Crystal nephropathy
		Mitomycin- C	Thrombotic microangiopathy
10	Diuretics	Loops, Thiazides	AIN
		Triamterene	Crystal nephropathy
11	Drugs of Abuse	Cocaine, Heroin, Ketamine, Methadone, Methamphetamine	Rhabdomyolysis
12	Proton Pump Inhibitors	Omeprazole, Pantoprazole	AIN
13	Others	Allopurinol	AIN
		Haloperidol	Rhabdomyolysis
		Phenytoin	AIN
		Quinine	Thrombotic microangiopathy
		Ranitidine	AIN

*AIN- Acute Interstitial Nephritis, NSAID- Non-steroidal Anti-inflammatory drugs, CIN- Chronic Interstitial Nephritis, ACE I- Angiotensin converting enzyme inhibitor,

ARB- Angiotensin II receptor blockers.

2.2.1 Oxidative stress induced nephrotoxicity-

The mechanism of drug induced nephrotoxicity may differ between various drugs or drug classes and they are generally categorized based on histological components of kidney that is affected. General mechanisms that cause nephrotoxicity includes changes in glomerular haemodynamic, Tubular cell toxicity, Inflammation, Crystal nephropathy, Rhabdomyolysis & Thrombotic microangiopathy[20]. Usually drug induced kidney injury consists of two patterns of renal injury: - ATN and AIN. Whereas AIN develops from medications that incite an allergic reaction, ATN develops from direct toxicity on

tubular epithelial cells. Among Several cellular mechanisms underlying ATN, oxidative stress plays an important role[21]. Oxidative stress is defined as disturbance in production of reactive oxygen species (free radicals) and antioxidant defences[22]. Most of the drugs administered are lipophilic in nature and can enter into cell easily through the plasma membrane. To reach target site for adsorption, distribution and excretion drug should be converted into hydrophilic molecules. This conversion of non-polar compounds to polar compounds is termed as drug metabolism or biotransformation[23]. Drug and xenobiotic metabolism occur through two phases namely Phase I and Phase II. Biotransformation of drugs, xenobiotics and other substances by multiple renal enzyme systems including CYP450 and flavin containing monooxygenase favours formation of toxic metabolites and reactive oxygen species (ROS) or free radicals. These free radicals react with cellular macromolecules such as DNA, lipids, proteins etc. to cause cellular damage. The presence of these ROS tilts the balance in favour of oxidative stress, which outstrips antioxidants and increase renal injury via nucleic acid alkylation or oxidation, protein damage lipid peroxidation and DNA strand breaks[24]. Renal proximal convoluted tubular (PCT) cells, especially the P-S3 segment are frequently affected due to this direct nephrotoxic effect[25].

2.2.2 Anti-oxidants and Nephroprotection-

An antioxidant is a substance that is present in low concentration and significantly delays and prevents oxidation of oxidizable substrate[26]. Generally, antioxidants in body work at following different levels:

1. Prevention- keeping formation of ROS to minimum.
2. Interception- scavenging radical species either by using catalytic or non-catalytic molecules.
3. Repair- repairing damaged target molecules[27].

Antioxidants are classified into primary and secondary antioxidants. Primary antioxidants are mainly chain breakers, able to scavenge radical species by hydrogen donation while secondary antioxidants are singlet oxygen quenchers, metal chelators, oxidative enzyme inhibitors or UV radiation absorbers[28].

2.3 *Vishaghna dravyas* from *Charakokt Panchashat Mahakashay*-

The drug which has the potency to pacify the toxic effects is termed as *Vishaghna*. In *Sutrasthana*, *Charaka* has mentioned *Panchashat Mahakashay*, each containing 10 *dravyas*. This classification of *dravyas* is based on their similarity in action i.e. *karma. Vishaghna Mahakashay* is one of these 50 *mahakashays*. *Dravyas* mentioned in remaining

mahakashays also possess the *vishaghna dravyas* from *Charakokt Panchashat Mahakashayas.*

Table 2 – *Vishaghna dravyas* from *Charakokt Panchashat Mahakashayas* [29] [30]

Sr. No.	*Dravya*	Latin name	*Mahakashay*
1	*Madhuk*	*Glycyrrhiza glabra*	*Jeevaniya, Sandhaniya, Varnya, Kanthya, Kandughna, Snehopaga, Vamanopaga, Asthapanopaga, Mutravirajniya, Angamardprashaman, Shonitasthapan,*
2	*Haridra*	*Curcuma longa*	*Lekhaniya, Kushthaghna, Vishaghna*
3	*Ativisha*	*Aconitum heterophyllum*	*Lekhaniya, Arshoghna*
4	*Karanj*	*Pongamia pinnata*	*Lekhaniya, Bhedaniya, Kandughna*
5	*Arka*	*Calotropis procera*	*Bhedaniya, Swedopaga*
6	*Swarnakshiri*	*Argemone Mexicana*	*Bhedaniya*
7	*Patha*	*Cissampelos pareira*	*Sandhaniya, Stanyashodhana, Jwarahar*
8	*Manjishtha*	*Rubia cordifolia*	*Sandhaniya, Varnya, Vishaghna, Purishsangrahaniya*
9	*Dhataki*	*Woodfordia fruticosa*	*Sandhaniya, Mutravirajniya, Purishsangrahaniya*
10	*Priyangu*	*Callicarpa macrophylla*	*Sandhaniya, Purishsangrahaniya, Shonitasthapan, Mutravirajniya, Dahaprashaman, Prajasthapan*
11	*Endri*	*Bacopa monnieri*	*Balya, Prajasthapan*
12	*Chandan*	*Santalum album*	*Varnya, Kandughna, Vishaghna, Trishnanigrahan, Dahaprashaman, Angamardprashaman*
13	*Padmak*	*Prunus cerasoides*	*Varnya, Vedanasthapan*
14	*Ushir*	*Vetiveria zizaniodis*	*Varnya, Shukrashodhan, Chhardinigrahan, Dahaprashaman, Angamardprashaman*
15	*Sariva*	*Hemidesmus indicus*	*Varnya, Stanyashodhana, Dahaprashaman*
16	*Hanspadi*	*Adiantum lunulatum*	*Kanthya*
17	*Jati*	*Jasminum grandiflorum*	*Kushthaghna*
18	*Nimb*	*Azadirachta indica*	*Kandughna*
19	*Shigru*	*Moringa oleifera Lam.*	*Krimighna, Swedopaga, Shirovirechanopaga*
20	*Nirgundi*	*Vitex negundo*	*Krimighna, Vishaghna*
21	*Rasna*	*Pluchea lanceolata*	*Vishaghna, Anuvasnopaga, Vayasthapan*
22	*Sukshma Ela*	*Elletaria cardamomum*	*Vishaghna, Shwashar, Angamardprashaman*
23	*Palindee*	*Operculina terpethum*	*Vishaghna*
24	*Katak*	*Strychnos potatorum*	*Vishaghna*

25	*Shirish*	*Albizzia lebbeck*	*Vishaghna, Vedanasthapan*
26	*Shleshmatak*	*Cordia dichotoma F.*	*Vishaghna*
27	*Elvaaluk*	*Gisekai pharnaceoides*	*Shukrashodhan, Vedanasthapan*
28	*Samudraphen*	*Sepia offincinalis*	*Shukrashodhan*
29	*Kadamb*	*Anthrocephalus indicus Miq.*	*Shukrashodhan, Vedanasthapan*
30	*Bakul*	*Mimusops elengi*	*Shukrashodhan, Mutravirechaniya*
31	*Shalparni*	*Desmodium gangeticum*	*Snehopaga, Shwayathuhar, Angamardprashaman, Vayasthapan*
32	*Punarnava*	*Boerhavia diffusa*	*Swedopaga, Kasahar, Vayasthapan*
33	*Hijjal*	*Barringtonia acutangula*	*Vamanopaga*
34	*Gambhari*	*Gmelina arborea*	*Virechanopaga, Shwayathuhar, Dahaprashaman*
35	*Jyotishmati*	*Celastrus panniculatus*	*Shirovirechanopaga*
36	*Kshavak*	*Centipeda minima*	*Shirovirechanopaga*
37	*Aparajita*	*Clitoria terneata*	*Shirovirechanopaga*
38	*Vriksharuha*	*Dendrophthoe falcata*	*Shukrajanan, Hikkanigrahan, Mutravirechaniya*
39	*Kamal*	*Nelumbo nucifera*	*Purishsangrahaniya, Purishvirajniya, Mutravirajniya, Dahaprashaman*
40	*Chorak*	*Angelica glauca*	*Shwashar, Sandnyasthapan*
41	*Tagar*	*Valeriana wallichii DC*	*Sheetaprashaman*
42	*Arjun*	*Terminalia arjuna*	*Udardprashaman*
43	*Arimed*	*Acacia farnisiana Willd*	*Udardprashaman, Sandnyasthapan*
44	*Kesar*	*Crocus sativus*	*Shonitasthapan*
45	*Gairik*	*Red Ochre*	*Shonitasthapan*
46	*Shaal*	*Shorea robusta Gaertn*	*Vedanasthapan*
47	*Ashok*	*Saraca asoka*	*Vedanasthapan*
48	*Brahmi*	*Centella asiatica L.*	*Sandnyasthapan, Prajasthapan, Vayasthapan*

After analysing above listed 48 *vishaghna dravyas*, 12 *dravyas* were found useful for *samprapti bhedana* of *garavishajanya shotha* in *vrikka* and they are listed below in table 3:

Table 3: *Guna- Karma* description of selected 12 *vishaghna dravyas* from *Charakokt Mahakashays*

Sr. No	***Dravya***	***Latin name***	***Rasa***	***Guna***	***Virya***	***Vipaka***	***Doshaghnata***	***Karma***
1	*Punarnava*[31]	*Boerhavia diffusa L.*	*Madhur Tikta Kashay*	*Laghu Ruksha*	*Ushna*	*Madhur*	*Tridoshashamak*	*Gara vishaghna Shothaghna Raktashodhak*

2	*Aparajita*[32]	*Clitoria terneata*	*Tikta Kashay*	*Laghu*	*Sheeta*	*Katu*	*Tridoshashamak*	*Shothaghna Mutraroganashak*
3	*Sariva*[33]	*Hemidesmus indicus*	*Madhur Tikta*	*Snigdha Guru*	*Sheeta*	*Madhur*	*Tridoshashamak*	*Raktashodhak*
4	*Patha*[34]	*Cissampelos pareira*	*Tikta*	*Ushna Laghu*	*Ushna*	*Katu*	*Tridoshashamak*	*Gara vishaghna Shothaghna*
5	*Katak*[35]	*Strychnos potatorum*	*Tikta*	*Laghu Vishad*	*Ushna*	*Madhur*	*Tridoshashamak*	*Gara vishaghna Shothaghna*
6	*Ela*[36]	*Elletaria cardamomum*	*Katu Madhur*	*Laghu*	*Sheeta*	*Madhur*	*Vata shamak*	*Mutrakruchhha, Mutrajanan*
7	*Madhuk*[37]	*Glycyrrhiza glabra*	*Madhur*	*Guru Snigdha*	*Sheeta*	*Madhur*	*Pitta-Vata Shamak*	*Raktashodhak, Shothaghna*
8	*Gambhari*[38]	*Gmelina arborea Linn*	*Tikta Madhur Kashay*	*Guru*	*Ushna*	*Katu*	*Tridoshashamak*	*Shothaghna, Amapachan*
9	*Manjishtha*[39]	*Rubia cordifolia*	*Madhur Tikta Kashay*	*Guru Ruksha*	*Ushna*	*Katu*	*Kapha-Pittashamak*	*Raktashodhak, Shothaghna*
10	*Rasna*[40]	*Pluchea lanceolata*	*Tikta*	*Guru*	*Ushna*	*Katu*	*Vata- Kapha Shamak*	*Shothaghna, Amapachan*
11	*Haridra*[41]	*Curcuma longa*	*Katu Tikta*	*Laghu Ruksha*	*Ushna*	*Katu*	*Kapha- Pitta Shamak*	*Raktashodhak Shothaghna*
12	*Chandan*[42]	*Santalum album Linn*	*Tikta Madhur*	*Laghu Ruksha*	*Sheeta*	*Katu*	*Kapha-pittashamak*	*Raktashodhak*

The antioxidant as well as nephroprotective activity of above listed 12 *vishaghna dravyas* have been reported and their details are mentioned in Table 4.

Table 4 – Antioxidant and Nephroprotective activities of selected 12 *vishaghna dravyas*

Sr No	***Dravya***	**Latin Name**	**Experimental Study**	**Activity proven**
1	*Punarnava*	*Boerhavia diffusa Linn.*	In vitro study on hydroalcoholic extract of *Boerhavia diffusa* L [43].	Antioxidant
			In vivo study on extract of *Boerhavia diffusa* L. against acetaminophen induced nephrotoxicity in rats [44]	Nephroprotective

2.	*Aparajita*	*Clitoria terneata*	In vivo study on extracts of *Clitoria terneata*[45]	Antioxidant & Nephroprotective
3	*Sariva*	*Hemidesmus indicus*	In vitro ex-vivo study on methanolic extract of root bark of *Hemidesmus indicus* R. Br[46].	Antioxidant
			In vivo study on extract of *Hemidesmus indicus* in Cisplatin induced nephrotoxicity[47]	Nephroprotective
4	*Patha*	*Cissampelos pareira*	In vitro study of alkaloids from *Cissampelos pareira* L[48].	Antioxidant
			In vivo study on hydroalcoholic extract of *Cissampelos pareira* in gentamicin induced nephrotoxicity in rats [49]	Nephroprotective
5	*Katak*	*Strychnos potatorum*	In vivo study on extract of *Strychnos potatorum* seeds [50]	Antioxidant
			In vivo study of ethanolic extract of *Strychnos potatorum* seeds in rat models [51]	Nephroprotective
6	*Yashtimadhu*	*Glycyrrhiza glabra*	In vitro study on extracts of ariel parts and roots of *Glycyrrhiza glabra* [52]	Antioxidant (Radical scavenging)
			In vivo study on aqueous extract of G*lycyrrhiza glabra* in CCl_4 induced nephrotoxicity in rats [53]	Nephroprotective
7	*Manjishtha*	*Rubia cordifolia*	In vivo screening of extract of *Rubia cordifolia* in Cisplatin induced nephrotoxicity in swiss albino mice [54]	Nephroprotective
8	*Ela*	*Elletaria cardamomum*	In vitro study of methanolic extract of green cardamom [55]	Antioxidant
			In vivo study on extract of cardamom in gentamicin induced nephrotoxicity in rats [56]	Nephroprotective
9	*Haridra*	*Curcuma longa*	In vitro study on curcumin [57]	Antioxidant, anti-inflammatory
			In vitro study of curcumin in Cisplatin induced nephrotoxicity [58]	Nephroprotective, Antioxidant & anti-inflammatory
10	*Gambhari*	*Gmelina arborea*	In vitro assessment of methanolic extract of *Gmelina arborea* [59]	Antioxidant
			In vivo assessment of ethanolic extract of *Gmelina arborea* [60]	Nephroprotective
11	*Rasna*	*Pluchea lanceolata*	In vitro study on root extract of *Pluchea lanceolata*[61]	Antioxidant

			In vivo study on extract of *Pluchea lanceolata* in Benzo (a) pyrene induced nephrotoxicity [62]	Nephroprotective
12	*Chandan*	*Santalum album Linn*	In vitro assessment of aqueous extract of sandalwood [63]	Antioxidant

3. DISCUSSION:

Medicinal plants and plant based medicinal preparations plays major role in ayurvedic treatment regimen. Use of plants for treatment was known since Vedic era but comprehensive classification of medicinal plants was first put forward by *Acharya Charaka*. In this review article, 500 *dravyas* from *Charakokt Mahakashays* were screened for *vishaghna* property. As per *Bhavprakash Nighantu*, 48 out of these 500 possess *vishaghna* property and they are enlisted in table 2. After scrutinizing these 48 *dravyas* for their *rasapanchaka* and *doshaghnata*, 12 *dravyas* were found useful in *garavishajanya shotha* in relation to *vrikka*. These *dravyas* are mentioned in table 3. Along with *vishaghna* property all the *dravyas* except *Sariva, Patha* and *Chandan* possess *shothaghna* property.

Vitiation of *tridosha* and *rakta dhatu* is responsible for causation of *garavishajanya shotha*. Hence, *dravya* should possess *vishaghna, shothaghna, raktashodhak* property to correct this vitiation. *Punarnava* (*Boerhavia diffusa* L.) due to its *tikta, madhur rasa* acts on vitiated *pitta* and *rakta*, being *ushna virya* it acts on aggravated *kapha* and *vata*. As it pacifies *tridosha* and as it possesses *gara vishaghna*, *shothaghna* as well as *rakta shodhak* properties as mentioned in table 3, it can be useful in treating *garavishajanya shotha*. *Patha* (*Cissampelos pareira*) due to *tikta rasa* pacifies aggravated *pitta* and *rakta*, by virtue of *ushna virya* it pacifies *kapha* and *vata*. As mentioned in table 3, *Patha* possesses *gara vishaghna* property. Hence being a *gara vishaghna* and *tridoshashamak* it can help in relieving *garavishajanya shotha*.

Ayurveda has given importance to *mutravaha srotas disorders* and has explained various herbs for their management. According to *Ayurveda, mutra* has predominance of *agni* and *jal mahabhuta*. Hence *dravyas* having *sheeta virya*, *madhur vipak, katu rasa* are helpful for *mutrajanan*. By increasing urine output, these *mutral dravyas* help in reducing *shotha*. Herbs like *Aparajita (Clitoria terneata), Ela (Elletaria cardamomum), Chandan (Santalum album)* primarily act on *mutravaha srotas*. *Aparajita* due to its *sheeta virya* acts as *mutral*. Due its *tikta rasa* and *tridoshahar* property it can reduce *garavishajanya shotha*. *Ela* being *sheeta virya* and *madhur vipaki* acts as *mutral*.

It is seen earlier that vitiation of *vata dosha* especially *apan vayu* plays important

role in genesis of *garavishajanya shotha*. Hence *dravyas* acting specifically on vitiated *vata dosha* can be helpful. *Rasna (Pluchea lanceolata*), *Katak* (*Strychnos potatorum*), *Gambhari* (*Gmelina arborea* L.) possess *vata shamak* property. *Katak* being *ushna virya* and *madhur vipaki* alleviates *vata dosha* whereas *Rasna* and *Gambhari* being *ushna virya* and due to *guru guna* acts on vitiated *vata*. *Dravyas* like *Haridra* (*Curcuma longa*), *Manjishtha* (*Rubia cordifolia*) being *katu* and *ushna* bring about the *samyak pachana* and *srotovishodhan*, which can be helpful in management of *garavishajanya shotha*.

Oxidative stress plays an important role in drug induced kidney damage. Antioxidants are the counter system that protect the body against the damage caused due to oxidative stress. Antioxidants are available in both endogenous as well as exogenous form. But synthetic antioxidants are reported unsafe to human health due to their carcinogenic potential. Hence, these undesirable effects of modern medicine have diverted the attention towards herbal medicines. Number of medicinal plants have reported to possess anti-oxidant properties. As drug induced nephrotoxicity has been correlated with *garavishajanya shotha, dravyas* acting on *garavishajanya shotha* can be used in management of drug induced nephrotoxicity. *Dravyas* described in table 3 have been reported for their antioxidant as well as nephroprotective activity in different in vitro as well as in vivo models, which are summarized in table 4. They protect the renal damage by different mechanisms. Nephroprotection and antioxidant activity of these twelve *vishaghna dravyas* is due to the various phytoconstituents present in them.

4. CONCLUSION:

Twelve Vishaghna dravyas from *Charakokt mahakashay* viz *Punarnava, Sariva, Aparajita, Patha, Haridra, Yashtimadhu, Rasna, Ela, Chandan, Katak, Manjishtha, Gambhari* can be helpful in management of *garavishajanya shotha* as they possess *tridoshashamak, raktashodhak, mutral* and *shothaghna* properties. These twelve *vishaghna dravyas* are also useful for management of drug induced nephrotoxicity due to their antioxidant and nephroprotective potential.

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