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REVIEW ARTICLE

PHARMACOLOGICAL ACTION OF *VISHAGHNA DRAVYAS* FROM *CHARAKOKTA MAHAKASHAYA* IN DRUG INDUCED HEPATOTOXICITY W.S.R. TO *GARAVISHJANYA SHOTHA* – A REVIEW

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ABSTRACT

Most of the metabolic processes including detoxification of various drugs and xenobiotics occur in the liver. During the detoxification process the reactive chemical intermediates damage the liver. Drug induced hepatotoxicity causes liver damage due to oxidative stress. Hepatotoxicity is an injury to the liver that is associated with impaired liver functions and is a major concern at present. In this modern era, herbal antioxidants have attracted the researches due to its potential and efficacy against drug induced liver injury. Ayurveda describe Vishaghna dravyas as they possess the property to pacify the visha (Toxin) and prevent the reoccurrence of toxic manifestations. Hepatoprotective and Antioxidant activity of Vishaghna Dravyas in Charakokta Mahakashaya has been reported. Most of the Vishaghna dravyas shows pharmacological actions like Shothaghna, Raktashodhaka, Tridoshashamaka, Pittashamaka etc. Drug induced hepatotoxicity can be correlated with the concept of Garavisha in ayurveda. Shotha is one of the manifestations found in Garavisha as well as DIH. Hence Vishaghna dravyas in Charakokta Mahakashaya can be useful in Garavishajanya Shotha and DIH. This review article is an attempt to discuss role of Vishaghna dravyas from Charakokta Mahakashaya as Antioxidant and Garavishaghna in oxidative stress induced hepatotoxicity with special reference to Garavishjanya Shotha.

KEY WORDS: Garavishajanya Shotha, Drug-induced Hepatotoxicity, Oxidative Stress, Antioxidants, Vishaghna Dravyas, Charakokta Mahakashaya.

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1. INTRODUCTION:

Humans are exposed to various xenobiotics from air (air pollutants), nutrients (food additive, preservatives), therapy for disease (drugs) etc. These xenobiotics damage various organs like liver. Liver is a dual organ having both secretary and excretory function. It plays a major role in the metabolism and excretion of drugs. In this modern era, the incidence of Drug Induced Hepatotoxicity (DIH) is increasing day by day due to easy availability of over the counter drugs like Paracetamol. Oxidative stress plays a major role in the formation of DIH. Application of antioxidant signifies a rational curative strategy to prevent and cure liver disease involving oxidative stress [1]. *Ayurveda* emphasizes more on preventive and promotive aspect of health. In *ayurveda*, *Visha* is classified as *Akritrim* and *Kritrim Visha*. *Garavisha* is also known as *Kritrima Visha.* When administered in the body it shows acute, sub acute and chronic toxic effects and also produces various disorders like *Shopha, Yakrita-pleehavikara, Udara, Pandu* etc. *Panchashata Mahakashaya* is described in *Charaka Samhita* which is the unique contribution in *ayurveda*. *Vishaghna dravyas* in *Charakokta Mahakashaya* are useful in the management of deleterious effect of *visha.* The primary objective of this review article is to explore the pharmacological action of *Vishaghna Dravyas* from *Charakokta Mahakashaya* in oxidative stress induced hepatotoxicity with special reference to *Garavishajanya Shotha*.

2. REVIEW OF LITERATURE:

2.1. *Garavishajanya Shotha* with special reference to Drug Induced Hepatotoxicity

In ayurvedic classics *Garavisha* is known as *Kritrimvisha* (Artificial Poison)[2]. *Garavisha* is considered as one of the form of *Kritrimavisha* which is the combination of two or more than two poisonous or non-poisonous drugs and ultimately affects the whole body by vitiating all the *dhatus* in the body [3]. When administered in the body it shows toxic effects and produces various disorders like *Shopha, Pandu, Yakrit-Pleehavikara* etc. [4]. One of the manifestations of *Garavisha* is *Yakrit-Pleehavikara* which can be correlated with DIH in present scenario. *Charaka Samhita* and *Madhavnidan* mentioned *Garavisha* as cause of *Nija Shotha* [5],[6]. In *Madhavnidan Shotha* is described as a separate disease and is classified as *Nija* and *Agantuja Shotha* [7].

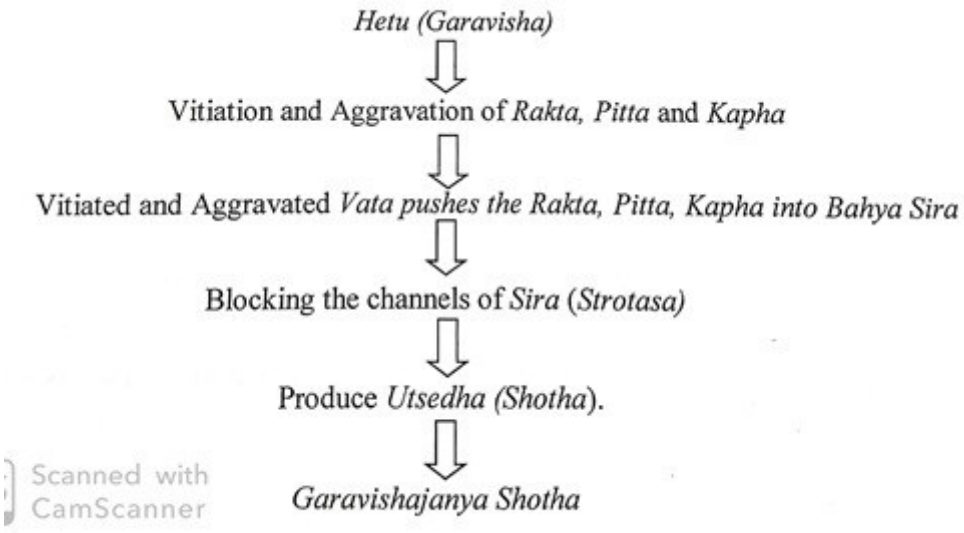

Fig. 1: Etiopathogenesis of *Garavishajnya Shotha*

In short etiopathogenesis of *Garavishajanya Shotha* in *Yakrita* is as follows:

1. *Hetu - Garavisha*
2. Factors responsible for *Samprati*:
    a) *Dosha - Vata, Pitta, Kapha*
    b) *Dushya - Rakta*
    c) *Vyadhi Adhishthana - Yakrita*
3. Type of *Strotodushti - Sanga*

2.2.1. Drug Induced Hepatotoxicity:

Liver often plays an important role in the metabolism of drugs and xenobiotics, leading to a particular risk of toxic effect. Drug induced hepatotoxicity is seen in the form of DILI. Drug induced liver injury (DILI) is defined as a liver injury caused by exposure to a drug or non infectious toxic agent, and it is associated with different levels of organ dysfunction [9]. Liver injury is defined as Alanine aminotransferase (ALT) level of more than three times the upper limit of the normal range, an Alkaline phosphatase (ALP) level of more than twice the upper limit of the normal or Total Bilirubin (TBL) level of more than twice the upper limit of the normal if associated with any elevation of the Alanine aminotransferase or Alkaline phosphatase level [10].

Hepatotoxicity is of three major classes in which liver damage is defined by biochemical pattern as follows:

1. Hepatocellular Injury: Sr. ALT or ALP levels are elevated
2. Cholestatic Injury: ALP and Bilirubin levels in the serum increases.
3. Mixed Injury: Both ALT and ALP levels in the serum increases [11].

In addition to the biochemical pattern, a histological pattern of liver damage may be identified. Recently, the Drug Induced Liver Injury Network (DILIN) reported a series of possible histological pattern in a prospective

systemic analysis of 249 biopsies performed on patients with suspected DILI : 1. Acute Hepatitis; 2. Chronic Hepatitis; 3. Acute Cholestasis; 4. Chronic Cholestasis; 5. Cholestatic Hepatitis; 6. Granulomatous Changes; 7. Steatosis; 8. Steatohepatitis; 9. Coagulative/Confluent necrosis; 10. Massive /Sub-massive necrosis; 11. Vascular injury; 12. Hepatocellular alteration; 13. Nodular Regenerative hyperplasia; 14. Mixed injury; 15. Unclassifiable injury; 16. Minimal non-specific changes; 17.Normality. Among these dominant histological patterns are acute hepatitis, chronic hepatitis and cholestatic hepatitis [12].

Grossly the pathological changes by hepatotoxins are classified in following two categories-

a. Acute Liver Disease characterized by Cholestasis, Hepatocellular Necrosis, Fatty change, Granulomatous reaction or vascular disease.
b. Chronic Liver disease characterized by Variable degree of fibrosis, Cirrhosis, Neoplasia [13].

More than 1000 drugs and toxins are suspected to induce liver damage [14]. Classification of Hepatotoxic drug Reaction based on pathological changes seen in Acute Liver Disease and Chronic Liver Disease are mentioned in Table No.1 and Table No.2[15].

Table No 1: Classification of Hepatic Drug Reaction in Acute Liver Disease

Pathologic Changes	Drugs
1. Zonal Necrosis	Carbon tetrachloride
	Acetaminophen
	Halothane
2. Massive Necrosis	Halothane
	Acetaminophen
	Methyldopa
3. Fatty Change	Tetracycline
	Salicylates
	Methotrexate
	Ethanol
4. Hepatitis	Methyldopa
	Isoniazid
	Halothane
	Ketoconazole

5. Granuloma Formation	Sulfonamide Methyldopa Quinidine Allopurinol
6. Cholestasis	Sex Hormone (including oral contraceptives) Chlorpromazine Nitrofurantoin
7. Veno-occlusive disease	Cytotoxic Drugs
8. Hepatic/ Portal Vein Thrombosis	Oral Contraceptives

Table No 2: Classification of Hepatic Drug Reaction in Chronic Liver Disease

Pathological Changes	Drugs
1. Fibrosis- Cirrhosis	Methotrexate
2. Focal Nodular Hyperplasia	Vinyl Chloride Vitamin A Sex Hormone
3. Adenoma	Sex Hormone
4. Hepatocellular Carcinoma	Sex Hormone

2.2.2. Role of Oxidative Stress in Hepatotoxicity:

Oxidative Stress is defined as an imbalance between the production of free radical and antioxidant defenses [16]. High exposure of humans to xenobiotics such as drugs, pesticides, environmental pollutants etc. have increased at present, which is the important cause of liver diseases. Liver being closely associated with the gastrointestinal system receives much of the blood from the portal vein, which drains the xenobiotic compounds to the liver [17]. Biotransformation of lipophilic xenobiotics to more hydrophilic substance before excretion in urine or bile is an important function in the liver. This biotransformation occurs through two major metabolic pathways namely Phase I and Phase II. Phase I enzyme reaction takes place among other cytochrome-P450 (CYP-450) are involved in majority of reaction which converts xenobiotics to reactive metabolites namely Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS). These Reactive

Metabolite Species (RMS) via Phase II enzymes conjugate with hydrophilic molecules and then excreted outside the body. However, when human body is exposed to xenobiotics frequently the Glucuronidation (A major metabolic reaction of liver for disposal of xenobiotic substance) is saturated and detoxification pathway (Phase I and Phase II) get overwhelmed [18]. Due to this excess production of free radicals occur. Free radicals are unpaired electron with unstable nature. Once free radical produces it starts attacking healthy nearby cells and attempt to replace their missing electron. When attacked molecule loses its electron it becomes a free radical itself. This can cause a chain reaction resulting in disruption of nearby cells. This chain reaction is known as oxidative stress. Nowadays oxidative stress is one of the important causes of many diseases including DIH. Hepatocytic Proteins, Lipids and DNA are among the cellular structures that are primarily affected by ROS and RNS, the process results in structural and functional abnormalities in the liver [19].

2.2.3. Hepatoprotective Activity of Antioxidant:

A complex antioxidant system has been developed in mammals to relieve oxidative stress. Antioxidants are the molecule that in low concentration can prevent or delay the oxidation of an oxidizable substrate [20]. Antioxidants may exert their effect on biological system by different mechanism including electron donation, metal ion chelation-antioxidants or by gene expression regulation.

Mechanism of Action:

Two principle mechanism of actions have been proposed for antioxidants-

a. The first is chain breaking mechanism by which the primary antioxidant donates an electron to the free radical present in the system.
b. The second mechanism involves removal of Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) initiators (Secondary antioxidant) by quenching chain-initiating catalyst [21]

2. 3. *Mahakashaya*

Acharya Charaka mentioned 500 *dravyas* in *Panchashata Mahakashaya* which is distributed in 50 groups. These groups of *Mahakashaya* are categorized according to their *karma* (Action). Each group of *Mahakashaya* includes 10 *dravyas.* Among them one of the group is *Vishaghna Mahakashaya* which shows antitoxic action [22]. According to *Chakrapani* the word *Vishaghna* is defined as the substance which possesses the property to pacify the *visha* (Toxin) and prevent the reoccurrence of toxic manifestations [23]. Along with *Vishaghna Mahakashaya* antitoxic

action also found in *dravyas* of remaining *Mahakashaya* which is listed in Table No.3.

Table No 3: *Vishaghna Dravyas* in *Charakokta Mahakashaya*[24],[25]

Sr. No	*Dravya*	Latin Name	Name of *Mahakashaya*
1.	*Aparajita*	*Clitoria ternatea*	*Shirovirechanopaga*
2	*Arjuna*	*Terminaliya arjuna*	*Udardaprashamana*
3	*Arka*	*Calatropis procera*	*Bhedaniya, Swedopaga*
4	*Ashoka*	*Saraca asoka*	*Vedanasthapana*
5	*Ativisha*	*Aconitun heterophyllum*	*Lekhaniya, Arshoghna*
6	*Bakula*	*Mimusops elengi*	*Shukrashodhana, Mutravirechaniya*
7	*Brahmi*	*Centella asiatica L*	*Sandnyasthapana, Prajasthapana, Vayasthapana*
8	*Chandan*	*Santalum album*	*Varnya, Kandughna, Vishaghna, Trishnanigrhana, Dahaprashamana, Angamardaprashamana*
9	*Choraka*	*Angelica glauca*	*Shwashara, Sandnyasthapana*
10	*Dhataki*	*Woodfordia fruticosa*	*Sandhaniya, Mutravirajaniya, Purishsamgrahaniya*
11	*Ela*	*Elettaria cardamomum*	*Vishaghna, Angamardaprashamana*
12	*Elwaluka*	*Gisekai pharnaceoides*	*Shukrashodhana, Vedanasthapan*
13	*Endri*	*Bacopa monnieri*	*Balya, Prajasthapana*
14	*Gairika*	*Red ochre*	*Shonitasthapana*
15	*Gambhari*	*Gmelina arborea*	*Virechanopaga, Shwayathuhara, Dahaprashamana*
16	*Hansapadi*	*Adiantum lunulatum*	*Kanthya*
17	*Haridra*	*Curcuma longa Linn*	*Lekhaniya, Kushthaghna, Vishaghna*
18	*Hijjal*	*Barringtonia acutangular*	*Vamanopaga*
19	*Irimeda*	*Acasia farnisiana willd*	*Udardaprashamana, Sandnyasthapana*
20	*Jati*	*Jasminum grandiflorum*	*Kushthaghna*
21	*Jyotishmati*	*Celastrus panniculatus*	*Shirovirechanopaga*
22	*Kadamba*	*Anthocephalus indicus*	*Shukrashodhana, Vedanasthapana*
23	*Katak*	*Strychnos potatorum*	*Vishaghna*
24	*Kshavak*	*Centipeda minima*	*Shirovirechanopaga*
25	*Kamal*	*Nelumbo nucifera*	*Purishsangrahaniya, Purishvirajaniya, Mutravirajaniya, Dahaprashamana*
26	*Kesara*	*Crocus sativus*	*Shonitasthapana*

27	*Karanja*	*Pongamia pinnata*	*Lekhaniya, Bhedaniya, Kandughna*
28	*Madhuka*	*Glycyrrhiza glabra*	*Jeevniya, Sandhaniya, Varnya, Kanthya, Kandughna, Snehopaga, Vamanopaga, Asthapanopaga, Mutravirjaniya, Angamardprashamana, Shonitsthapana.*
29	*Manjistha*	*Rubia cordifoliya*	*Sandhaniya, Varnya, Vishaghna, Purishsamgrahaniya*
30	*Nimba*	*Azadirechta indica*	*Kandughana*
31	*Nirgundi*	*Vitex negundo*	*Krumighna, Vishaghna*
32	*Padmak*	*Prunus cerasoides*	*Varnya, Vedanasthapana*
33	*Palindee*	*Operculina terpethum*	*Vishaghna*
34	*Patha*	*Cissampelos pareira*	*Sandhaniya, styanashodhaka, Jwarahara*
35	*Priyangu*	*Callicarpa macrophylla*	*Sandhaniya, Purishsamgrahaniya, Shonitsthapana, Mutravirajaniya, Dahaprashamana, Prajasthapana*
36	*Punarnava*	*Boerhavia diffusa*	*Swedopaga, Kasahara, Vayasthapana*
37	*Rasna*	*Pluchea lanceolate*	*Vishaghna, Anuvasanopaga, Vayasthapana*
38	*Samudraphena*	*Sepia offincinalis*	*Shukrashodhana*
39	*Sariwa*	*Hemidesmus indicus*	*Varnya, Stanyashodhana, Dahaprashamana*
40	*Shalaparni*	*Desmodium gangeticum*	*Shalparni, Shwayathuhara, Angamardaprashamana, Vayasthapana*
41	*Shaal*	*Shorea robusta gaertn*	*Vedanasthapana*
42	*Shigru*	*Moringa oleifera Lam*	*Krumighna, Swedopaga, Shirovirechanopaga.*
43	*Shirisha*	*Albizzia lebbeck*	*Vishaghna, Vedanasthapana.*
44	*Shleshmataka*	*Cordia dichotoma F*	*Vishaghna*
45	*Swarnkshiri*	*Argemone mexicana*	*Bhedaniya*
46	*Tagara*	*Valeriana wallichii*	*Shitaprashamana*
47	*Ushira*	*Vetivera zizaniodis*	*Varnya, Shukrashodhana, Chhardinighrahana, Dahaprashamana, Angamardaprashamana.*
48	*Vrukshruha*	*Dendrophthoe falcate*	*Shukrajanana, Hikkanigrahana, Mutravirechaniya*

After scrutinizing 48 *dravyas* from *Charakokta Mahakashaya*, 12 *dravyas* were found to be Hepatoprotective and Antioxidant which are enlisted in Table No. 4. These 12 *Dravyas* from *Charakokta Mahakashaya* possess *Vishaghna, Shothaghna, Tridoshashamaka* and

Raktashodhaka properties which pacify the etiopathogenesis of *Garavishajanya Shotha* are enlisted in Table No. 5.

Table No 4: Twelve *Vishaghna Dravya*s reported for Hepatoprotective - Antioxidant activity.

SR NO.	DRAVYA	EXPERIMENTAL STUDIES	PROVEN ACTIVITY	REFERENCE
1.	*Haridra*	i. Curcuma longa Linn extract on CCl_4 induced hepatotoxicity. ii. Antioxidant and Radical Scavenging properties of Curcumin.	Hepatoprotective & Antioxidant	[26] [27]
2.	*Manjishtha*	i. Hepatoprotective effect of Rubiadin a major constituent of Rubia Cordifoliya Linn. **ii.** Antioxidant activity of Rubiya Cordifolia against Lead toxicity.	Hepatoprotective & Antioxidant	[28] [29]
3.	*Nimba*	i. Effect of Azadirecta Indica on PCM induced hepatic damage in albino rats. ii. Antioxidant activity in bark and roots of Neem.	Hepatoprotective & Antioxidant	[30] [31]
4.	*Yashtimadhu*	Glycyrrhiza Glabra extract on CCl_4 induced oxidative stress mediated hepatotoxicity.	Antioxidant & Hepatoprotective	[32]
5.	*Aparajita*	i. Clitoria Ternatea leaf extract against PCM induced Damage in Mice. ii. Cytotoxic and Antioxidant properties of Clitoria Ternatea L.	Hepatoprotective & Antioxidant	[33] [34]
6.	*Ativisha*	i. Aconitum Heterophyllum root in glycerol induced acute renal failure in rats.	Antioxidant &	[35] [36]

		ii. Pharmacological and other important findings on the medicinal plant Aconitum heterophyllum.	Hepatoprotective	
7.	*Brahmi*	In Vitro activity of ethanolic extract of Bacopa Monnieri Linn aerial parts	Antioxidant & Hepatoprotective	[37]
8.	*Jati*	i. Evaluation of Jasminum grandiflorum for hepatoprotective activity in Isoniazid induced liver damage. ii. Antiulcer and in vitro Antioxidant activity of Jasminum grandiflorum.	Hepatoprotective & Antioxidant	[38] [39]
9.	*Kadamb*	i. Antihepatotoxic effect of Chlorogenic acid from Anthocephalus Cadamba. ii. Hypolipidemic and Antioxidant activity of Anthocephalus Indicus (Kadamba) root extract.	Hepatoprotective & Antioxidant	[40] [41]
10.	*Sariwa*	Antioxidant and Hepatoprotective activity of Hemidesmu Indicus R.Br.	Antioxidant & Hepatoprotective	[42]
11.	*Shaliparni*	i. Hepatoprotective activity of Desmodium Gangeticum in PCM induced liver damage in rats. ii. Anti-inflammatory and Antioxidant activities of Desmodium Gangeticum fraction in carrageenan induced inflamed rats.	Hepatoprotective & Antioxidant	[43] [44]
12.	*Shirisha*	Hepatoprotective and Antioxidant Effects of Albizzia Lebbeck against Thioacetamide induced Hepatotoxicity	Hepatoprotective & Antioxidant	[45]

Table No 5: Pharmacological Properties of Twelve *Vishaghna Dravyas* in *Charakokta Mahakashaya*

DRAVYA	***VISHAGHANA***	***SHOTHAHARA***	***RAKTASHODHKA***	***RASA***	***VIRYA***	***VIPAKA***	***DOSHAGHNTA***
Haridra[46],[47]	✓	✓	✓	TK	*Ushna*	*Katu*	KP
Manjishtha[48]	✓	✓	✓	K_sTM	*Ushna*	*Katu*	KP
Nimba [49],[50],[51]	✓	✓	✓	TK_s	*Shita*	*Katu*	PK
Madhuka[52]	✓	✓	✓	M	*Shita*	*Madhura*	PV
Aparajita [53]	✓	✓	-	TK K_s	*Shita*	*Katu*	VPK
Ativisha[54]	✓	✓	-	TK	*Ushna*	*Katu*	VPK
Brahmi [55]	✓	✓	✓	TK_s	*Shita*	*Madhura*	VPK
Jati[56],[57]	✓	✓	-	Tk	*Ushna*	*Katu*	VPK
Kadamb[58]	✓	✓	-	TK_s	*Shita*	*Katu*	VPK
Sariva[59]	✓	-	✓	MT	*Shita*	*Madhura*	VPK
Shaliparni[60],[61]	✓	✓	-	MT	*Shita*	*Madhura*	VPK
Shiriha[62]	✓	✓	-	K_sTM	*Ushna*	*Katu*	VPK

T-*Tikta* (Bitter), K-*Katu* (Pungent), M-*Madhura* (Sweet), Ks- *Kashaya* (Astringent), KP-*Kaph pitta,* VPK: *Vata-Pitta-Kapha*

3. DISCUSSION:

During metabolism free radical production occurs continuously in all cells. Body is able to remove these free radicals at certain degree and these are not harmful to body in specific physiological condition like appropriate physical exercise. However, a lots of risk factors such as drugs, environmental pollutants, alcohol etc. induce oxidative stress in liver, which result in various liver diseases like DIH. Antioxidants prevent free radical induced tissue damage. The action of antioxidant is different as they are categorized. Enzymatic antioxidant breaks the free radical and remove them. Enzymes convert oxidative products to hydrogen peroxide (H_2O_2) and then to water. Non enzymatic antioxidant breaks the continuity of free radical chain reaction. In radical scavenging process the small molecule antioxidants neutralize the reactive oxygen species and carry them away. Free radicals absorbed by large molecule antioxidant and prevent them from attacking other nearby healthy cells. Hence by these mechanisms antioxidants acts as hepatoprotective in oxidative stress induced hepatotoxicity. Nowadays, herbal antioxidants have attracted the researches due to its potential and efficacy. Natural antioxidants from food, medicinal plants possess strong antioxidant and free

radical scavenging abilities. Twelve *Vishaghna Dravyas* which are mentioned in Table No, 4 can be useful in the management of DIH as their Hepatoprotective and Antioxidant activity reported previously.

Twelve *Vishaghna Dravyas* mentioned in Table No. 5 possess *Shothaghna* property except *Sariva*. Despite the fact *Sariva* (*Hemidesmus Indicus*) has proven Anti-inflammatory action [63]. Hence in the management of *Garavishajanya Shotha* eleven *dravyas* in Table No.5 along with *Sariva* can be useful. Etiopathogenesis of *Garavishajanya Shotha* occurs mainly due to vitiation of *Tridosha* and *Raktadushti*. *Brahmi, Jati, Kadamba, Aparajita, Ativisha, Shirisha, Shaliparni* are *Tridohashamaka* and *Haridra, Manjistha, Sariwa, Nimba, Yashtimadhu* have *Raktashodhaka* properties. Hence these *dravyas* can alleviate etiopathogenesis of *Garavishajanya Shotha.* From Table No. 4 and Table No.5, it is found that most of the *Vishaghna dravyas* reported for hepatoprotective and antioxidant activity are predominant in *Tikta* and *Madhura Rasa*. These two *Rasa* possesses *Vishaghna* property. *Tikta-Madhura Rasa* are *Pittashamaka*. *Pitta* and *Rakta* has *Ashrayashrayi Sambandha*. Hence treatment used to cure diseases of *Pitta,* ultimately pacify the *Raktadushti.* As *Yakrita* is *Moolsthana* of *Raktavahastrotas*, *Vishaghna dravyas* pacifying *Raktadushti* also helps to improve function of *Yakrita.* Hence *Pittashamaka* treatment can be useful in DIH.

Out of twelve, three *Vishaghna Dravyas* namely *Haridra, Majistha, Nimba* are more effective in *Garavishajanya Shotha* (DIH) as they are *Vishaghna, Shothahar*, *Raktashodhaka* and *Kapha-Pittashamaka*. Due to *Tikta Rasa*, *Haridra* acts as *Pittavirechaka.* Hence it is useful in the *Kamala* (Jaundice) one of the mimic clinical presentation of DIH. *Manjistha* specifically act on *Raktavahasrotasa*. Due to its *Tikta, Kashaya* and *Madhura Rasa* it pacifies vitiated *Kapha-Pittadosha* in *Raktadhatu* and *Rakta* get purified (*Raktashodhaka*). Hence it can help in relieving important pathological factor of *Garavishajanya Shotha. Nimba* stimulates *Yakrita (Yakrutottejana)* due to its *Tikta- Kashaya* properties.

4. **CONCLUSION:**

Twelve *Vishaghna Dravyas* mentioned in *Charakokta Mahakashaya* viz. *Haridra, Manjistha, Nimba, Yashtimadhu, Aparajita, Ativisha, Brahmi, Jati, Kadamba, Sariwa, Shaliparni* and *Shirish possesses* hepatoprotective and antioxidant activity. These twelve *dravyas* are *Vishaghna, Shothaghna, Raktashodhaka* and *Tridoshashamaka.* Hence can be useful in the management of *Garavishajanya Shotha* (DIH). Among these twelve *dravyas Haridra, Manjistha and Nimba* are more effective.

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