



## HEPATOPROTECTIVE POTENTIAL OF SHIRISHADI YOGA IN ACETAMINOPHEN-INDUCED HEPATOXICITY – REVIEW

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## ABSTRACT

*Ayurveda*, an ancient holistic system from India, emphasises balancing the mind, body, and spirit for health, focusing on disease prevention through diet, exercise, and mental well-being. Paracetamol (acetaminophen), a widely used pain reliever, can cause liver toxicity when overused, leading to acute liver failure. *Agada Tantra*, *Ayurveda*'s toxicology branch, addresses various poisonings, including synthetic toxins like food adulteration and drug interactions, termed "*Gara Visha*." *Gara Visha* shares similarities with drug-induced hepatotoxicity. *Shirishadi Yoga*, an *Ayurvedic* formulation, contains hepatoprotective herbs with anti-poison, anti-inflammatory, and blood-purifying properties. It balances *Doshas* and detoxifies the liver, potentially preventing liver damage by suppressing toxic metabolites and enhancing glutathione synthesis. Its ingredients, known for antioxidants, immunomodulatory, and hepatoprotective actions, make *Shirishadi Yoga* a valuable remedy for liver protection, particularly in *Gara Visha*-related disorders.

**Keywords:** *Gara Visha*, Acetaminophen, *Shirishadi Yoga*, *Yakrit*

## INTRODUCTION

*Ayurveda* is an ancient holistic medical system from India that focuses on balancing the mind, body, and spirit to promote overall health. It emphasises disease prevention through proper diet, exercise, and mental well-being. Paracetamol (acetaminophen), a widely used pain reliever, can cause hepatotoxicity when taken in excess, leading to liver damage or acute liver failure. With over 89 million prescriptions in 2003<sup>1</sup>, acetaminophen remains one of the most commonly dispensed medications, and it is a leading cause of acute liver failure in the U.S.<sup>2</sup>.

*Agada Tantra*, a branch of *Ayurveda*, specializes in toxicology, addressing poisonings from plants, animals, and chemicals. It focuses on detoxification, antidotes, and preventive measures. *Vishas* (toxins) are classified into different types: *Sthavara*, *Jangama*, *Akritrima*, *Kritrima*, and *Gara Visha*. *Gara Visha* refers to synthetic poisons made from non-toxic ingredients, which include food adulteration and incompatible food and medicines.

*Shirishadi Yoga* is an *Ayurvedic* formulation containing hepatoprotective herbs with properties like *Vishaghna* (anti-poison), *Shothaghna* (anti-inflammatory), *Krimighna* (antimicrobial), *Deepana* (digestive), and *Raktashodhaka* (blood purifier). The herbal drugs in this formulation help detoxify and protect the liver, balancing the *Doshas* and promoting overall health.

## OBJECTIVES

To review the hepatoprotective potential of *Shirishadi Yoga* in Acetaminophen-induced hepatotoxicity.

## MATERIALS & METHODS

A review of *Ayurvedic* Literature and its corresponding commentaries has been conducted in depth. Peer-reviewed medical publications and textbooks of contemporary medical sciences have also been cited as sources for this topic.

## CONCEPTUAL REVIEW

### *Yakrit* In *Ayurveda*

*Yakrit* is explained as one among the *Koshtanga*, situated on the right side of the heart, by *Ashtangahridaya*.<sup>4</sup> As per *Sushruta Samhita*, *Yakrit* is situated below the heart on the right side and *Pliha* on the left side.<sup>5</sup> The anatomy of the liver is not well described. Even yet, our *Acharyas* were aware of it since the liver is also given significant weight in relation to metabolic processes in *Ayurvedic* texts. It is stated that *Pitta* seats on the liver. The liver is responsible for *Ranjakapitta's* entire range of functions. The liver is thought to be the source of *Raktavaha Srotas*. Thus, the liver plays a significant role in all *Raktavaha* and *Pittavaha Srotas disorders*. The liver is accorded with the same physiological importance in *Ayurvedic* texts as in modern ones.

**Table 01: Similarities between *Ranjaka Pitta* and Bile** <sup>6</sup>

Characteristics	<i>Ranjaka Pitta</i>	Bile
Site	<i>Yakrit</i> (liver)	Liver
Derived from	<i>Pitta</i>	A bitter greenish-brown alkaline fluid aids digestion and is secreted by the liver and stored in <sup>[1]</sup> the gall bladder.
Function	Imparts colour to the <i>Rasa</i> ( <i>Rasa Ranjana</i> ), Imparts colour to the stool	Helps in the emulsification of fats. <sup>[2]</sup> Imparts colour to the stool
Obstruction Results in	Pale colour stools ( <i>Tilapishtanibha Varchas</i> )	Clay Colored stool

### *Yakrit Roga*

There is no separate description of liver problems in

the classic *Ayurvedic* texts.

Possible reasons for not describing the *Yakrit Roga* as a separate group of disorders may be

- Most of the Ayurvedic classification of disease is based on symptoms.
- In pathogenesis, more importance is given to physiology than structure involved.

### 1. Brihatrayi

- Charaka has given a detailed description of Kamala in the context of Pandu Roga.
- In Sushruta Samhita - Kamala is mentioned as a synonym of Pandu Roga. In the same context, a description of the liver and spleen is found. The further stages of Kamala, i.e., Panaki, Kumbha Kamala, Halimaka, Lagharaka and Alasaka and the explanation about Raktavaha Srotodushti & treatment of Kamala are mentioned.
- In Ashtanga Sangraha & Ashtanga Hridaya - (600AD) - followed by the view of Charaka & Sushruta, description of 4 types of Pandu & Kamala are found. In Nidana Sthana, the Lodhra word is used for Kamala. An explanation of Swatantra and Paratantra Kamala is also mentioned.

### 2. Laghu Trayi

- Madhava Nidana (700 AD): Followed the view of Charaka, Sushruta and Vagbhata. A full description of Kamala and its stages with Nidana, Rupa, and Samprapti was given.
- Sharangadhara Samhita (1400 AD): Described Kamala in the context of Pandu Roga.
- Bhava Prakasha (1600 AD): Kamala was described along with Pandu Roga in Madhyamakhanda.

### 3. Others

- Bhela Samhita (700 AD): Kamala has been described in Pliha Halimaka Chikitsa Adhyaya.
- Harita Samhita (1400 AD): Eight types of Pandu, including two types of Kamala and Halimaka, have been described.

### Gara Visha and Hepatotoxicity

Gara Visha is becoming increasingly important in the present period because it can be conceptually interpreted as encompassing things like food adulteration, incompatible food, drug interactions, mechanical irritant poisoning, cosmetics, psychotropic medications,

occupational poisoning, etc.

According to Ayurveda in Agada Tantra (Toxicology), drug-induced hepatotoxicity may be correlated with Gara Visha. Gara Visha is a type of artificial slow-acting poison, and it is usually produced due to a combination of toxic or non-toxic substances, the waste products of the body, Bhasma and Alpa Virya (Low potent) Visha, Virudhahara, and the use of Virudha Aushadhi are also one of the vital causes. Signs and symptoms of Gara Visha Janaya Yakrit Roga have a resemblance with drug-induced hepatotoxicity. After long time use of Gara Visha and Virudha Aushadhi, the patient shows symptoms of Udara Roga (Yakrit Vridhi, Pliha Vridhi), Mandagni, Pandu, Adhyamana, Grahni Roga, Jaundice and Yakrit Vikara<sup>7</sup>.

Gara Visha in Today's World:

- Food adulteration/ Food preservatives
- Agricultural poisoning
- Incompatible food
- Different pollutions
- Mechanical irritant poisons
- Cosmetics
- Psychoactive drugs
- Alcohol
- Occupational poisoning, etc.

### Pathophysiology of Gara Visha:

Due to its "Kalantara Vipaka"<sup>8</sup> characteristics, Gara Visha cannot be wholly metabolized once it enters the body and experiences improper digestion and assimilation. As a result, it cannot be properly excreted from the body. The liver is an organ that performs various bodily tasks, including metabolic processes, immunological function, detoxification, and the creation and storage of diverse compounds required for the body<sup>9</sup>. The liver is vulnerable to possible harm from these toxins because it is the primary organ in the body responsible for detoxifying and metabolizing drugs. The liver is responsible for eliminating all bodily toxins within a specific bond. These toxins will then start to impact the hepatocytes.<sup>10</sup> This will eventually lead to the development of liver-related disorders since it will impair all other liver functions. In the end, Gara Visha impacts the liver in the body.

### Pathophysiology of Acetaminophen-induced hepatotoxicity

Acetaminophen-induced hepatitis occurs due to an overdose, leading to toxic liver injury. Normally, paracetamol is metabolized by glucuronidation and sulfation pathways, but a small portion is converted by the cytochrome P450 enzyme (CYP2E1) into a toxic metabolite, N-acetyl-p-benzoquinone imine (NAPQI). In overdose, NAPQI accumulates as glutathione, the detoxifying agent becomes depleted. Excess NAPQI binds to liver cell proteins, causing oxidative stress, mitochondrial dysfunction, and hepatocyte necrosis, particularly in the liver's centrilobular (zone 3) regions.

The necrotic cells trigger an inflammatory response, activating immune cells like Kupffer cells, which release pro-inflammatory cytokines (TNF- $\alpha$ , IL-6),

exacerbating liver damage. This results in hepatitis, with elevated liver enzymes (AST, ALT), jaundice, and potentially liver failure. Early treatment with N-acetylcysteine (NAC) replenishes glutathione, preventing severe damage. Without intervention, extensive necrosis may lead to acute liver failure or death.

### Shirishadi Yoga – Drug Review

Shirishadi Yoga is a formulation containing drugs with Vishaghna properties mentioned in different Ayurvedic Samhitas. This Yoga contains Shirisha (Ch. Su. 4/16), Haridra (Ch. Su. 4/16), Daruharidra (Raj Nighantu Pippalyadi Varg 202), Nimba (Kaidev Nighantu Aushadha Varga 883), and Manjistha (Ch. Su. 4/16) in combined decoction form. Most of the ingredients of this formulation are hepatoprotective and have antioxidant action.

**Table 02: Ingredients of Shirishadi Yoga**

Ingredients	Scientific name	Family	Part used
Shirisha	<i>Albizia lebbek Benth</i>	Leguminosae	Bark
Haridra	<i>Curcuma longa Linn.</i>	Zingiberaceae	Rhizome
Daruharidra	<i>Berberis lycium DC.</i>	Beberidaceae	Root
Manjistha	<i>Rubia cordifolia Linn.</i>	Rubiaceae	Root
Nimba	<i>Azadirachta indica A. Jugs</i>	Meliaceae	Leaf

**Table 03: Pharmacodynamics of the ingredients of Shirishadi Yoga**

Sr No.	Drug	Rasa	Guna	Virya	Vipaka	Karma
1.	Shirisha <sup>11</sup>	Tikta (Bitter), Katu (Pungent), Kashaya,	Laghu (Light)	Anusna	Katu	Vishaghna (Antipoisonous), Tvagdosha (For skin disorder), Tridoshara (Balance Vatta Kapha Pitta humor, Sothahra (Anti-inflammatory), Varnya (Complexion promoter)
2.	Haridra <sup>12</sup>	Tikta (Bitter), Katu (Pungent)	Laghu (Light), Ruksha (Dry)	Ushna (Hot)	Katu	Kushthaghna (Antileprotic), Kandughna (Antipruritic), Vishaghna (Antipoisonous), Lekhaniya (Aids in reducing corpulency), Krimighna (Antihelmentic), Kaphavatarakta doshahara (Balance Kapha Vata and Rakta humor)
3.	Daruharidra <sup>13</sup>	Tikta (Bitter), Kashaya (Astringent)	Laghu (Light), Ruksha	Ushna (Hot)	Katu	Kandughna (Antipruritic), Vishahara (Antipoisonous), Shophahara (Antiinflammatory),

			(Dry)			<i>Kaphapittahara</i> (Balance <i>Kapha Pitta</i> humor)
4.	<i>Manjishtha</i> <sup>14</sup>	<i>Tikta</i> (Bitter), <i>Kashaya</i> (Astringent), <i>Madhura</i> (Sweet)	<i>Guru</i> (Heavy), <i>Ruksha</i> (Dry)	<i>Ushna</i> (Hot)	<i>Katu</i>	<i>Shothahara</i> (Antioedematous), <i>Vranaropana</i> (Wound healing), <i>Kushthaghna</i> (Antileprotic), <i>Deepana</i> (Gastrostimulant), <i>Pachana</i> (Digestive), <i>Stambhana</i> (Antihemorrhagic), <i>Krimighna</i> (Antihelminthic), <i>Raktashodhaka</i> (Blood purifier), <i>Varnya</i> (Complexion promoter), <i>Rasayana</i> (Rejuvenant), <i>Kapha-Pittashamana</i> (Balance <i>Kapha Pitta</i> humor)
7.	<i>Nimba</i> <sup>15</sup>	<i>Tikta</i> (Bitter), <i>Kashaya</i> (Astringent),	<i>Laghu</i> (Light),	<i>Shita</i> (Cold)	<i>Katu</i> (Pungent)	<i>Kaphapittahara</i> (Balance <i>Kapha Pitta</i> humor), <i>Kandughna</i> (Antipruritic), <i>Kushtaghna</i> (Antileprotic), <i>Varanpachna</i> , <i>Vranshodhna</i> (wound purification), <i>Rochan</i> (appetiser), <i>Grahi</i> , <i>Dahprashman</i> (Relieving burning sensation), <i>Raktvikar shodhna</i> (Blood purifier), <i>Vednasthapna</i> (Analgesic), <i>Jwarghan</i> (antipyretic), <i>Krimighna</i> (Antihelminthic), <i>Vishahara</i> (Antipoisonous),

## DISCUSSION

Antitoxic medicines should have properties like *Deepana*, *Pachana*, *Srotoshodana*, *Raktashodhaka*, *Vishahara*, etc. This formulation has *Katu Tikta*, *Kashaya* and *Madhura rasa*, *Katu Vipaka*, *Ushna Virya*, and *Laghu Ruksha Teekshna Guna*. The properties of *Vishaghna*, *Shothaghna*, *Krimighna*, *Deepana*, *Pachana*, *Vranahara*, *Garanashaka*, and *Raktashodhaka* may have influenced the composition of the individual medications in *Shirishadi Yoga*. Therefore, *Shirishadi Yoga* is thus capable of taking action due to its *Vishaghna Guna*. Literature reveals that various ingredients of *Shirishadi Yoga* have antioxidants, immuno-modulatory, anti-inflammatory, anti-ulcerative & hepatoprotective actions.

*Shirishadi Yoga* may act by – 1. Prevent synthesis of prostaglandins, which may help as an anti-inflammatory. 2. It may suppress CYP450, which is essential in producing toxic metabolites (NAPQI). 3. Maybe by increasing the synthesis of Glutathione

(GSH). Thus, *Shirishadi Yoga's actions* may contribute towards its hepatoprotective activity.

## CONCLUSION

Overall, the discussion regarding the efficacy of *Shirishadi Yoga* in acetaminophen-induced liver damage can conclude that *Shirishadi Yoga* is effective in acetaminophen-induced hepatotoxicity. The potential for clinical trials should also be investigated since extensive research investigations employing experimental liver injury models may provide a clear justification for the therapeutic use of *Shirishadi Yoga* as a hepatoprotective medication in a laboratory context.

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