

## PIPPALI: A POTENT DRUG USED FOR HEPATIC DISORDER W.S.R YAKRITODARA - A REVIEW

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### ABSTRACT

Ayurveda is a widely practiced system of traditional medicine in India. The knowledge about medicinal plants in the early age was documented systematically and organized scientifically in Ayurvedic Samhitas which has been used for various disease conditions for a long time. Nowadays hepatobiliary disorder especially enlargement of the liver is a burning health problem found in society, it may be due to our modernize lifestyle. Significant and safe hepato-protective agents are unavailable in modern therapeutics. Therefore, due importance has been given globally to develop plant-based hepato-protective drugs effective against a variety of liver disorders. For this some plant based drugs have studied and it is found that Pippali is one of the potent herbal drugs, which can improve the regeneration process by restricting fibrosis and having hepatoprotective action. In Ayurveda, Pippali has been used for the treatment of *Gulma* (Abdominal tumor), *Udara sula* (Abdominal pain), *Arsha* (Piles), *Pandu* (Anemia), *Yakrutvikar* (hepatic disorder), *Pleehavridhi* (Spleen enlargement), *Krimiroga* (worm), *Hridourbalya* (heart disease), *Raktavikara* (Blood disorder), *Amavata* (Rheumatoid arthritis), *Vatarakta* (Gout), *Kasa* (Cough), *Swasa* (Asthma), *Hikka* (Hic cough), *Yakhma* (Tuberculosis), *Mootravikara* (Urinary track disorder), *Kushtha* (Skin disease), *Jeernajwara* (Chronic fever), *Vishamjwara* (Malaria). The present review article is aimed at compiling data based on reported works on promising hepatoprotective effect of Pippali in *Yakritadora*.

**Keywords:** Ayurveda, Pippali, Hepatobiliary disorder, *Yakrutbrudhhi*

### INTRODUCTION

Plants have formed the basis of sophisticated traditional medicine system and natural product make excellent lead to for a new drug development<sup>1</sup>. In worldwide, approximately 80% of world Inhabitants lean on traditional medicine for their primary health care and play an important role in the health care system of the remaining 20% of population<sup>2</sup>. The WHO is encouraging, promoting and facilitating the

effective use of herbal medicine for the developing countries health program<sup>3</sup>. The human race started using plants and plant products successfully as a source for treatment of disease and injuries as an effective therapeutic tool from the early days of civilization to modern age<sup>4,5</sup>. In Charaka Samhita, a reference is available regarding the enlargement of *Yakrita* (liver) in *Udara- Roga*. While explaining the

*nidana, lakshana* of *Plihodara* it has been mentioned that *the nidana, laxana, samprapthi and chikitsa of Yakritodora* are similar to that of *Plihodara*. Acharya Sushruta and Bhavaprakasa have also included this disease indirectly in eight types of *Udara Roga*. Bhavamisra has mentioned that it is situated right and below to the *hridaya* and is the *sthana* of *pitta and shonita*<sup>6</sup> Susruta mentioned *yakrit* as the place of *ranjaka pitta*<sup>7</sup> and *rakta*<sup>8</sup> while Charaka mentioned *Yakrit* and *Pleeha* as the *moola* of *raktavaha Srotas*<sup>9</sup> But Bhavamisra who for the first time introduced the term '*yakrit vikara*' in his text Bhavaprakash. Madhavakara, in *parishista prakarana*, explains *Yakrit roga* as a separate entity<sup>10</sup> in Madhava Nidana. Significant and safe hepatoprotective agents are unavailable in modern therapeutics. Therefore, due importance has been given globally to develop plant-based hepatoprotective drugs effective against a variety of liver disorders. The present review is aimed at compiling data based on reported works on promising hepatoprotective effect of Pippali in *Yakritadara*.

#### **NIDANA OF YAKRITHODARA:**

The cause of *Yakrutodara* has described as due to excess intake of *Vidahi* (the food substances which causes internal burning sensation like *Madya, Kulattha*, spices etc) and *Abhishyandhi ahara* (the food which causes obstruction to the *srotas* by secretion & which causes *Kaphaparakopa* like *dadhi, masha* etc in Ayurvedic classics.

**FATTY LIVER:** Fatty liver, also known as fatty liver disease is a condition of the liver wherein large vacuoles of triglyceride fat accumulate in liver cells via the process of steatosis (i.e., abnormal retention of lipids within a cell). The prevalence of fatty liver disease in the general population ranges from 10% - 24%. Obese patients (60- 90%) and up to 50% of type 2 diabetics have fatty liver. By considering the contribution of alcohol, fatty liver may be termed:

1. Alcoholic fatty liver disease (ALD/FALD) or Alcoholic steatosis

2. Non-alcoholic fatty liver disease (NAFLD)

#### **ETIOLOGY:**

1. Alcoholic Fatty liver disease: It depends on consumption and probability of developing alcoholism, and is going to conjointly have an effect on levels of liver enzymes concerned with the metabolism of alcohol. Other factors which influence include hepatitis, obesity & diet.
2. Non-Alcoholic fatty liver disease: The causes of non-alcoholic disease are not defined; the known risk factors of these problems are like Overweight, Insulin resistance syndrome, High sterol or triglyceride.

**SAMPRAPTHI OF YAKRITHODARA:** After intake of the substances which increases *Kapha* and *Pitta dosha* like *vidahi* and *abhishyandhi aahara* the *bhutaagni* gets *mandya* since the liver is the main seat of *Bhutaagni* impaired fatty acid metabolism takes place in the liver. *Kapha* gets accumulated in the *Pitta sthana* accumulation of fat occurs due to *avarana* causing *Yakrithvridhi, Agnimandhya, Balaksheena* etc symptoms thereby producing the disease *Yakrithodara*.

#### **SYMPTOMS AND SIGN OF YAKRITODARA**

(hepatomegaly): In addition to enlargement of the liver, the patient may have a mild fever, diminished digestive process, weakness, extreme anaemia. Bhavaprakas has described four types of *Yakrit vridhi* such as *Raktaja Yakrit vridhi, Pittaja Yakrit vridhi, Kaphaja Yakrit vridhi, Vataja Yakrit vridhi*. The patients of *Raktaja Yakrit vridhi* have the symptoms of tiredness, giddiness, burning sensation, discoloration, heaviness, unconsciousness. *Pittaja Yakrit vridhi* patients having the symptoms like fever, thirst, burning sensation, unconsciousness, and yellowishness. The patients of *Kaphaja Yakrit vridhi* having symptoms like thick, hard, and heaviness in the liver with enlargement, mild pain and loss of appetite. *Vataja Yakrit vridhi* patients show the symptoms like pain feeling around the liver area<sup>11</sup>. According to description Hepatobiliary disease includes a heterogeneous group of diseases of the

liver and biliary system caused by viral, bacterial, and parasitic infections, neoplasia, toxic chemicals, alcohol consumption, poor nutrition, metabolic disorders, and cardiac failure. One of the predominant diseases of the liver is cirrhosis. Cirrhosis of the liver is a chronic and usually relentlessly progressive disease characterized by loss of normal liver structure, fibrosis, impairment of the blood supply, and regeneration of disorganized liver lobules. These changes eventually result in liver failure. This disease has ranked among the 10 leading causes of death in the United States since 1950, and in middle-aged adults, it has ranked even higher in some years. In 1983, cirrhosis was the cause of 28,000 deaths, making it the ninth leading cause of death in the United States<sup>12</sup>

Cirrhosis may be caused by viral hepatitis, hemochromatosis, obstructive lesions of the biliary system, congestive heart failure, and chronic alcoholism. It is assumed that most cases of liver cirrhosis are due to alcohol consumption, and rates of prevalence, incidence, and mortality for liver cirrhosis are used as indicators of alcoholic cirrhosis. Early stages of alcoholic liver injury are reversible, but advanced stages are usually relentlessly progressive. The only known prevention for alcoholic cirrhosis is to limit consumption of alcohol. For many years cirrhosis among alcoholics was attributed to nutritional deficiencies associated with alcoholism and not to the direct effects of alcohol on the liver<sup>13</sup>.

**PIPPALI:** Plants have been the source of medicines for thousands of years. Species of the genus *Piper* are among the important medicinal plants used in various systems of medicine<sup>14,15</sup>. *Piper longum* L. (Piperaceae), commonly known as "long pepper", is widely distributed in the tropical and subtropical regions of the world, throughout the Indian subcontinent, Sri Lanka, Middle Eastern countries and the Americas. It is said that the Roman emperors valued it even more highly than black pepper due to its high commercial and economic importance. Vernacular names: English: Long pepper, Hindi: Pippali, Sanskrit: Pipali Habitat: The native of the plant is con-

sidered to be South Asia and is found both wild as well as cultivated, throughout the hotter parts of India from central to the north-eastern Himalayas. The herb also grows wild in Malaysia, Singapore, Bhutan, Myanmar and elsewhere.

#### **BOTANICAL DESCRIPTION:**

It is having slender, aromatic, perennial climber, with woody roots and numerous wide-ovate, cordate leaves. The inflorescence is a cylindrical, pedunculate spike, the female flower is up to 2.5 cm long and 4-5 mm in diameter but the male flower is larger and slender. The fruits are small, ovoid berries, shiny blackish green, embedded in fleshy spikes<sup>16</sup>

#### **DISTRIBUTION:**

It occurs in the hotter part of India from the central Himalayas to Assam, Khasi and Mikir hills, lower hills of Bengal and evergreen forest of Western Ghats from Konkan to Travancore<sup>17</sup>.

#### **AYURVEDIC PROPERTIES:**

*Rasa: Katu,*

*Guna: Laghu, snigdha, tikshna*

*Veerya: Anushnashita*

*Vipaka: Madhur*

*Dosha: Kapha and Vata shamaka*<sup>18</sup>

**ROGAGHNATA :** Pippali having therapeutic action like *Gulma* (Abdominal tumor), *Udara sula* (Abdominal pain), *Arsha* (Piles), *Pandu* (Anemia), *Yakrutvikar* (hepatic disorder), *Pleehavidhi* (Spleen enlargement), *Krimiroga* (worm), *Hridourbalya* (heart disease), *Raktavikara* (Blood disorder), *Amavata* (Rheumatoid arthritis), *Vatarakta* (Gout), *Kasa* (Cough), *Swasa* (Asthma), *Hikka* (Hic cough), *Yakhma* (Tuberculosis), *Mootravikara* (Urinary track disorder), *Kushtha* (Skin disease), *Jeernajwara* (Chronic fever), *Vishamjwara* (Malaria).

#### **HEPATOPROTECTIVE ACTIVITY:**

The fruit extract improved the regeneration process by restricting fibrosis, but offered no protection against acute damage or against cirrhotic changes in

rodents. Treatment with the ethanol extract of *P. longum* inhibits liver fibrosis induced by carbon tetrachloride (CCl<sub>4</sub>)<sup>19,20</sup>. Piperine exerted a significant protection against tert-butyl hydroperoxide and carbon tetrachloride hepatotoxicity by reducing both in vitro and in vivo lipid peroxidation, enzymatic leakage of GPT and AP, and by preventing the depletion of GSH and total thiols in the intoxicated mice. Piperine showed lower hepato-protective potency than silymarin<sup>21</sup>. It has been reported to possess antiasthmatic, anti-inflammatory, hepatoprotective, hypocholesterolemic and immunomodulatory activities. It contains various alkaloids like piperine, piperlongumine, piperlonguminine, etc. which helps in the regeneration of hepatocytes.<sup>22</sup> A study showed a significant hepatoprotective effect on *Piper longum* Linn. Milk extract treatment in CCl<sub>4</sub> induced hepatic damage. An evident decrease in the level of serum enzymes, total bilirubin, and direct bilirubin was observed. Histo-pathological findings indicated that administration of *Piper longum* Linn. Milk extract offered protection to the hepatocytes from damage induced by CCl<sub>4</sub>, with mild fatty changes in the hepatic parenchymal cells, which cor-

roborated the changes observed in the hepatic enzymes<sup>23</sup>

#### BIOAVAILABILITY ENHANCEMENT:

Piperine was found to enhance the bioavailability of structurally and therapeutically diverse drugs, possibly by modulating membrane dynamics due to its easy partitioning and increase in permeability of other drugs such as vasicine, indomethacin, diclofenac sodium etc.<sup>24,25</sup>. It was suggested that piperine might be inducing alterations in membrane dynamics and permeation characteristics, along with induction in the synthesis of proteins associated with the cytoskeletal function, resulting in an increase in the small intestine absorptive surface, thus assisting efficient permeation through the epithelial barrier<sup>26,27</sup>. The study showed that piperine enhances the serum concentration, extent of absorption and bioavailability of curcumin in both rats and humans with no adverse effects<sup>28</sup>.

#### FORMULATIONS:

Some important formulations which contain Pippali as ingredient or anupana used for the treatment of hepatic disordered such as

Sl.No	Dosage Form	Formulation	Reference	Dose
1.	<i>Churna</i>	Pippali Churna	Bhaisajya Ratnabali <sup>29</sup>	Not Mention
2.	<i>Churna</i>	Sudarsanachurna	AFI Part-I <sup>30</sup>	2-4 gm
3.	<i>Vati</i>	Manakadi Gutika	Bhaisajya Ratnabali <sup>29</sup>	Not Mention
4.	<i>Avaleha</i>	Guda Pippali	Bhaisajya Ratnabali <sup>29</sup>	5 gm
5.	<i>Rasousadhi</i>	Vidyadhara rasa	Bhaisajya Ratnabali <sup>29</sup>	60 mg
6.	<i>Rasousadhi</i>	Plihasardularasa	Bhaisajya Ratnabali <sup>29</sup>	125 mg
7.	<i>Rasousadhi</i>	Louhamrutunjayarasa	Bhaisajya Ratnabali <sup>29</sup>	250 mg
8.	<i>Louha</i>	Yakruta Plihari Louha	Bhaisajya Ratnabali <sup>29</sup>	250 mg
9.	<i>Louha</i>	Sarbeswar Louha	Bhaisajya Ratnabali <sup>29</sup>	250 mg
10.	<i>Ghruta</i>	Pippali Ghruta	Bhaisajya Ratnabali <sup>29</sup>	Not Mention
11.	<i>Ghruta</i>	ChitrakaPippali Ghruta	Bhaisajya Ratnabali <sup>29</sup>	Not Mention
12.	<i>Rasousadhi</i>	Jwararyabhra rasa	AFI Part-I <sup>30</sup>	125-250 mg
13.	<i>Louha</i>	Putapaka Visamajwarantaka Louha	AFI Part-I <sup>30</sup>	250 mg
14.	<i>Louha</i>	Yakrudari Louha	AFI Part-I <sup>30</sup>	250 mg
15.	<i>Louha</i>	Rohitaka Louha	AFI Part-I <sup>30</sup>	250 mg
16.	<i>Louha</i>	Sarvajwarahara Louha	AFI Part-I <sup>30</sup>	250mg

## CONCLUSION

Hepatobiliary disorder especially enlargement of the liver is a burning health problem found in society. One of the Significant and safe hepato-protective plant is Pippali. It has got a variety of pharmacologically and medicinally significant constituents, which are being utilized in the field of Ayurveda for different diseases. It is also used as a bioavailability enhancer and has been used in Hepatic disorders due to its hepatoprotective action in various formulations. It contains various alkaloids like piperine, piperlongumine, piperlonguminine, etc. which helps in the regeneration of hepatocytes. Histopathological findings indicated that administration of Piper longum Linn. Milk extract offered protection to the hepatocytes from damage induced by CCl<sub>4</sub>, with mild fatty changes in the hepatic parenchymal cells, which corroborated the changes observed in the hepatic enzymes. So, Pippali is one of the best drugs for the treatment of Hepatic disorders. The above review provides information of its uses in Hepatic disorders, which may be helpful for further study and to develop plant-based hepato-protective drugs effective against a variety of liver disorders.

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