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SINGLE AND COMPOUND FORMULATIONS IN THE MANAGEMENT OF KAMALA (JAUNDICE) OF MEDIEVAL COMPENDIA: A REVIEW

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ABSTRACT:

Medieval period is known as Madhya Kala (8th to 15th century) of Ayurveda. This period is also known as Sangraha Kala. In this period a number of commentaries on Brihat Trayi and Laghu Trayi were written. The commentators also expressed their own concepts while writing their treaties. Some important compendia on Ayurveda like Siddhayoga Vrindamadhava, Chakradatta, Vangasena, Gadnigraha, Sharangdharasamhita, Rasaratnasammuchaya, etc. were compiled. In the present review, some of the compendia of this era were reviewed with special reference to Kamala. Review is also extended to recent researches on hepatoprotective activity of mentioned drugs. Most of the compendia explained Kamala in Pandu Adhayaya. Single drugs like Amalaki, Guduchi, Nimba, Triphala, Daruharidra, etc. were quoted for the treatment of Kamala. Many of the herbo-mineral preparations like Yogarajrasayana, Manduravatakam, Arogyavardhini etc. are also described in this period. Recent researches have validated the single drug claims and certain classical formulations indicated for their hepato-protective activity.

KEY WORDS: Hepatoprotective activity, Jaundice, Kamala, medieval

INTRODUCTION

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Ayurveda has golden period during the Ancient era, the science was developed in incredible form. The medieval period marks the invasion of Muslims into India. By this time, the traditional indigenous classical learning had already received a setback.[1]

Acharya P.V. Sharma described the Medieval period as *Madhya Kala* from 8th – 15th century. The Ayurveda system of medicine did not progress as vigorously as it did in the ancient period because of lack of royal patronage. However, some important compendia on Ayurveda like Siddhayoga by Vrinda Madhava (9th century), Chakradatta by Chakrapanidutta (11th century), Chikitsasarasamgraha by Vangasena (12th century), Gadanigraha by Shodhala (12th century), Sharangdharasamhita by Sharangdhara (13th century), Rasaratnasammuchaya by Rasavagbhata (13th century), etc. were compiled. The Unani system of medicine flourished in India during the medieval period. The Unani medicine system came to India along with the Muslims by about the eleventh century and soon found patronage for its growth.

Liver disorders are considered as the one of the prevalent cause for human suffering and death. In Ayurvedic classics, the etiology and pathology of hepatic disorders are well defined. *Yakrita* (liver) is the main seat of the vital *Ranjaka Pitta* and *Rakta Dhatu*. Discrepancy in liver function may cause number of diseases. Diseases like *Pandu* (anaemia), *Raktapitta* (haemorrhagic disorders), *Kamala* (jaundice), *Yakritadalyudara* (hepatomegaly or cirrhosis of liver), *Halimaka* (fulminant hepatic failure), *Kumabha Kamala* (chronic hepatic failure), *Panaki* (hepatorenal syndrome), *Mukha-mandika Grahaja Vyadhi* (Childhood cirrhosis) and *Shotha* (Oedema/ anasarca due to liver failure) comes under liver disorder. The symptoms include increased bile, serum bilirubin, poor liver function, etc.

MATERIALS AND METHOD

The disease *Kamala* and formulations suggested are reviewed from Ayurvedic texts of medieval period namely Siddhayoga of Vrindamadhava,[2] Chikisasara Samgraha of Vangasena,[3]

Chakradatta,[4] Gadanigraha of Shodhala,[5] one of the *Laghutrayi* Sharangdhara Samhita[6] and Rasaratnasammuchaya by Rasavagbhata.[7] Also recent monographs, published scientific articles and internet sources, were utilized to compile current scientific evidences.

Perceptive of *Kamala* from medieval era

Description of *Kamala* (jaundice) included in *Pandu* (anaemia) chapter by all the treaties of medieval era same as ancient period.

Pathology of *Kamala*

Pathology as described by Acharya Charaka was followed. *Kamala* develops after *Pandu* with overindulgence in foods and habits which vitiates *Pitta* and vitiated *Pitta* burns up the *Rakta* and *Mamsa* (muscle tissue) and produces disease *Kamala*. It also manifests without *Pandu*.

Types of *Kamala*

There are two basic types of *Kamala*- *Koshthashrita* (haemolytic jaundice) and *Shakhashrita Kamala* (obstructive jaundice). Other complicated types of jaundice include *Kumbhakamala*, which is chronic stage of *Koshthashakhashrita Kamala* and *Halimaka* representing chronic stage of *Shakhashrita Kamala*. These two types of *Kamala* described in majority text of medieval era in short. No detail of pathology regarding *Shakhashrita Kamala* and *Koshthashrita Kamala* are explained. Vangasena and Chakradatta only narrate these varieties.

a. *Koshthashrita Kamala* is associated with accelerated destruction of red blood cells and decreased hemoglobin and promotes *Mala Rupa Ranjaka Pitta* due to faulty diet and life style that increases *Pitta* leading to enhanced bilirubin formation.
b. The *Shakhashrita Kamala* is attributed to the obstruction in the biliary flow due to *Kapha Dosha* obstructing the channels of biliary system, the stool will be clay coloured (*Tilapishtanibham*) in such condition.

Main features of *Kamala* explained in text of medieval era are deep yellow discolouration of eyes, skin, nails and faeces, reddish yellow urine, weakness of sense organ, burning sensation indigestion, weakness, debility, anorexia etc.

Management of *Kamala*

Majorities of scientist of medieval era emphasised on Panchakarma i.e. *Shodhana* (purification) in *Kamala* and almost all Acharyas described *Virechana* (medicated controlled purgation) followed by *Pitta* pacifying measures.

Conservative treatment of *Kamala*:

A. Single herbs

Guduchi (*Tinispora cordifolia* (Wild.) Miers.), *Nimb* (*Azadirachta indicia*. Juss.), and *Daruharidra* (*Berberis aristata* DC.) are described in all texts. *Vasa* (*Adhatoda vasica* Nees.) and *Alambusha* (*Mundi* - *Spharanthus indicus* L.) are only

mentioned by Sharangdhara. Most of the compendia quoted *Madhu* (honey) and *Gomutra* (cow urine) as *Anupana* (adjuvant) for single and simple drug recipes [Table 1].

Table 1: Single drugs mentioned in various texts of medieval era

Name of drugs	Siddhayoga	Vangasena	Chakradutta	Gadanigraha	Sharangadhara
Guduchi	√ (*Madhu*)	√ (*Madhu*)	√ (*Madhu*)	√	√
Triphala	√ (*Madhu*)	√ (*Madhu*)	√ (*Madhu*)	√	√ (*Madhu*)
Daruharida	√ (*Madhu*)	√ (*Madhu*)	√ (*Madhu*)	√	√
Nimba	√ (*Madhu*)	√ (*Madhu*)	√ (*Madhu*)	√	√
Vasa					√ (*Madhu*)
Alambusha					√
Shilajatu	√			√ (*Gomutra*)	
Suvarna Makshika				√ (*Gomutra*)	
Roupya Makshika				√ (*Gomutra*)	

B. Single minerals:

Use of *Shilajatu* in *Kamala* is denoted by Gadanigraha and Siddhayoga. Along with *Shilajatu* Gadnighraha also denoted use of *Raupya* and *Suvarn Makshika* in *Kamala* with *Gomutra* [Table 1]. These single herb or mineral practices are very popular among traditional/ folklore practitioners for *Kamala*.

Table 2: *Choorna* (powder) formulations

Name of *Choorna*	Siddhayoga	Vangasena	Chakradutta	Gadanigraha	Sharangadhara
Navayas	√	√			
Darvyadhya				√	
Dhatri Lauha		√	√		
Vidangadi Lauha		√	√		
Ayorajadi			√		
Punarnava Mandura	√		√		
Vyoshadi	√				
Lauhadi	√				
Eladi	√				
Hapushadi					√

Navayas, Darvyadhya, Dhatri Lauha, Vidangadi Lauha, Ayorajadi Choorna, etc. are the herbomineral *Choorna* formulations described in this period for the management of *Kamala* [Table 2].

Table 3: *Kwatha* (decoction) formulations

Name of *Kwatha*	Siddhayoga	Vangasena	Chakradutta	Gadanigraha	Sharangadhara
Phalatrikadi	√	√	√		√
Darvi-Tiktadi		√		√	
Punarnavadi		√			
Darvyadi			√		

Total four decoctions are mentioned for *Kamala*. Out of them *Phalatrikadi* is mostly quoted by referred texts. *Darvi-Tiktakadi* is mentioned in Vangasena and Gadanigraha [Table 3].

C. *Vati/Guti/Modaka* (tablets):

Table 4: *Vati/Guti/Modaka* (tablets) formulations mentioned in various treaties of medieval era

Name of *Vati/Guti/Modaka*	Siddhayoga	Vangasena	Chakradutta	Sharangadhara
Ashtadashanga Gulika		√		
Nimbadi Gulika		√		
Bibhitakyadi Gulika		√		
Mandura Gulika		√		
Mandura Vataka	√	√		√
Brihata Mandura Vataka		√		
Mandura Vajra Vataka	√	√	√	
Madebhasingh Rasa				
Trailokyanath Rasa				
Shri Bahushala Guda				√
Chandraprabha Guggulu				√

Vangasena is the one who mentioned majority of *Vati* formulations in the management of *Kamala*. These include *Ashtadashanga Gulika*, *Mandura Vataka*, *Brihata Mandur Vataka*, *Nimbadi Gulika*, *Mandur Gulika*, *Bibhitakyadi Gulika*, *Mandur Vajra Vataka* [Table 4].

Table 5: *Ghrita* (medicated ghee) formulations

Name of *Ghrita*	Siddhayoga	Vangasena	Chakradutta	Gadanigraha	Sharangadhara
Haridradi	√	√	√	√	
Guduchi		√		√	
Amrutadi					
Kalyanaka			√		
Panchagavya			√		
Mahatiktaka			√		
Draksha			√		
Murvadi	√		√		
Vyoshadi	√				
Kamdeva					√

This dosage form mostly advocated for *Abhyantara Snehapana* (internal oleation) before *Shodhana*. *Haridradi Ghrita* is mentioned in all treaties, except Sharangadhara. Chakradutta advised maximum 6 *Ghrita* formulations. *Kamdeva Ghrita* is the only formulation advised by Sharangadhara [Table 5].

Table 6: *Avaleha* (elinctures) formulations

Name of *Avaleha*	Siddhayoga	Vangasena	Chakradutta	Gadanigraha	Sharangadhara
Sitadhyavaleha		√			
Amalakyavaleha		√			
Khadiravaleha		√			
Kalyanaka Guda		√			
Dhatryadhyavaleha	√			√	
Triphaladhyavaleha				√	
Yogaraj Rasayana			√		
Ayorajadi Yoga	√				
Kutajavaleha					√

Amalakyavaleha, *Dhatryadhyavaleha*, *Bibhitakaavaleha*, *Triphaladhyavaleha*, *Sitadhyavaleha*, *Khadiraavaleha*, *Kalyanaka Guda*, *Yogaraj Rasayana*, *Ayorajadi Yoga*, and *Kutajavaleha* are the *Avalehas* mentioned by different treaties of medieval era [Table 6].

D. *Arishta*:

Very few *Arishta* formulations were described in *Kamala*. *Dhatryarishta* is described in Chakradutta while *Dashamoolarishta* by Sharangadhara.

Specification in treatment:

a. *Anjana* (collyrium): In majority of text, application of *Dronpushpi Swarasa* (fresh juice of *Leucas cephalotes* (Roxb.) Spreng,) as *Anjana* in *Kamala* and powders of *Haridra* (*C. longa*), *Swarna Gairika* (red ochre) and *Amalaki* (*E. officinalae*) are described to reduce the symptoms of *Kamala*.

b. *Nasya* (nasal insufflations): *Karkotaka Moola* (root of) and *Devadali Phala* (fruit of *Luffa echinata* Roxb.) are suggested for *Nasya* in *Kamala*. Many old Vaidyas from Southern part of Maharashtra practicing this even today.

Inhalation of *Kumari Swarasa* (leaf juice *Aloe barbadensis* Miller.) or *Arkamoola* (roots of *Calotropis procera* (Aiton) W.T.) or *Jeemutaka Phala* (*L. echinata*) is advised by Sharngadhara in *Kamala*.

Formulations quoted in Rasaratnasamucchaya

Rasaratnasamucchaya one of the most popular text of Rasashastra, provides number of herbomineral or mineral formulations for the management of various diseases. In the management of *Kamala* - *Hansa Mandura, Panchanana Rasa, Kamalapranuda Rasa, Sindurbhushana Rasa, Sudhapanchaka Rasa, Kanakasundara Rasa, Jivananama Rasa, Mehari Rasa, Sarvangasundara Rasa, Taleshwara Rasa, Mahataleshwara Rasa, Arogyavardhini, Madansanjivani Rasa, Khandakhadhyadhya Lauha Kalpa, Lauha Kalpa, Parada Bhasma* with disease oriented *Anupana* were mentioned.

Rasaratnasamuchhaya quoted one herbal recipe – *Baladi Kwatha* for the management of *Garbhini Kamala*.

RESEARCH PERSPECTIVE

Most of the researches had been carried out on single drugs and very few researches on compound formulations for evaluation of hepato-protective activity.

A. Single herbs:

1. ***Apamarga* (*A. aspera*):** Ethanolic extract from the leaves of *A. aspera* at a dose level of 200 mg/kg, 400mg/ kg body weight in albino rats was administered orally once for 3 days. Substantially elevated serum marker enzymes such as SGOT, SGPT, ALP, due to paracetamol treatment were restored towards normal. Biochemical parameters like total protein, total bilirubin, total cholesterol, triglycerides, and urea were also restored towards normal levels. In addition, test drug extract significantly decreased the liver weight of paracetamol intoxicated rats. The results strongly indicate that extract of *A. aspera* has got a potent hepatoprotective action against paracetamol induced hepatic damage in rats.[8]

2. ***Arka* (*C. procera*):**

Pre treatment with ethanolic extract of *C. procera* flower (CPA) in CCl_4 induced hepatic injury albino rats and mice, reduced biochemical marker of liver. Histopathological observations also revealed that CPA protected the animals from liver damage. *C. procera* possess hepatoprotective property possibly because of its anti-oxidant activity.[9] Daily oral administration of aqueous suspension of dried latex of *C. procera* produced a dose-dependent reduction in the serum levels of liver enzymes and inflammatory mediators and attenuated the necro-inflammatory changes in the liver.[10]

3. ***Guduchi* (*T. cordifola*):**

Ethanolic extract of *T. Cordifola* stem exhibits hepatoprotective activity against CCl_4 induced hepatotoxicity in rats.[11] A clinical trial conducted on total 30 patients of obstructive jaundice with impairment of hepatic function and immune-suppression divided in to two groups. Hepatic function remained comparable in two groups after surgical procedure of drainage. *T. cordifolia* appeared to improve surgical outcome by strengthening host defence.[12]

4. ***Haridra* (*C. longa*):**

Hepatoprotective effect of turmeric was being exhibited against CCl_4 induced liver damage by reducing the elevation of serum enzymes level.[13] Curcumin and turmeric having hepatoprotective potentialities against other hepatotoxins include alfatoxin B1, paracetamol, iron and

cyclophosphamde.[14] Water extract of the fresh rhizome has been shown potency to inhibit alkaline phosphatise in alfatoxin B1 hepatotoxicity.[15] Methanolic extract of the dried rhizome is active versus alpha alpha-naphthylisothiocyanate induce hepatotoxicity in rats.[16]

5. ***Pippali* (*P. longum*):** The ethanolic extract and butanol fraction of *P. longum* showed significant hepatoprotective activity by lowering serum enzymes – SGOT, SGPT in rats treated with CCl_4 when compared to control and Liv 52 treated rats.[17] In another experimental study on rat, ethanolic extract of *P. longum* exhibited hepatoprotective effect against CCl_4 induced hepatotoxicity.[18]
6. ***Kutaki* (*P. kurroa*):** In D-galactosamine-induced hepatitis in rats, a significant increase of lipid peroxidation and a decrease in liver antioxidant enzymes levels are observed. Pre-treatment with the ethanol extract of *P. kurroa* prevented these alterations.[19] Oral pre-treatment with alcoholic extract of *Picrorrhiza kurroa* rhizomes and roots significantly prevented the D-galactosamine-induced alterations in respiration and oxidative phosphorylation of liver mitochondria.[20] *Kutaki* root powder showed biological plausibility of efficacy, as supported by clinical trial in viral hepatitis, hepatoprotection in animal model and an approach for standardizing extracts based on picroside content.[21]
7. ***Daruharidra* (*B. aristata*):** A combination of *Ghanasatva* (aqueous extract) of *Daruharidra* and leaf juice of *Punarnava* exhibited improvement in patients suffering from hepatocellular jaundice after three months of treatment.[22] Pre treatment of animals with berberine prevented the acetaminophen- or CCl_4-induced rise in serum levels of ALP, AST and ALT, suggestive of hepatoprotection. Post-treatment with three successive oral doses of berberine reduced the hepatic damage induced by acetaminophen, while CCl_4-induced hepatotoxicity was not modified, suggesting a selective curative effect against acetaminophen.[23] An alkaloid isolated from the plant *B. aristata* - Berberine was administered simultaneously with N-nitrosodiethylamine (NEDA), the markers of liver injury were reduced significantly. A similar decrease was noted in the serum levels of lipid peroxide, bilirubin and SGPT. Morphology of liver tissue and levels of marker enzymes indicated that berberine offered protection against chemical carcinogenesis.[24]

8. ***Devadali* (*L. echinata*):** The petroleum ether, acetone and methanolic extracts of *L. echinata* showed a significant hepatoprotective activity comparable with those of Silymarin.[25] Research studies have confirmed the *Kamalahara* activity with *Devadali Swarasa.* In a study on the therapeutic effect of *L. Echinata* fruits in 6 patients of viral hepatitis, results reveals that a single administration of drops squeezed form water soaked dry fruits into the nostrils led to a reduction in bilirubin and SGPT levels significantly within 3 to 7 days and this response was accompanied by substantial relief in clinical symptoms especially anorexia and malaise. The nasal secretions contained total bilirubin ranging from 1.62 to 5.5 mg percent, the levels not being higher than the serum levels. The observations thus could justify the simple explanation of the relief of jaundice by enhanced nasal excretion of bilirubin. The possibility of the absorption of the active principle of the plant through the nasal mucosa and then action on the liver has been proposed.[26]
9. ***Kumari* (*A. barbadensis*):** Aqueous extract of *A. barbadensis* showed significant hepatoprotective activity against CCl_4 induced hepatotoxicity. It is significantly capable of restoring integrity of hepatocytes indicated by improvement in physiological parameters, excretory capacity of hepatocytes and also by stimulation of bile flow secretion.[27]
10. ***Nimba* (*A. indica*):** Fresh juice of tender leaves of *A. indica* (200 mg/kg body wt. p.o.) inhibited paracetamol (2 g/kg body wt. p.o.)-induced lipid peroxidation and prevented depletion of sulfhydryl groups in liver cells. It also decreased serum marker enzymes of hepatic damage (aspartate transaminase, alanine transaminase and alkaline phosphatase). *A. indica* pre-treatment stabilized the serum levels of these enzymes. Histopathological observations of liver tissues corroborated these findings. [28]
11. ***Vasa* (*A. vasica*):** *A. vasica* aqueous leaf extract showed significant hepatoprotective effect at doses of 50t at doses op.o., on liver damage induced by d-galactosamine in rats.[29] Pre treatment with Vasicinone isolated form leaves of *Vasa* may act as hepatoprotective in CCl_4 induced acute hepatotoxicity in mice.[30]

B. Formulations:

1. ***Amalkadi Ghrita* (AG):** Administration of AG to rats markedly prevented CCl4-induced elevation of levels of serum GPT, GOT, ACP, ALP, and bilirubin. The decreased level of total proteins due to hepatic

damage induced by CC_{l4} was found to be increased in AG-treated group. The results are comparable to that of silymarin. A comparative histopathological study of liver exhibited almost normal architecture. Hepatoprotective effect of AG is probably due to combined action of all ingredients.[31]

2. ***Navayas Choorna* (NYC):** Traditional herbal formulation was evaluated for hepatoprotective activity against CCl_4 intoxication in albino rats. Pre-treatment with NYC reduced significantly the enzyme levels of SGOT, SGPT and ALP. The results were comparable with standard drug (Liv 52).[32]
3. ***Arogyavardhini*:** In a clinical study, *Arogyavadhini* reported to be beneficial in the management of acute viral hepatitis.[33]
4. ***Panchatiktaka Ghrita*:** In a clinical study, *Panchatiktaka Ghrita* lowered elevated levels of liver enzymes significantly without producing any adverse effect; study concluded that, it can be used as a hepatoprotective drug in patients of hepatitis.[34]
5. ***Phalatrikadi Kwatha*:** *Phalatrikadi* significantly improved clinical manifestations in the patients of acute viral hepatitis. Also reduced level of marker enzymes of hepatotoxicity. Decoction is effective in checking the progress of the viral hepatitis.[35]
6. ***Punarnava Mandura*:** A combination therapy of *Punarnava Mandura* with *Arogyavardhini Vati* would be helpful to arrest the multiplication of viruses and regeneration of hepatocytes.[36]
7. ***Panchagavya Ghrita*:** Treatment with *Panchagavya Ghrita* significantly reduced the CCl4 induced hepatotoxicity in rats. A comparative histological study of liver from different groups further confirmed the hepatoprotective activity of *Panchagavya Ghrita*.[37]

A critical review of most of the popular compendia indicated the drugs namely *Guduchi*, *Haridra*, *Nimba*, *Triphala*, *Daruharidra*, *Vasa*, *Katuki* and *Pippali* are frequently denoted which reflects their popularity. Recent research studies significantly validated the hepatoprotective activities of these drugs. Among herbo-mineral formulations more data was documented on the role of *Arogyavardhini* in the management of viral hepatitis. *Arogyavardhini* which has become very popular as hepatoprotective recipe was originally formulated and mentioned in the treatment of *Kushtha.*

Medieval era of Ayurveda is also known as *Sangraha Kala*. In this period a number of commentaries on *Brihat Trayi* and *Laghu Trayi* were written. The commentators also expressed their own

concepts while writing treaties. In the same period *Nighantus* were also composed. Vrindamadhava exploits Charakasamhita, Susrutasamhita and Vagbhata to compile Siddhayoga Sangraha. Chakradutta was written in 11th century on the basis of Siddhayoga. Chakradutta quoted more number of *Yogas* (formulations) in comparison to Siddhayoga. Vangasena's Chikitsasara Sangraha or Vangasenasamhita is found similar to Siddhayoga Sangraha and Chakradutta.[38]

Compendia of this period documented easy to adopt simple recipes for the management of diseases.

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