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Clinical study to evaluate the effectiveness of *Gavakshi Moola* (*Citrullus colocynthis*) *Draava* with *Ksheera* in *Kamala* (hepatocellular jaundice)

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ABSTRACT

Hepatocellular jaundice is a sign that usually accompanies diseases of liver, the organ that detoxifies metabolites, synthesizes proteins, produces biochemicals necessary for digestion, decomposes red blood cells and produces hormones,[1] hence is constantly under the risk of various diseases. Causes of hepatocellular jaundice are numerous with the most common being viral hepatitis, alcohol and drug toxicity. Kamala described among the *Pittaja Nanatmaja Vyadhi* has *Haridra Varna* of *Netra, Twak, Nakha, Anana, Mutra* as the cardinal sign, hence analogous to jaundice. The administration of *Gavakshimoola Draava* for 3 days is described in the management of *Kamala*. A clinical trial was conducted on 15 subjects and the results obtained were statistically analysed. Statistically significant reduction of *Lakshana* of *Kamala* and serum levels of bilirubin with p-value < 0.05 was noted.

Key words: *Gavakshi Moola Draava, Hepatocellular Jaundice, Kamala.*

INTRODUCTION

Jaundice, synonymously known as icterus, is a yellowish or greenish discoloration of tissues corresponding to high bilirubin levels. Clinically jaundice can be classified based on the underlying cause as hepatocellular, obstructive, hemolytic and based on its onset and manifestation as acute or chronic.[2]

Hepatocellular jaundice is characterized by disproportionate rise in the enzymes Aminotransferases in comparison to Alkaline phosphatase, accompanied by raised serum bilirubin levels. It is constituted by yellowish discoloration of tissues, pruritus, bleeding tendencies, anorexia, fatigue, abdominal pain, weight loss or gain, change in mental status.[3] Treatment aims at combating the underlying cause.

Kamala is a *Pitta Pradhana Vyadhi*. It is classified as *Koshtashrita* and *Shakhashrita*. It can manifest as *Swatantra* as well as *Paratantra Vyadhi. Swatantra* due to the causative factors directly vitiating *Pitta Dosha* and *Paratantra* as a consequence of *Pandu Roga.* The *Lakshana* of *Koshtashrita Kamala* are *Haridra Netra, Twak, Nakha, Anana, Peetata* of *Mutra, Shakrut, Indriya Shakti Nasha, Daha, Avipaka, Sadana.* The *Chikitsa Siddhanta* is *Samshodhana* with *Tikta, Mrudu Rechaka Dravya* followed by *Pathya Ahara.*

Draava prepared out of roots of *Gavakshi* is indicated in the management of *Kamala* and is to be administered with *Ksheera*.[4] It comprises of *Tikta Rasa, Katu Vipaka, Laghu Ruksha Guna, Ushna Veerya,* has *Pitta-Kapha Shamaka, Rechaka* activities. *Goksheera* comprises *Madhura Rasa, Sheeta Virya,*

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Mrudu Guna, Pitta-Vata Shamaka Karma. Taking into consideration the combined *Pitta Shamaka, Rechaka* action of *Gavakshi* with *Ksheera* and the *Pradhana Dosha (Pitta)* in *Koshtashrita Kamala* the aforesaid intervention was evaluated.

OBJECTIVE

To assess the effectiveness of *Gavakshi Moola Draava* with *Ksheera* in *Kamala* (hepatocellular jaundice).

MATERIALS AND METHODS

Source of data

Subjects of *Kamala* from out-patient and in-patient Department of Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Hassan.

Diagnostic criteria

a) On the basis of lakshanas of *Kamala*

1. Peeta Netra
2. Peeta mutra
3. Avipaka
4. Aruchi

b) Elevated Liver Function Tests

Inclusion criteria

- Subjects of either gender, between the age of 18 to 60 years .
- Subjects who were ready to sign the informed consent form.
- Child-Turcotte-Pugh Score of 5-10
- Hepatocellular jaundice due to viral hepatitis, alcoholic liver disease

Exclusion criteria

- Subjects with uncontrolled Diabetes mellitus, Malignant Hypertension
- Serum Bilirubin levels above 10 mg/dL
- Known cases of hepatic cancer, liver metastasis, Ca pancreas.
- Pregnant or lactating women

Laboratory investigation

- Liver function test
- Prothrombin Time

Plan of treatment

a) Freshly prepared *Draava* of roots of *Gavakshi* in the dose of ½ *Karsha* (6 ml) was administered in empty stomach (morning) with 3 *Pala Ksheera* for 3 days.

b) *Pathya Ahara* was advised during the treatment.

Post treatment assessment - On the 4th day

Assessment criteria

Subjective parameters

- *Netra peetata*
- *Twak peetata*
- *Nakha peetata*
- *Anana peetata*
- *Peeta mootrata*
- *Daurbalya*
- *Avipaka*
- *Aruchi*
- *Angasada / Gaurava*
- Abdominal pain
- Fever
- Chills and rigor
- Pruritus

Objectives parameters

- Serum bilirubin
- Transaminases
- Alkaline phosphatase

OBSERVATIONS AND RESULTS

A total of 15 subjects of *Kamala* were registered for the study; of which 2 dropped out and 13 completed the trial. Statistical analysis was done using SPSS Ver.20 with Wilcoxon signed rank test on ordinal data,

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Mc Nemar test on nominal data and paired t test on numerical data.

Table 1: Result of Wilcoxon signed rank test showing the effect of intervention on *Lakshana* of *Kamala.*

Variable	Negative ranks			Positive ranks			Ties	Total	Z value	P value	Remarks
	N	MR	SR	N	MR	SR					
Angasada / *Gaurava* at-bt	10	5.50	55	0	0.00	0.00	3	13	-2.87	0.004	S
Aruchi at – bt	13	7	91	0	0.00	0.00	0	13	-3.20	0.001	S
Avipaka at – bt	13	7	91	0	0.00	0.00	0	13	-3.21	0.001	S
Daurbalya at – bt	9	5	45	0	0.00	0.00	4	13	-2.71	0.007	S
Mootra (urine color chart) at – bt	13	7	91	0	0.00	0.00	0	13	-3.19	0.001	S
Abdominal pain at – bt	5	3	15	0	0.00	0.00	8	13	-2.04	0.041	S
Fever at – bt	3	2	6	0	0.00	0.00	10	13	-1.63	0.102	NS

Statistically significant reduction of lakshana, viz., *Angasada, Aruchi, Avipaka, Daurbalya, Peeta Mootrata* and abdominal pain was noted.

Table 2: Result of Mc Nemar test showing the effect of intervention on *Lakshana* of *Kamala*

Variable	Bt		At		N	P value	Remarks
	Present	Absent	Present	Absent			
Peeta Netra	13	0	4	9	13	0.004	S
Peeta Twak	9	4	5	4	13	0.125	NS
Peeta Nakha	2	11	0	2	13	0.500	NS
Peeta Anana	8	5	3	5	13	0.063	NS
Chills & rigor	2	11	0	2	13	0.500	NS
Pruritus	1	12	0	1	13	1.00	NS

Statistically significant reduction of *Peetata* of *Netra* was noted. Reduction in *Peetata* of twak*, Nakha, Anana,* chills & rigor and pruritus were statistically insignificant due to small sample.

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DISCUSSION

Kamala is a condition described among the *Rakta Pradoshaja Vyadhi.* It occurs due to *Prakupita Pitta Dosha.* The word *Kamala* can be split as '*Kamam'* meaning desire and '*Laati'* meaning loss.[5] Thus interpreting it as a condition where the affected individual loses the desire towards food. The explanation of *Kamala* is found in the context of *Pandu Roga* in the classics. Manifestation of *Kamala* can be understood as an increase in *Mala Roopi Pitta.* Bilirubin is a breakdown product of senile RBCs physiologically. An increase in the breakdown of RBCs or a reduced uptake by the hepatocytes for further metabolism or an obstruction to the eliminatory pathway leads to the clinical condition jaundice.

Probable mode of action[6]

Rasa - *Gavakshi* pocesses *Tikta Rasa* which is *Pitta Shamaka*. The *Mahabhoota* dominant in *Tikta Rasa* is *Vayu* and *Akash* making it *Sowmya, Laghu* and *Ruksha* that oppose the qualities of *Teekshna, Sasneha* of *Pitta*. It produces *Vishodhana* of *Rasanendriya* promoting *Bhaktaruchi* that helps mitigate *Aruchi* in *Kamali*.

Guna & Veerya - The individual suffering from *Kamala* experiences reduced appetite and improper digestion. The *Laghu Guna* and *Ushna Veerya* of *Gavakshi* helps in *Jataragni Deeepana*. *Sara Guna* causes *Vata, Mala Pravartana.* Thus, contributing to the *Rechana Karma* in turn eliminating *Malaroopi Pitta.*

Vipaka - Transformation of *Tikta Rasa* to *Katu Vipaka* is graded as *Alpa* thus not causing *Pitta Prakopa.*

Karma - *Gavakshi* acts as *Pitta Rechaka*.

Gavakshi is a stimulant purgative that irritates the intestinal mucosa and stimulates motor activity.

Local action - Mild inflammation causes capillary dilatation and exudation of protein that helps in dilution of toxins. Hydrophilic action increases water in colon making propulsion easy.

Action on nerves - Defecation centre in medulla oblongata is irritated. The contraction of gall bladder by the activity of cholecystokinin and vagal stimulation results in bile secretion into duodenum. Increased peristalsis results in expulsion of secretions accumulated in the intestinal lumen.

Dodging enterohepatic circulation - Increased peristalsis leads to reduced stasis of intestinal contents. The bilirubin in the secreted bile, normally is reabsorbed through enterohepatic circulation. Due to the rapid expulsion of faeces bilirubin fails to enter this circulation. Thus, resulting in reduction of serum levels of bilirubin.

Pharmacological activity of *Gavakshi* - *Citrullus colocynthis* has purgative, cathartic, anti-inflammatory, hepatoprotective activities attributable to its active principles.

Table 3: Active principles and pharmacological activity of *Citrullus colocynthis*

Qurcitin and Rutin	The flavonoids have been reported to inhibit oxidation. Quercetin contains a polyphenolic chemical substructure that scavenges free radicals. This makes *Citrullus colocynthis* an anti-oxidant
Cucurbitacin B and Colocynthin	Lipid peroxidation which is the oxidative degradation of lipids is inhibited by cucurbitacin B and colocynthin. In vitro studies show reduction of hepatitis induced by carbon tetrachloride proving its hepatoprotective activity
Colocynthin	Colocynthin stimulates gallbladder contraction promoting bile flow and also causes increased hepatocellular secretions making it both excretory and secretory cholagogue
Cucurbitacin D, E	Cucurbitacin D, E interact with albumin leading to increase in the binding of bilirubin to albumin. Thus, helping in inhibition of seepage of unconjugated bilirubin into tissues and improved hepatic uptake.
L-citrulline	L-citrulline is one of the three dietary amino acids in urea cycle. It increases the rate of oxidative ATP Production, reducing fatigue. In a dose of 3000mg/day L-citrulline also improves circulatory health.

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Rationale: Reduction of serum bilirubin in 3 days

Physiologically bilirubin production follows 2 pathways[7]

- From senescent RBCs: This is termed as late labelled bilirubin, which makes up 78% of the bilirubin in the body. This is expelled out of the body over a duration of 120 days.
- From immature, defective RBCs and hepatic cytochromes: This is termed as early labelled bilirubin, which makes up 22% of the bilirubin in the body. This is expelled out of the body within a duration of less than 10 days.

Formation of immature RBCs in deficient state of Vit B12 and Folic acid is common in chronic alcoholic individuals. Hepatitis results in increased formation of hepatic cytochromes. These contribute to increased production of shunt/ early labelled bilirubin. With the help of secretory and excretory cholagogue properties of *Citrullus colocynthis,* the elimination of bilirubin is hastened resulting in reduction of serum levels of bilirubin.

CONCLUSION

Gavakshi Moola is a *Tikta Rasa Pradhana Dravya* with *Rechana Karma*, thus, helps in elimination of *Mala Roopi Pitta. Gavakshi Moola Draava* with *Ksheera* helped in alleviating *Lakshana* of *Kamala* (hepatocellular jaundice) viz., *Avipaka, Aruchi, Angasada, Daurbalya, Peeta Mootrata, Peeta Netrata, Peeta Anana,* abdominal pain, fever, chills & rigor. Statistical significance in reduction of constitutional symptoms and serum levels of bilirubin in hepatocellular jaundice was noted.

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