WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 3, 1115-1129. Review Article ISSN 2277– 7105

LODHRADI KASHAYA AS A POTENT ANTIDIABETIC AGENT: A DRUG REVIEW

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Article Received on
12 January 2022,

Revised on 02 Feb. 2022,
Accepted on 22 Feb. 2022

DOI: 10.20959/wjpr20223-23335

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ABSTRACT

Lodhradi Kashaya is a herbal preparation described in *Vasavarajeeyam* containing four components *Lodhra*, *Musta*, *Haritaki* and *Katphala* given in decoction form which should to be prepared daily and given to *Madhumeha* or diabetic patients due to its anti-hyperglycemic actions. Various experimental studies on animals and humans reveal the anti-diabetic, antioxidant, hepatoprotective and renoprotective properties of *Lodhra*, *Musta*, *Haritaki* and *Katphala* individually and also in combination. Studies show that it acts by stimulating the beta cells of the pancreas and increasing sensitivity of the peripheral tissue to insulin thus enhancing glucose utilisation. The pharmacodynamics analysis show that there is predominance of *Kashaya* (100%), *Tikta* and *Katu Rasa* (75%); *Laghu* (100%), *Ruksha* (75%) and *Tikshna* (25%) *Guna*; *Anushna Virya* and *Katu Vipaka* (75%). 100% of the components are *Kapha Shamaka*, 75% are *Pitta Shamaka* and 50% are *Vata Shamaka*, hence it can be said that *Lodhradi Kashaya* is *Tridosha Shamakaa* predominantly *Kapha Shamaka*. Most of the drugs are having *Kapha-medahara* property which ultimately corrects the vitiated *Slesma*, *Meda* and *Mamsa dhatu*. Hence effective in controlling *Madhumeha*. Thus, *Lodhradi Kashaya* can be used as a potent anti diabetic agent.

KEYWORDS:– *Lodhradi Kashaya*, Pharmacodynamics analysis, Anti-diabetic actions, Evidences.

INTRODUCTION

For successful treatment, Ayurveda give second position to *Dravya* (drug), first position to physician (*Vaidya*), third position to attendant (*Upasthata*) and fourth or last position to the patient (*Rogi).*[1] The comprehensive knowledge about the drug is very important to physician for the success in treatment.[2] An unknown drug is as fatal as poison, weapons, fire and the thunderbolt.[3] Hence before using any drug, we need to know the details about the same in every aspect. Diabetes is a very effectively growing lifestyle disorder in today's world. There are many conventional anti-diabetic agents available at present. However due to their adverse effects, cost, and decreasing efficacy over time, there is a search for safer, acceptable and effective anti-hyperglycemic agents. In Ayurveda, the treatment of *Madhumeha* (hyperglycemia) and *Prameha* (polyuria) are well described. Various plant- based medicines were developed and had been used for last thousands of years, and are well-documented for their clinical effects in Ayurvedic classics. 'Vasavarajeeyam' is one among those classics. It was written by Vasavaraj in 16th century. It is one of the authoritative books of Ayurveda specified in the First Schedule of Drug and Cosmetic Act 1940.[4] It has specified effective drug formulations for various diseases. Among them, one of the important poly-herbal formulation described for the treatment of *Madhumeha* is *Lodhradi Kashaya*.

Components of lodhradi kashaya

It contains *Lodhra*, *Haritaki*, *Musta*, and *Katphala* in equal amount and is prescribed in decoction form.[5] The drugs are cheaply available and it can be easily prepared at home. As the starting drug in description is *Lodhra* hence it gives the name to the preparation *Lodhradi Kashaya*.

Table no. 1: Showing composition of *lodhradi kashaya.*

Sl. No.	Name	Latin name	Family	Parts used	Proportion
1	Lodhra	*Symplocos racemosa Roxb*	Symplocaceae	Stem bark	1 part
2	Haritaki	*Terminalia chebula*	Combretaceae	Fruit pericarp	1 part
3	Musta	*Cyperus rotundus* Linn	Cyperaceae	Rhizome	1 part
4	Katphala	*Myrica esculenta*	Myricaceae	Stem bark	1part

Method of preparation of lodhradi kashaya

The collected plant materials are cleaned and dried in the sunlight. The dried plant materials are then ground into a moderately coarse powder using a mechanical pulveriser. The powder is mixed properly and packed.

Dose - 12 gms of the drug powder is to be boiled with 200ml water and reduced to 50ml. Always fresh *kwath* is made for use and taken twice daily.

Analysis of pharmacodynamics of lodhradi kashaya

According to Ayurveda the pharmacological activity of a drug may depend upon any one of the *Rasa*, *Guna*, *Virya, Vipaka* or *prabhaba.*[6,7,8] The pharmacological properties of the drug *Lodhradi Kashaya*, as described in Ayurveda, are summarised in the *Rasapanchaka* table below-

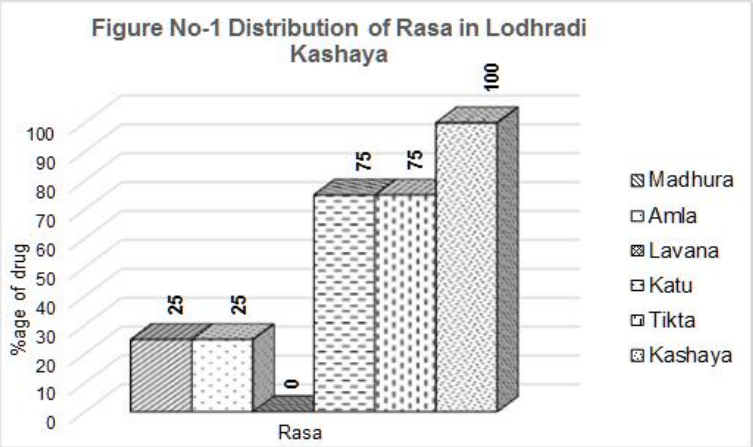
Table no. 2: Showing the *rasapanchaka* of *lodhradi kashaya.*

Drug	Rasa	Guna	Virya	Vipaka	Dosha Karma	Karma
Lodhra[9]	Kashaya	Laghu, Ruksha	Seeta	Katu	Pitta-kapa shamaka	*Grahi, Chakshusya, Raktapitta-Ashruk-Jwara-Atisara-Sotha Nashaka*
Musta[10]	Katu, Tikta, Kashaya	Laghu, Ruksha	Seeta	Katu	Pitta-kapa shamaka	*Pittakaphahara, Sthaulyahara, Sothahara, Dipana, Pacana, Grahi, Trishnanigrahana, Krumighna, Tvak dosahara, Jvaraghna, Visaghna*
Haritaki[11]	Madhura, Amla, Katu, Tikta, Kashaya	Laghu, Ruksha	Ushna	Madhura	Tridosha shamaka	*Rasayana, Deepan, Pachana, Medhya, Chakshushy, Laghu, Ayushya, Brinhana, Anulomana.*
Katphala[12]	Katu, Tikta, Kashaya	Laghu, Tikshna	Ushna	Katu	Vata-Kapha Shamaka	*Swasa- Prameha-Kasa-Kantharoga Nasak. Ugradahahara, Mukharogasamaka, Dhatuvikarajit. Gulma, Meha, and agnimandya nasak.*

Rasa – The analysis of *Rasa* of individual components of *Lodhradi Kashaya* shows that the preparation as a whole in predominant in *Kashaya* (100%), *Katu* and *Tikta* (75%) *Rasa*.

Table no. 3: Showing *rasa* of *lodhradi kashaya*.

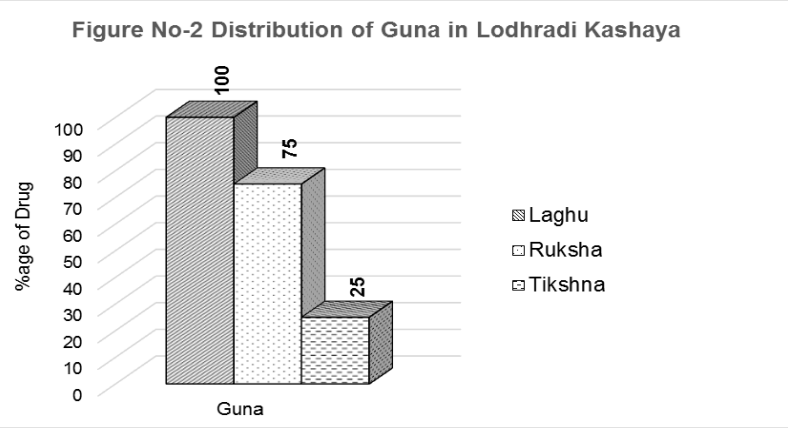
Rasa	No of parts	Percentage
Madhura	1	25
Amla	1	25
Lavana	0	0
Katu	3	75
Tikta	3	75
Kashaya	4	100



Guna – 100% components of *Lodhradi Kashaya* possess *Laghu guna* while 75% possess *Ruksha guna* hence the preparation is predominant in *laghu ruksha guna*.

Table no. 4: Showing *guna* of *lodhradi kashaya.*

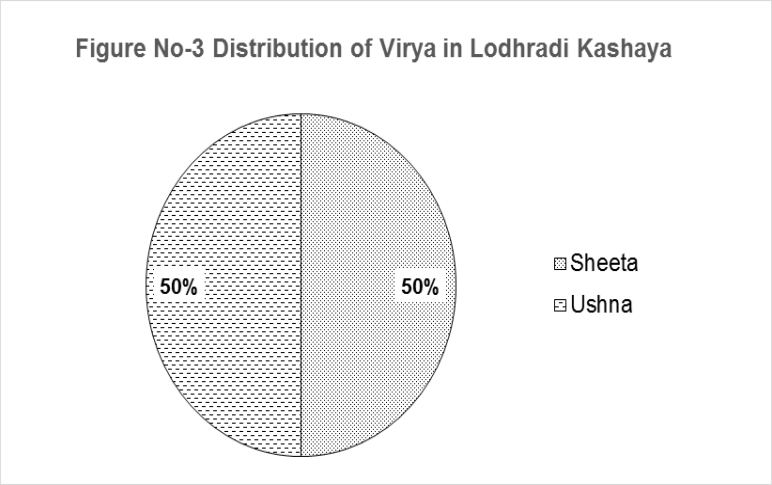
Guna	No of parts	Percentage
Laghu	4	100
Ruksha	3	75
Tikshna	1	25



Virya – 50% components of *Lodhradi Kashaya* have *Sheeta Virya* while 50% have *Ushna Virya*, hence the preparation can be considered as *Anushna Sheeta*.

Table no. 5: Showing *virya* of *lodhradi kashaya.*

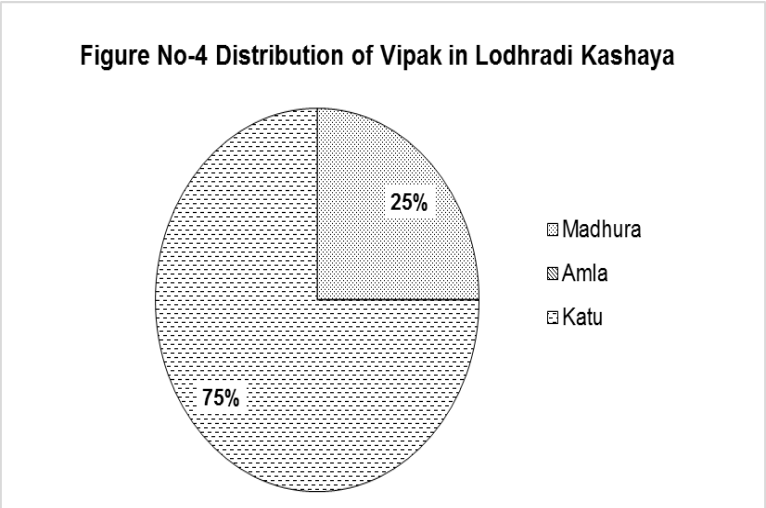
Virya	No of parts	Percentage
Sheeta	2	50
Ushna	2	50



Vipaka – 75% of components of *Lodhradi Kashaya* possess *Katu Vipaka* and 25% possess *Madhura Vipaka*, hence the preparation as a whole can be considered as *Katu Vipaka*.

Table no. 6: Showing *vipaka* of *lodhradi kashaya.*

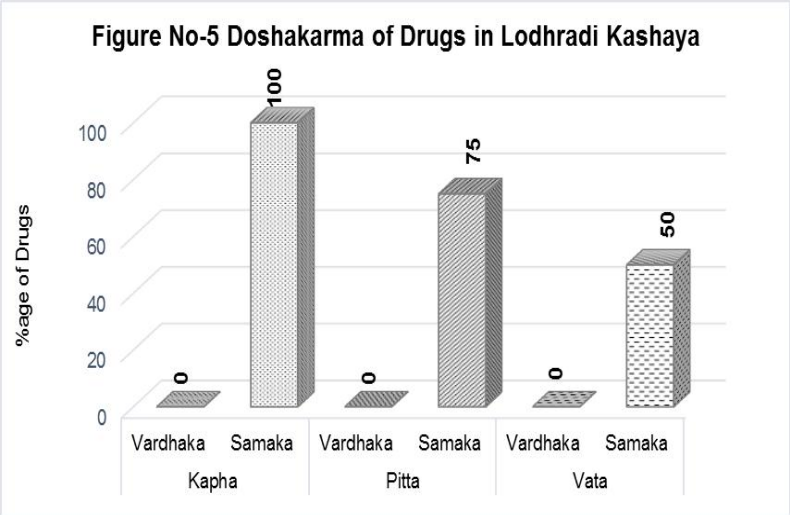
Vipaka	No of parts	Percentage
Madhura	1	25
Amla	0	00
Katu	3	75



Doshakarma – 100% of the components are *Kapha Shamaka*, 75% are *Pitta Shamaka* and 50% are *Vata Shamaka*, hence it can be said that *Lodhradi Kashaya* is *Tridosha Shamaka* predominantly *Kapha Shamaka*.

Table no. 7: Showing *doshakarma* of *lodhradi kashaya.*

Dosha	Doshakarma	No of parts	Percentage of drugs
Kapha	Vardhaka	0	0
	Shamaka	4	100
Pitta	Vardhaka	0	0
	Shamaka	3	75
Vata	Vardhaka	0	0
	Shamaka	2	50



Antidiabetic activity of components of lodhradi kashaya

Lodhra - Pharmacological studies on anti-diabetic property of *Lodhra*

1) *Mehaghna* activity of *Lodhra* was demonstrated in a clinical study where *Lodhra* bark was used in the form of *Kashaya*, aqueous extract, ethanolic extract, Glibenclamide. Diabetes was induced to Wister Albino Rats by intraperitoneal injection of Alloxan monohydrate at the dose of 150 mg/kg body weight. After 21 days of experimental study group treated with *Kashaya* of *Lodhra* bark gave significant results in all parameters with p value <0.001.[13]

2) Studies show anti-diabetic effects of Symplocos racemosa Roxb. methanol extracts of the bark (MESR) in streptozotocin (STZ) induced diabetic Albino Wistar rats in 14 days. MESR, administered at doses of 250 & 500 mg/kg to STZ-treated diabetic rats caused significant ($p < 0.01$) reduction of blood glucose levels. MESR showed a dose related

significant ($p < 0.01$) reduction in triglycerides compared to pretreatment levels. The reduced glucose levels suggested that MESR might exert insulin-like effect on peripheral tissues by either promoting glucose uptake metabolism by inhibiting hepatic gluconeogenesis. The altered serum lipid profile was reversed towards normal after treatment with the MESR. MESR exhibited hypocholesterolemic and hypotriglyceridemic effects, while increased the levels of HDL in STZ - induced diabetic rats.[14]

3) Studies also show the antidiabetic efficacy of the hexane extract of Symplocos cochinchinensis leaves in high fat diet–low streptozotocin (STZ) induced type 2 diabetic rats. After 28 days of treatment with the hexane extract at 250 and 500 mg/kg reduced the plasma glucose level by 17.04% and 42.10%, respectively. A significant reduction in plasma insulin, plasma and hepatic total cholesterol (TC), triglycerides (TG) and free fatty acids (FFA) and a significant increase in liver glycogen were observed in treated diabetic rats.[15]

Musta - Pharmacological studies

1) In a study, Oral daily administration of 500 mg/kg of the hydro-ethanolic extract of *Cyperus rotundus* (once a day for seven consecutive days) significantly lowered the blood glucose levels in alloxan induced hyperglycemia in rats. This antihyperglycemic activity can be attributed to its antioxidant activity as it showed the strong DPPH radical scavenging action in vitro.[16]

2) In another study, ethanolic extract of *Cyperus rotundus* (EECR) rhizomes was evaluated for antidiabetic activity in streptozotocin (STZ)-induced diabetic swiss mice for 3 weeks. The ethanolic extract at dose levels of 250 and 500 mg/kg body weight revealed significant antidiabetic activity, improvement in body weight, and reduction in elevated biochemical parameters such as SGPT, SGOT, cholesterol, and triglyceride levels.[17]

3) Studies also show that the water extract of *Cyperus rotundus* 0.5 g/kg could significantly reduce the plasma glucose levels of either type 1 or type 2 diabetic rats. The toxicity test summarized that the single oral LD was more than 5 g/kg. The mechanism testing demonstrated that the extract at a dose of 5 mg/ml could inhibit the intestinal glucose absorption significantly in everted sac model and the extract since 1 mg/ml could enhance the glucose utilization of muscle like insulin did. Thus *C. rotundus* extract has a hypoglycemic or anti-diabetic effect by inhibiting intestinal glucose absorption and

promoting glucose consumption.[18]

4) In another animal study 25 Male rats were divided into 5 groups: normal control, diabetic control, diabetic of C. rotundus (200 mg/kg b.w), diabetic of C. rotundus (400 mg/kg b.w), diabetic of glibenclamide (0.6mg/kg).Treatments were administered orally for 6 weeks. A single injection of alloxan to rats (150mg/kg b.w) caused pathological alterations in all studied parameters and histological structure of the pancreas. On the other hand, results showed that oral administration of C. rotundus rhizomes extract in dose of 200 and 400 mg/kg caused significant reduction in glucose, HbA1C%, α-amylase level and plasma lactate together with significant elevation in serum insulin, serum pyruvate with an improvement in insulin resistance. In line with amelioration of the diabetic state, C. rotundus rhizomes extract improved of the liver and kidney functions, and oxidative marker levels. Moreover, the extract succeeded to reduce the elevated serum total cholesterol, triglyceride (TG) and low-density lipoprotein- cholesterol (LDL-C) levels and to elevate the reduced high-density lipoprotein- cholesterol (HDL-C) level of diabetic rats.[19]

Haritaki

Acharya Vagbhatta has advised the use of *Haritaki* powder with honey in all *Prameha*.[20]

Pharmacological studies showing antidiabetic effect

1) In a double-blind clinical study 100 patients of diabetes mellitus were selected randomly and Powder of *Terminalia chebula* in the dose of 10 gm twice per day was administered with water and honey. It was found that the effect of *Terminalia chebula* powder with water and honey as vehicle in both fasting and post prandial state in urine and blood sugar was satisfactory.[21]

2) In a study it was found that the chloroform extract of *T. chebula* seeds produced dose-dependent reduction in blood glucose of streptozotocin-induced diabetic rats at the doses of 100, 200 and 300 mg/kg and comparable with that of standard drug, glibenclamide in short term study. Blood samples were collected from the eye retro-orbital plexus of rats before and also at 0.5, 1, 2, 4, 6, 8 and 12 h after drug administration and the samples were analyzed for blood glucose by using glucose-oxidase/peroxidase method using a visible spectrophotometer. The results indicated a prolonged action in reduction of blood glucose by *T. chebula* and is probably mediated through enhanced secretion of insulin

from the β-cells of Langerhans or through extra pancreatic mechanism. It also produced significant reduction in blood glucose in long term study where the extract (300 mg/kg) was administered to streptozotocin-induced diabetic rats, daily for 8 weeks. Blood glucose was measured at weekly intervals for 4 weeks. Urine samples were collected before the induction of diabetes and at the end of 8 weeks of treatments and analyzed for urinary protein, albumin and creatinine levels. Significant renoprotective activity was observed in *T. chebula* treated rats.[22]

3) Studies show that oral administration of ethanolic extract of the fruits (200 mg/kg body weight/rat/day) for 30 days significantly reduced the levels of blood glucose and glycosylated hemoglobin in streptozotocin (STZ)-induced diabetic rats. Determination of plasma insulin levels revealed the insulin stimulating action of the fruit extract. Also, the alterations observed in the activities of carbohydrate and glycogen metabolising enzymes were reverted back to near normal after 30 days of treatment with the extract. Electron microscopic studies showed significant morphological changes in the mitochondria and endoplasmic reticulum of pancreatic B cells of STZ- induced diabetic rats. Also, a decrease in the number of secretory granules of B-cells was observed in the STZ- induced diabetic rats and these pathological abnormalities were normalized after treatment with T. chebula extract. The efficacy of the fruit extract was comparable with glibenclamide, a well-known hypoglycemic drug.[23]

4) In another study the aqueous extract of the fruits of Terminalia chebula Retz. has been evaluated for its antidiabetic activity in streptozotocin (STZ) induced mild diabetic rats and compared with a known drug, tolbutamide. The oral effective dose (ED) of the extract was observed to be 200 mg/kg body weight, which produced a fall of 55.6% ($p<0.01$) in the oral glucose tolerance test. Oral administration of ED of aqueous extract of T.chebula (AETC) daily once for two months reduced the elevated blood glucose by 43.2% ($p<0.01$) and significantly reduced the increase in glycosylated hemoglobin (HbA1c) ($p<0.01$). The same dose also showed a marked improvement in controlling the elevated blood lipids as well as decreased serum insulin levels in contrast to the untreated diabetic animals. Hepatic and skeletal muscle glycogen content decreased by 75% and 62.9% respectively in diabetic controls, these alterations were partly prevented (34.9% and 21.17%) in AETC treated group when compared to the healthy controls. The in vitro studies with pancreatic islets showed that the insulin release was nearly two times more

than that in untreated diabetic animals. The treatment did not have any unfavorable effect on other blood parameters of liver and kidney function tests. LD 50 was found to be above 3 g/kg body weight i.e. 15 times of ED, because there were no deaths of animals even at this dose indicating high margin of safety.[24]

Katphala - Pharmacological studies

1) In a study it was found that Methanolic extract *of Myrica esculenta leaves* showed dose-dependent antidiabetic activity by significant decrease in blood glucose level, body weight and blood cholesterol level of streptozotocin induced diabetes in rats in extract treated group as compared to the positive vehicle treated group.[25]

Lodhradi kashaya ¯ Experimental study on the hypoglycemic effects

Apart from the experimental studies of individual drugs showing their anti-diabetic properties studies also provide evidence of the antidiabetic activity of *Lodhradi Kashaya* in *vati* form. In a study *Lodhradi Kashaya Ghanavati* (LKGV) was prepared, containing *Lodhra* (*Symplocose racemosa*), *Haritaki* (*Terminalia chebula*), *Musta* (*Cyperus rotundus*), and *Katphal* (*Myrica esculanta*) by the standard procedure of *Kashaya Ghanavati*. Hyperglycemia was induced to create an equivalent to the diabetic state by giving streptozotocin (STZ) solution (intra-peritoneal [i.p.]) 65 mg/kg, 15 min after initial administration of 120 mg/kg nicotinamide i.p. After assessment of hyperglycemia as an approximate induction of diabetes, group of animals (III, IV, and V) were treated with dose titrations using 50, 150, and 275 mg/kg of LKGV. For treatment comparison, Group VI animals were treated with a standard hypoglycemic drug, glibenclamide 10 mg/kg. Blood sugar, the level was assessed by glucometer on the 7th, 14th, 21st, and 28th day. LKGV extract produced a significantly reduction of fasting blood glucose with various doses in STZ-induced diabetic rats. In a 4-week study, LKGV produced a significant reduction in blood glucose compared to glibenclamide. (Brahmakar R.B. *et al* has reported the hypoglycemic effects of Lodhradi Kashaya. In their study, Lodhradi Kashaya Ghana Vati (LKGV) showed a significant decrease in blood sugar level both compared to a diabetic non-treated control group and to a group treated with a standard anti-diabetic drug, glibenclamide, in a streptozotocin-induced hyperglycemic rat model. It is reported that LKGV acts by stimulating the pancreatic beta cells of the pancreas and increasing sensitivity of the peripheral tissue to insulin.[26]

The above sited research articles prove the antidiabetic property of each component of

Lodhradi Kashaya and *Lodhradi Kashaya* as a whole. Above cited experimental study also proves the hypoglycemic potential of the trial drugs.

DISCUSSION

The drug Lodhradi Kashaya contains four constituents namely *Lodhra, Musta, Haritaki* and *Katphala*. Each one is reported in Ayurvedic classics to have action of reducing *Prameha*.

From ***Rasa panchaka* analysis** it has been observed that-

- There is predominance of *Kashaya* (100%), *Tikta* and *Katu Rasa* (75%); *Laghu* (100%), *Ruksha* (75%) and *Tikshna* (25%) *Guna*; *Anushna Virya* and *Katu Vipaka* (75%). 100% of the components are *Kapha Shamaka*, 75% are *Pitta Shamaka* and 50% are *Vata Shamaka*, hence it can be said that *Lodhradi Kashaya* is *Tridosha Shamaka* predominantly *Kapha Shamaka*. Hence effective in controlling *Madhumeha*.
- Most of the drugs are having *Kapha-medahara* property which ultimately corrects the vitiated *Slesma*, *Meda* and *Mamsa dhatu*.
- All the herbs are having *Deepan-pachan* property. Thus, the medicine is potential to correct the *Agni* i.e. *Jatharagni* and *Dhatwagni*. They help in smooth management of body metabolism. Ultimately it helps in proper nourishment of *Dhatus*. It has the capacity to improve the tones of *sapta-dhatus*.
- *Madhumeha* is a disease related to *Mutravaha srotas* with cardinal symptom of polyuria (*prabhuta mutrata*). Most of the drugs are having *Grahi* and *Stamhbhana* property with predominance of *Kashaya* (astringent) and *Tikta* (bitter) *Rasa* as well. These helps to decrease excess urination and prevent the system from vitiation.
- *Haritaki* clears all the *srotas* (paths) so it is called as *pathya.* It alleviates the *margavarodha* (obstructions) in *Madhumeha.* It also nourishes all *dhatus* with its *Rasayana* property.
- *Musta* is potent in *Trishna nigrahana*. So, it corrects the *purvarupa* stage like *Trishna, Galatalu sosha* etc. in *Madhumeha*.
- *Katphala* has *Ugradahahara* property and Musta also have *Sheeta* property. It cures the burning and tingling sensations in upper and lower extremities (*hastapada daha).*
- *Lodhra* is having *chakshushya (*good for eyes) property, which may alleviate the chances of retinal complications in type 2 DM.

Hence from Ayurvedic point of view *Lodhradi Kashaya* is capable enough to fulfil all the treatment modalities of *Madhumeha* (type 2 DM).

Modern science strengthens the concept of *Madhumehaghna* (antidiabetic) property of all the four herbs. It is believed that the basis of the chemical constitution of different herbal drugs and various medicinal/ plant extracts contain active flavonoids, alkaloids, phenolic compounds, terpinoids, saponins, and phytosterol type chemical constituents that are effective in the management of diabetic complications. This effect might be attributed to the amelioration of persistent hyperglycemia, oxidative stress, and modulations of various metabolic pathway involved in the pathogenesis of diabetic complications.[27]

The experimental studies on antidiabetic activities of *Lodhra* (*Symplocos racemose*), *Musta* (*Cyperus rotundus*), *Haritaki* (*Terminalia chebula*) and *Katphala* (*Myrica esculenta)* has been cited. Experimental study on *Lodhradi Kashaya* showed a significant reduction in blood glucose levels in DM animal models.

The above data proves the antidiabetic property of the drug *Lodhradi kashaya*.

CONCLUSION

Lodhradi kashaya is a herbal drug containing *Lodhra, Musta, Haritaki* and *Katphala* has such composition which strongly possesses the hypoglycaemic properties according to the text. As per the experimental studies all ingredients individually and the drug are effective hypoglycaemic agents.

Along with hypoglycaemic properties the compound drug possess antioxidant, Hepato-protective and reno-protective effects which in turn provide a productive, peaceful and blissful life to the patients.

Physicochemical analysis of the drug demonstrate that the pH is favourable for early absorption in stomach as it remains acidic. It is used in *Kashaya* form which also enhances the absorption of the drug. Thus, it can be used as herbal tea regularly by the diabetic patients. And can be given for prolonged period as an alternative oral hypoglycaemic drug. Moreover, this drug can be prescribed combined with modern drugs like sulphonyluria and biguanides to minimise the dosage and potentiate the hypoglycaemic action as well.

Lastly it is to be concluded that *Lodhradi kashaya* can be safely prescribed for long term to one and all without any hesitation and may prove the bacon hope for diabetes.

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