Pramehahara Yoga (Anti-diabetic formulations) – A *Laghutrayi* review

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Abstract

Background: Diabetes is a major non-communicable disease reaching epidemic proportions. Inspite of vigorous development in modern medical science and technology, management of diabetes has remained inadequate. *Ayurveda* with vast documentation of treatment in management of *Prameha* may hold the key to this problem.

Aim: This review is expected to enrich the documentary evidences about classical references on formulations related to *Prameha* (Diabetes mellitus) enumerated in *Laghutrayi*.

Methodology: *Laghutrayi* texts are considered as one among the best *Ayurveda* treatises for understanding treatment principles of any disease. A total of 117 *Pramehahara* (anti-diabetic) formulations have been compiled from *Laghutrayi* by searching specific keywords from individual text's hardcopy. Key words searched in *phalashruti* (verse with indications) included "*prameha*", "*meha*", "*madhumeha*" with suffixes like "*hanti*", "*harati*", "*jayati*", "*jit*", "*nihanti*", "*nashayet*", "*nivrittaye*", "*ghna*".

Results: A total of 117 *Pramehahara Yoga* (anti-diabetic formulations) have been compiled from *Laghutrayi*. *Kvatha* (decoction) is the highest enumerated dosage form (55 formulations) in *Laghutrayi*. Honey is the most enumerated adjuvant in *Laghutrayi* (62 formulations). *Triphala* is the highest enumerated herbal formulation in *Laghutrayi* (18 formulations), followed by *Daruharidra* (12 formulations).

Conclusion: Validating these comprehensive observations of *Pramehahara yoga* (anti-diabetic formulations) mentioned in *Laghutrayi* may facilitate a better and precise treatment protocol in management of Diabetes mellitus.

Keywords: *Ayurveda*, *Prameha*, Diabetes mellitus, Antidiabetic formulations, *Laghutrayi*

Introduction

The term metabolic disorder is an umbrella term encompassing different types of disorders and diseases occurring due to disturbed metabolism. Cardiovascular diseases stand at the top of the list of non-communicable diseases followed by Diabetes in the second place. [1]

According to 10th edition of Diabetes atlas published by International Diabetic federation in 2021, it is estimated that 537 million adults between age group 20-79 years have diabetes worldwide. The second largest numbers of diabetes patients from age 20-79 years are in India (74.2 million). [2]

Sangraha kala was golden period for *Ayurveda* science's redactions and modifications in textual content. Ancient authors of *Ayurveda* could expound on all 8 branches of *Ayurveda* in their works. It must have felt humongous, hence authors in *sangraha kala* focused on few particular area of subject and explained them in detail. Gupta rule and establishment of Nalanda University became a primordial reason for science to flourish, thus marking Gupta rule as *sangraha kala*. [3]

Among these works, three works were more appreciated

than others and became famously known as "*Laghutrayi* " of *Ayurveda. Sharangadhara samhita, Bhavaprakasha* and *Madhava nidana* comprise as *Laghutrayi* (compendia minora). Precise explanation, repeated mentioning by contemporary authors, concised yet unsaturated comprehension of subject matter told by *Brihattrayi* (compendia majora) could have transcended these three works. *Ayurveda* may help in management of diabetes holistically by catering person specific treatment. Thus, present review was taken up as an attempt to understand drug design process in compiled formulations related to management of *Prameha* (Diabetes).

Methodology

Laghutrayi have been thoroughly scrutinised and formulations indicated for *Prameha* management were compiled. Chapters like *Prameha chikitsa* (Diabetes mellitus), *Prameha pidaka chikitsa* (Diabetic carbuncles), *Sthaulya chikitsa* (obesity) and *Mutravikara chikitsa* (urinary system diseases) were thoroughly reviewed as chances of finding *Prameha* indicated formulations were more in these chapters. Key words searched in *Phalashruti* (verse with indications) included "*prameha*", "*meha*", "*madhumeha*" with suffixes like "*hanti*", "*harati*", "*jayati*", "*jit*", "*nihanti*", "*nashayet*",

"*nivrttaye*", "*ghna*". Data was compiled and details like reference, ingredients, adjuvants, dosage form and indications were recorded digitally. Apart from *Sharangadhara samhita* and *Bhavaprakasha*, the text included in this review was *Madhava chikitsa*. Although *Madhava nidana* text is originally considered as *Laghutrayi*, it deals only with pathology of disease and does not enumerate any medcines. The author for both the works remains the same i.e., *Madhavakara. Madhava chikitsa* compendium did not receive as much popularity as the *Madhava nidana*, although it can be said to be a milestone in *Ayurveda* scripture, which initiated a new tradition of *Chikitsa grantha* (texts with treatment principles). This compendium appears to have been a role model for the *chikitsa* texts that were written in the later eras like the *Chikitsa kalika, Vrinda madhava and Chikitsasara sangraha.*

Results

Total formulations in management of *Prameha* compiled from *Madhava chikitsa* text are 21 formulations, [4] from *Sharangadhara samhita* - 27 formulations [5] and from *Bhavaprakasha* text - 69 formulations. [6] A total of 117 *Pramehahara* (anti-diabetic) formulations have been compiled from *Laghutrayi* (Figure – 1).
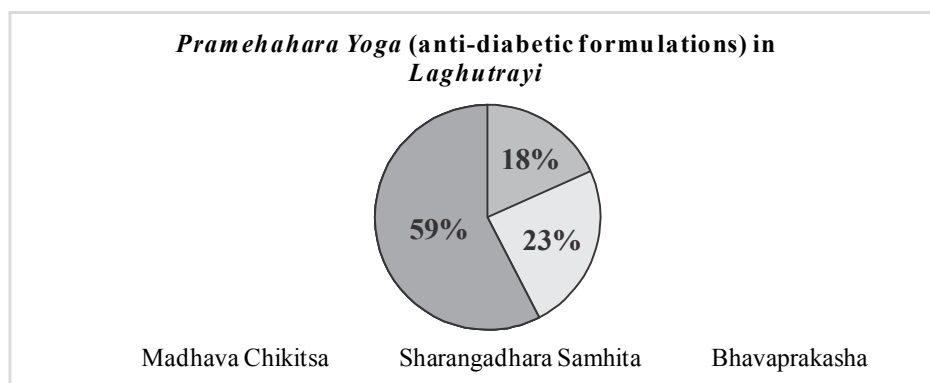

Figure – 1: Ant-diabetic formulations contributed from individual *Laghutrayi*

Discussion

Individual text's compiled formulations have been scrutinized to understand each author's method of drug

design in formulating a *Pramehahara yoga* (anti-diabetic formulation).

Madhava chikitsa: Anti-diabetic formulations compiled

from this text are represented in table - 1. This text was written by *Madhavakara* in 13th century AD. Herbal drug's anti-diabetic formulations amount upto 90.5% (19 formulations) and mineral drug's formulations contribute around 9.5% (2 formulations). This could have been due to author's personal affiliations towards hebal drugs or the influence of time period of the author. During this time-period mineral drugs in *Ayurveda* practise were not yet popularised, hence less enumerations.

Formulations with less than 10 ingredients were scrutinised for the sake of elementariness to extract most repeated drugs opted by the author of this text in designing a *Pramehahara yoga* (anti-diabetic formulation). *Arjuna* was the most enumerated herbal drug (6 formulations), followed by *Musta* (5 formulations) and *Triphala* (4 formulations). Apart from *Triphala* being mentioned as a single unit in formulations, independently *Amalaki* has been mentioned in 4 formulations, *Haritaki* in 3 formulations and *Vibhitaki* in 1 formulation. *Triphala* in *churna* form (powder) mentioned in *Madhava chikitsa* in the mangement of *Prameha* is distinctive, unlike *Kvatha* dosage form mentioned in *Brihattrayi*. Thus we can observe that author has opted *Triphala* as one among the main vehicle in formulation related to *Prameha*.

Amongst 21 formulations compiled in this text, 11 formulations are indicated in all types/stages of *Prameha* (includes *phalashruti* with mentioning of '*sarvaprameha*' and just '*prameha*'), 4 formulations in *kapha prameha*, 4 formulations in *pitta prameha* and 2 formulations in *kapha-pitta prameha*. No formulations specifically for *vataja prameha* is indicated.

Honey is the most opted adjuvant (20 formulations). Amongst dosage form enumerations (Figure – 2), *Kvatha* is the highest - 12 formulations, *Churna* - 4 formulations, *Svarasa* - 2 formulations and *Asava* – 1 formulation. *Kvatha* (decoctions) being the most repeated dosage form, might have been a preferred dosage form because of its better absorption and assimilation in body system and good retaining capacity of water soluble constituents present in raw materials. [7] *Svarasa* (juice) of only two drugs i.e., *Amalaki* and *Guduchi* has been mentioned. Both these are mentioned to cure all types *Prameha* (*sarvamehajit)*, thus proving its potency to act at multiple pathological pathways of *Prameha* disease.

Yava (Barley) as an ingredient in a *Churna yoga* has been a unique mentioning by this text. Barley is a cereal known for its glucose reduction effect. [8] Thus barley in antidiabetic formulations and also much importance towards food preparations with barley flour can be noticed. Mentioning of *Gobhakshita Yava;* a unique curating method of barley has been mentioned by *Brihattrayi,* options of adjuvants is unique in this text.

It could be observed that *Madhava chikitsa* text has some unique contributions in formulation design related to *Prameha* management when compared to *Brihattrayi* texts. *Haritaki churna* as single drug formulations in managing *Prameha* (*mehanivrittaye*), *Lohajam* i.e., *Loha bhasma* in managing *Sarva prameha* (all types of *prameha*), *Yava* (barley) as an ingredient in *Aushadha* (herbal) formulation and not just restricting it to *Ahara kalpana* (food recipie).
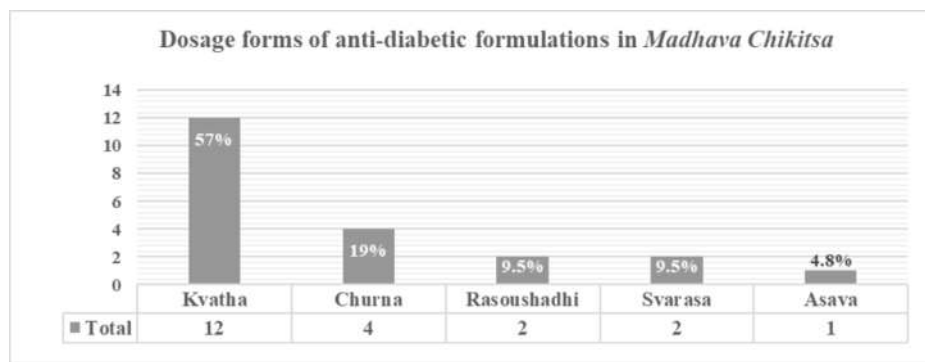

Figure – 2: Dosage forms of anti-diabetic formulations in *Madhava chikitsa*

*Sharangadhara samhita***:** Anti-diabetic formulations compiled from this text are represented in table - 2. This text was authored by *Sharangadhara* in 13th century AD. *Sharangadhara samhita* primarily includes principles of *Ayurveda* pharmaceutics and is considered a pioneer in this subject matter.

Herbal drug's anti-diabetic formulations amount upto 81.5% (22 formulations) and mineral drug's formulations contribute around 18.5% (5 formulations).

Formulations with less than 10 ingredients were scrutinised to extract most repeated drugs opted by the author. *Triphala* was the most enumerated herbal drug (5 formulations), followed by *Musta* (3 formulations) and *Daruharidra* (3 formulations). *Sharangadhara* has mentioned a specific ratio of the three ingredients involved i.e., *Haritaki* - (1 part), *Vibhitaki* - (2 part) and *Amalaki* (4 parts). Clinical studies on different proportions of ingredients of *Triphala* and their varied efficacy in *Prameha* management is a yet to be explored study.

Amongst 27 formulations compiled in this text, 23 formulations are indicated in all types/stages of *Prameha* (includes *phalashruti* with mentioning of '*sarva prameha*' and just '*prameha*'), 1 formulation in *Prameha* and *Medoroga (Nyagrodadhi ghana kvatha)*, 1 formulation in *Prameha* and *Prameha pidaka* (*Kaishora guggulu*), 1 formulation in chronic *Prameha (Mehabaddha rasa)* and 1 formulation in *Prameha* with complications (*Devadarvyarishta*).

Honey is the most opted adjuvant (6 formulations). Amongst 27 formulations*, in* 17 formulations, adjuvants are not mentioned.

Posology for formulation is a unique characteristic feature of this text. Posology has been specified for 8 formulations out of 27 formulations. Except *Mandura vataka,* for remaining 4 *rasoushadhi* (mineral drug) formulations, posology has been specified. Thus care and quantity specificity during prescribing formulation with mineral

drugs can be deduced. *Abhaya modaka* aimed at bringing about *sramsana* of *dosha* (evacuation of *dosha* through bowels) also has been specified quantity of medicine to be given.

Amongst dosage form enumerations (Figure – 3), *vati* is the highest - 5 formulations. For sake of elementariness all 5 *rasoushadhi* formulations has been categorised as single dosage form. Although 4 amongst them are *vati* and 1 is *asava*. Addition of *Makshika dhatu* in *Kumaryasava* is a unique drug design method while preparing *asava* dosage form. Disintegration of a mineral drug in such a dosage form has to be explored. *Sharangadhara samhita* paves way for varied dosage forms of formulations, not to be found in texts dated prior to this text. Thus proving to be a major contributor in terms of expanding *Ayurveda* pharmaceutical science.

Tryushana churna, Lavangadi churna, Sri bahushala guda, Surana vataka, Mandura vataka, Chandraprabha vati, Yogaraja guggulu, Kaishora guggulu, Paniya kalyanaka grita, Shatavari taila, Ushirasava, Kumaryasava, Vidangarisha, Devadarvyarishta, Babbulyarishta, Dashamularishta, Vasantakusumakara rasa, Mehabaddha rasa and *Abhaya modaka* are unique formulations (not to be found in *Brihattrayi* or *Ayurveda* texts prior to this text) mentioned in *Sharangadhara samhita.*
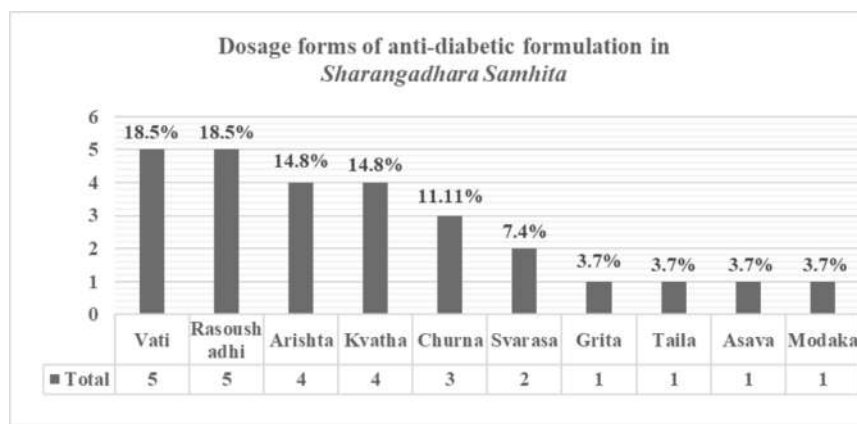
Figure – 3 : Dosage forms of anti-diabetic formulations in *Sharangadhara samhita*

Bhavaprakasha: Anti-diabetic formulations compiled from this text are represented in table - 3. This text was authored by *Bhavamishra* during 16th century AD.

Herbal drug's anti-diabetic formulations amount upto 91.3% (63 formulations) and mineral drug's formulations contribute around 8.7% (6 formulations).

Formulations with less than 10 ingredients were scrutinised to extract most repeated drugs opted by the author. *Triphala* and *Daruharidra* were the most enumerated herbal drugs (9 formulations) followed by *Haritaki* (8 formulations).

Amongst 69 formulations complied from this text, 22 formulations are indicated in all types/stages of *Prameha* (includes *phalashruti* with mentioning of '*sarvaprameha*' and just '*prameha*'), 21 formulations in *kapha prameha*, 14 formulations in *pitta prameha*, 1 formulation in *kapha pitta prameha*, 4 formulations in *prameha pidaka*, 1 formulation in *prameha & madhumeha* indication (*Simhamrita grita*), 1 formulation indicated exclusively in *madhumeha* (*Asanadi yoga*), 1 formulation in *pitta prameha* and *madhumeha* (*Gokshurakadya lehya*), 1 formulation indicated in *prameha- mutrakricchra* and *prameha pidaka* (*nyagrodadhi churna*), 1 formulation indication in *prameha* and *medoroga* (*yava pishta* with water), 1 formulation indicated in *daha* (burning sensation) condition in *prameha* (*nyagrodadhi gana*

kvatha's *basti*), 1 formulation in *prameha* with complications (*trikatukadi modaka*). *Sushruta samhita*'s method of prescribing single drug formulation in each of the 20 types of *prameha* can be observed in *Bhavaprakasha* text.

Honey is the most opted adjuvant (36 formulations). Amongst dosage form enumerations (Figure – 4), *Kvatha* (decoction) is the highest with 39 formulations. Other than *yava* (barley) as *ahara kalpana* (food dietetics), mentioning of *Chanakadi bhakshya* (snacks prepared out of *Cicer arietinum* Linn.) is unique in this text. Three *basti* (rectal enema) formulations have been mentioned, which is also a unique mentioning when compared with other two *Laghutrayi*.

Mentioning of compounded drug units included in formulations can be observed in this text like *Surasadi gana, Nyagrodadhi gana, Asanadi gana, Shala varga*. This might have been due to author's good competency in pharmacognosy, also as he has authored *Bhavaprakasha nighantu* (lexicon on drugs).
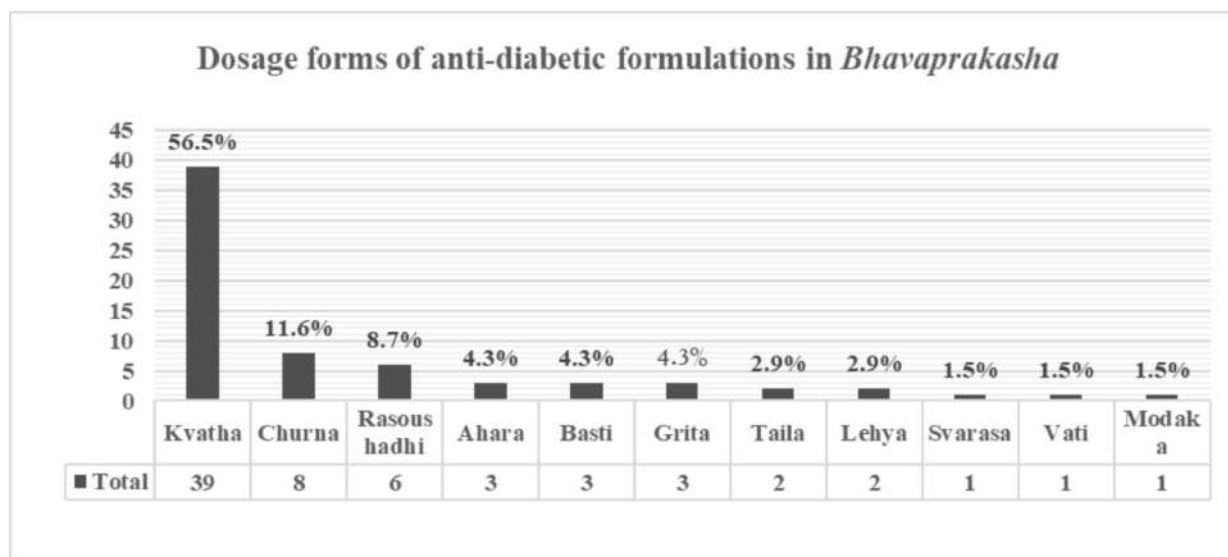
Figure – 4 : Dosage forms of anti-diabetic formulations in *Bhavaprakasha*.

Details of herbal drug most enumerated in *Laghutrayi*: Herbal drugs listed highest in *Pramehahara* (anti-diabetic) formulations of *Laghutrayi* have been scrutinized and their probable mode of action in Diabetes was attempted. *Triphala* has been enumerated highest (18 formulations), followed by *Daruharidra* (12 formulations), *Haritaki* (8 formulations), *Musta* (8 formulations) and *Arjuna* (6 formulations).

Triphala (combination of three fruits; *Phyllanthus emblica* Linn.*, Terminalia bellerica* Linn.*,* and *Terminalia chebula* Linn.) is a potential drug in management of diabetes. *Triphala* contains active ingredients like menthol and sorbitol which is believed to have hypoglycemic effect. [9] Beneficial effects of the *Triphala* in the diabetic neuropathy may be linked with presence of tannins mainly gallic acid and ellagic acid. [10] It shows significant results in antihyperlipidemia, antihyperglycemia and improvement in anthropometric parameters (decreased body weight, body mass index and waist circumference).[11]

Daruharidra (*Berberis aristata* DC) root extract's main constituents were identified as berberine, berbamine and palmatine. They were validated to have lowered the blood glucose significantly without any hypoglycemic effect on their control counterparts. [12]

Haritaki (*Terminalia chebula* Retz.) as an add-on treatment may significantly decrease cardiovascular morbidity by improving lipid profile. [13] Few extracts like ethyl acetate, methanol and methanol– water showed inhibitory potential against the key enzyme (á-glucosidase) linked to type 2 diabetes and also strong antioxidant activity. [14] It has shown potential therapeutic effect as antidiabetic, antilipidemic, hepatoprotective and renoprotective in higher doses when compared to lower doses.[15]

Musta (*Cyperus rotundus* Linn.) shows significant antidiabetic activity as well as anti-lipidemic activity along with reduction in elevated biochemical parameters such as cholesterol, and triglyceride levels. [16, 17] It also acts as an anti-protein glycoxidation agent by inhibiting the oxidative processes. [18] Administration of *Cyperus rotundus* root extract increased the level of HDL (high-density lipoprotein) cholesterol in young and aged rats in an experimental study. [19]

Arjuna (*Terminalia arjuna* Linn.) has a proven cardioprotective action in diabetic cases. [20] It is also proven helpful to stimulate insulin secretion, which may activate hexokinase, there by increasing utilization of glucose leading to decrease in blood sugar levels. [21] The

active ingredient of *Terminalia arjuna* L.; Arjunetin, Arjungenin, Ellagic acid and Arjunic acid have shown superior Dipeptidyl Peptidase-4 (DPP-IV) inhibitory activity as compared to synthetic DPP-IV inhibitors (Sitagliptin and Vildagliptin) based on results of docking studies. [22]

Details of mineral drugs most enumerated in *Laghutrayi*: Mineral origin drugs as a single ingredient formulation in *Prameha* (Diabetes mellitus) is unique mentioning and their probable mode of action in diabetes have been attempted to understand.

Shilajatu (Bitumen mineral) is composed mainly of humic substances, including fulvic acid, that account for around 60% to 80% of the total nutraceutical compound plus some oligoelements including selenium of antiaging properties. [23] Fulvic acid (FvA) has been shown to reduce hyperglycaemia in diabetic rats and increase superoxide dismutase (SOD) activity in pancreatic beta cells. [24, 25] Patients with diabetes are found with a change in gut microbial composition, and FvA may have influenced the bacterial community. [26] *Shilajatu* has been reported to reduce macrophage and lymphocyte activation and migration, as a part of its immunomodulatory activity. Moreover, being an antioxidant it may help prevent damage to the pancreatic islet cell induced by the cytotoxic oxygen radicals. [27, 28]

Svarna makshika bhamsa ($CuFeS_2$) efficacy was attempted to validate through animal study on healthy Charles foster albino rats. The effect of graded dose of *Svarna makshika bhamsa* (SMB) solution (5.85mg/kg, 11.25mg/kg and 22.5mg/kg), standard drug glibenclamide and a combination of standard drug and medium dose of SMB was observed. SMB showed marked decrease in blood sugar level from 7th day onwards of treatment in lower dose. [29] Thus proving its efficacy in management of diabetes.

Although no significant studies have been found to establish efficacy of *Loha bhasma* in diabetes, inter-relation between iron deficiency and increased HbA1C levels have been observed. [30,31] Thus paving a way to understand role of *Loha bhasma* in formulations related to *Prameha* management in *Laghutrayi*.

Clinical usage of *Prameha* formulations mentioned in *Laghutrayi*: Formulations with a nomenclature provided by *Laghutrayi* were reviewed for market availabity, although in general they are available they need extensive clinical research evidence. *Nishamalaki* (powder and tablet form), *Triphala* (powder and tablet form), *Chandraprabha vati, Shilajatu, Vasanatakusumakara rasa, Gokshuradi guggulu, Dhanvantara grita, Nyagrodadhi gana kvatha* are few of the formulations actively used by *Ayurveda* clinicians also available as market sample. *Simhamrita grita, Mehabadha rasa, Arjunadya taila, Arjunadya grita, Sara leha, Gokshurakadya leha, Asanadi yoga,* three different combinations of *Varadi kvatha* are not available as a market sample.

Conclusion

A total of 117 *Pramehahara* (anti-diabetic) formulations have been compiled from *Laghutrayi*. A total of 104 formulations with only herbal ingredients and 13 formulations with mineral origin drugs have been compiled from *Laghutrayi*. *Bhavaprakasha* text with highest enumerations (69 formulations), followed by *Sharangadhara samhita* (27 formulations) and *Madhava chikitsa* (21 formulations) respectively. *Triphala* is the highest enumerated herbal formulation in *Laghutrayi* (18 formulations), followed by *Daruharidra* (12 formulations). *Kvatha* (decoction) is the highest enumerated dosage form (55 formulations) in *Laghutrayi*. Honey is the most enumerated adjuvant in *Laghutrayi* (62 formulations). The present review may be of help in exploring formulations or drugs mentioned in *Laghutrayi* in future scientific studies and its utility in prevention or management of *Prameha* (Diabetes mellitus).

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