A CLINICAL STUDY TO EVALUATE THE ANTIHYPERGLYCEMIC ACTIVITY OF *BHANDIRA*

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ABSTRACT

Introduction: *Madhumeha (Diabetes mellitus) is a life style related, multifactorial disease with multiple facets involving all the Srotas, Dhatus and the Ojas. Madhumeha is a Vataja variety of Prameha, which manifests either due to Margavarana or due to Dhatu Kshaya.*

Diabetes mellitus is a clinical syndrome characterized by Hyperglycemia due to absolute or relative deficiency of insulin. Diabetes and its complication pose a major threat to future public health resources throughout the world. In this study an effort has been made to evaluate the Madhumehahara karma (Antihyperglycemic activity) of Bhandira (Clerodendrum infortunatum auct Non Linn)

Materials and methods: *The present study was an open labelled, single arm, clinical study in Madhumeha (Diabetes mellitus) (n=30) selected using convenience sampling technique with pre and post design conducted in a tertiary Ayurveda healthcare centre attached to a teaching institute, situated at the district headquarters in South India. 32 patients fulfilling the inclusion criteria suffering from Madhumeha w s r to Diabetes mellitus were selected with the intervention of Bhandira patra vati 3 Twice in a day (BD) for 30 days.*

Results: *The effect of therapy was assessed before and after treatment, the results were statistically analyzed; it showed significant changes in subjective parameters like praboota mutrata, avila mootrata, kshudadikya, karapada daha, and Objective parameter- Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS), Fasting Urine Sugar (FUS), Post Prandial Urine Sugar (PPUS)*

Conclusion: *Bhandira patra vati in a dose of 3 BD before food has shown better efficacy in subjective parameters like praboota mutrata, avila mootrata, kshudadikya, karapada daha, and Objective parameter like- FBS, PPBS, FUS, PPUS*

KEY WORDS: *Madhumeha, Anti-hyperglycaemic, Bhandira patra vati*

INTRODUCTION

Madhumeha is one among the '*Mahagada*'[1] which involves maximum number of *Srotas* and vitiates all most all the *Dhatus* and the *Ojus*. *Kapha* is the predominant *Dosha* and the important *Dushyas* are *Meda* and *Kleda*. The vitiated *Kapha* and *Pitta* obstruct the path of *Vata* causing its provocation which can be correlated to *Santarpanajanya* and *Apatarpanajanya* respectively.[2] Present study is emphasizing more on *Santarpanajanya Madhumeha*. The description of *Madhumeha* has many similarities with Diabetes mellitus in all most all the aspects; this is evident during conceptual study of the disease.

Diabetes mellitus is a metabolic disorder characterized by the presence of hyperglycaemia due to defective insulin secretion, defective insulin action or both. Type II Diabetes mellitus is the most common type accounting for almost 90% of all diabetes.[3]

Global prevalence of Diabetes mellitus is estimated to be around 374 million in 2017 and projected to increase to 587 million adults by 2045 equalling 8.4% of total population. It is more prevalent in low and middle income countries.[4] its incidence is also increasing at an alarming rate. There were 65 million prevalent cases of diabetes in India in 2016.[5] it has become utmost importance to find ways to combat this disease.

Bhandira is a gregarious shrub common throughout India.[6] It is easily available in all seasons and cost effective. One of its common folklore uses is in *prameha*.[7] Drug contains Scutellarin, Quercetin which are Flavonoids and proven as Nephro protective, anti oxidant and useful in reducing vascular inflammation.[8] The drug also contains Diterpenoids such as clerodin and clerodane which are proven to reduce blood sugar level in various experimental and animal studies,[9] One more anti diabetic chemical constituent found in *bhandira* is Hentriacontane which is a major chemical constituent in *Gymnema sylvestris* Hence this study has been conducted to evaluate the Antihyperglycemic activity of *Bhandira* in *Madhumeha*

AIMS AND OBJECTIVES
To Evaluate the *Madhumehahara karma* of *Bhandira patra vati* in *Madhumeha*

MATERIALS AND METHODS
Source of data: Patients attending the Outpatient department (OPD) of *Madhumeha* at a tertiary Ayurveda healthcare centre attached to a teaching institute, situated at the district headquarters in South India
Ethical Committee Approval Number –
SDM/IEC/25/2019
Clinical Trial Registry of India –
CTRI/2019/08/020941

CRITERIA OF EVALUATION
Diagnostic Criteria
For diagnosis detailed medical history and physical examination was done according to both Ayurvedic and Modern clinical methods

Inclusion Criteria
1. Subjects above 30 years of either gender suffering from Type 2 Diabetes mellitus will be taken.
2. RBS above $\geq$ **200 mg/dL.**[10]
3. FBS $\geq$ **126 mg/dL.**
4. PPBS level $\geq$**180 mg/dL.**
5. Those patients willing to participate in the study and who are ready to sign the informed consent form

Exclusion Criteria
1. Subjects with Type 2 Diabetes mellitus who are on insulin.
2. Subjects with Diabetic complications like Diabetic foot, Diabetic retinopathy, Diabetic neuropathy, Diabetic nephropathy and other secondary complications.
3. Patients with impaired Cardiac, Hepatic and Renal Functions
4. Pregnant and Lactating woman

STUDY DESIGN
The present study was an open labelled, single arm, clinical study in *Madhumeha* (Diabetes mellitus) (n=30) selected using convenience sampling technique with pre and post design conducted in a tertiary Ayurveda healthcare centre attached to a teaching institute, situated at the district headquarters in South India

LABORATORY INVESTIGATION
Following lab investigations will be performed for the diagnosis.
1. **Blood investigations:** FBS, PPBS
2. **Urine Investigations:** FUS, PPUS

DOSAGE AND DRUG ADMINISTRATION
Drug: *Bhandira patra vati*
Dosage: 3 BD (Each tablet of 500 mg)
Route of administration: Oral
Time of administration: BD Before food
Anupana: *Ushna jala*
Duration: 30 days

ASSESSMENT CRITERIA
Assessment will be done on 15th and 30th day of the treatment. Assessment table is given at (Table 1)

STATISTICAL ANALYSIS
- Friedman's test was applied to analyze the significance of change in Subjective parameters

- Wilcoxon signed rank test was done as post hoc with Bonferroni correction on parameters which show significance in Friedman's test, to interpret the time of significant change.
- Paired T test was done for analyzing the significance of objective parameters

OBSERVATION
In the present study total 60 subjects were screened, out of which 35 subjects were registered for the study, among them 32 subjects completed the study and 3 were dropped out

Among 35 completed subjects maximum (n=24) were from the age group of 31-60 years and predominance of Males (n=19) over females was found. 14 subjects were from middle class group and majority of them (n=19) were having sedentary life style. Diet wise distribution showed maximum (n=29) were having non veg diet. Considerable number of subjects (n=27) were not doing *vyayama* (Exercise), maximum number of subjects (n=27) were having family history

RESULTS
In the present study total 60 subjects were screened, out of which 35 subjects were registered for the study, among them 32 subjects completed the study and 3 were dropped out

32 subjects were administered with *Bhandira patra vati* in a dose of 3 BD Before food along with *Ushna jala* for a period of one month

Friedman's test was run on subjective parameters and has shown significant improvement in symptoms like *Praboota mootrata* Day and Night, *Avila mootrata, Kshudadikya, Karapada daha*. Results are placed at (Table 2)

Paired t Test was run on objective parameters like FBS, PPBS, FUS and PPUS and has shown significant improvements. Results are placed at (Table 3)

DISCUSSION
EFFECT OF THERAPY ON SUBJECTIVE PARAMETER
Effect on *Praboota mutrata*
There was significant reduction in frequency of micturition day time and night time (p < 0.001), Wilcoxon signed rank test as post hoc test with Bonferroni correction - 0.0166 also showed reductions in between D1 to D30 (p < 0.001)

Praboota Mootrata is due to increase of *Shareera Kleda* and due to *Draveekarana* of all *Dushyas*. The reduction in *Bahu mootrata* by *Bhandira patra vati* is by its *Tikta rasa* and *laghu, ruksha guna*, which does *Shoshana* of *Shareera*

Kleda and *Draveekrita Dushyas* leading to reduction in *Prabhoota Mootrata*

Effect on *Avila mootrata*
There was significant reduction in *Avila mootrata* (p < 0.001) Mean ranks also decreased significantly. Wilcoxon signed rank test as post hoc test with Bonferroni correction 0.016 showed significant reductions before and after treatment.

Avila mootrata is due to kapha dosha which results in turbid urine. *Bhandira* having *tikta rasa, ushna veerya* and *Katu Vipaka* helps in normalizing the urine by acting on vitiated *kapha dosha* which results in reduction of *avila mootrata*

Effect on *Kshudadikya*
There was significant reduction in *Kshudadhikya* with (p < 0.001) Wilcoxon signed rank test as post hoc test with Bonferroni correction 0.0016 showed reductions between D1 and D30

Bhandira having *tikta rasa, ushna veerya* helps in normalizing the vitiated pitta dosha thereby improving the normal appetite, it also acts as *deepana, pachana* thereby improving *Jataragni* and *dhatwagni* thus helps in treating the excessive hunger.

Effect on *Karapada daha*
There was significant reduction in *karapada daha* (p <0.001). Mean ranks also decreased significantly. Wilcoxon signed rank test as post hoc test with Bonferroni correction 0.0166 also showed reduction in D1 and D30 visits.

Karapada daha is due to pitta dosha which results in burning sensation in soles and palms *Bhandira* having *tikta rasa* acts as *pitta shamaka* also its having *teekshna guna*, *Ushna veerya* which acts as *sroto shodaka* thereby helps in reducing *karapada daha*

EFFECT OF THERAPY ON OBJECTIVE PARAMETER
Effect on FBS
There was gradual reduction in FBS with (p < 0.001) and mean difference of 26.25 which is statistically significant.

Effect on FUS
There was reduction in FUS with (p < 0.001) and mean difference of 0.45 which is statistically significant.

Effect on PPBS

There was significant reduction in PPBS with (p < 0.001) and mean difference of 43.88 which is statistically significant.

Effect on PPUS

There was reduction in PPUS with (p < 0.001) and mean difference of 0.50 which is statistically significant.

The drug contains Scutellarin, Quercetin which are Flavonoids and proven as Nephro protective, anti oxidant and useful in reducing vascular inflammation.[168]

The drug also contains Diterpenoids such as clerodin and clerodane which are proven to reduce blood sugar level in various experimental and animal studies

One more anti diabetic chemical constituent found in bhandira is Hentriacontane which is a major chemical constituent in *Gymnema sylvestris*

All these chemical constituents are effective in reducing the blood sugar level thereby helping in glycemic control.

BASED ON PROBABLE MODE OF ACTION OF *BHANDIRA*

Bhandira possess *Tikta Rasa*; *Laghu*, *Ruksha*, *Tikshna Guna*; *Ushna Veerya*; and *katu Vipaka*. It is *kaphavata shamaka*; *Vatahara* due to *ushna Veerya*; *Laghu*, *ruksha guna* produces *lekhana*, *rukshana* and *kaphahara* effect. Hence they act as *Kaphahara* and *Medhohara* according to *Samanya-Vishesha Siddhantha*.

Because of its Tikta rasa and Laghu, ruksha guna it helps in correction of *dhatwagni*. As *dhatwagni* is corrected *Dhatu kshaya* will be prevented and helps in nourishment of all the *dhatus*.

Preliminary phytochemical screening showed the presence of Carbohydrate, Saponins, Tannins diterpenoids and Flavonoids which exhibited highest reduction of blood glucose level with the percentage reduction of 46.99. [169]

The present study showed significant reduction in both subjective and objective parameters of *Madhumeha*. But only with medication it's not possible to control *Madhumeha* which requires regular medical care along with modification in Life Style, diet and exercise. This will help in management of the disease and also to reduce complications

CONCLUSION

Bhandira patra vati in a dose of 3 BD Before food along with *Ushna jala* for a period of one month has shown better results in subjective parameters like *Praboota mootrata* Day and Night, *Avila mootrata*, *Kshudadikya* and *Karapada daha* and also in objective parameters like FBS, PPBS, FUS and PPUS

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Table: 1 Self formulated Scale for assessment of Subjective parameters

SI NO	Assessment criteria	0	1	2	3
1.	*Prabhuta Mutrata* (polyuria) Frequency Day time- Night time-	3-5times Does not wake up	6-8 times Wake up once	9-11 times Wake up twice	>11times Wake up more than twice
2.	*Avila Mutrata* (Turbidity)	Crystal clear fluid	Faintly cloudy/smoky /hazy with slight turbidity	Turbidity clearly present but news print readable with difficulty through the tube	Turbidity clearly present & news print is not readable
3.	*Kshudhadhikya* (polyphagia)	Feels hunger at next *Annakala* only	Feels hunger for once in between the *Annakala*	Feels hunger twice in between *Annakala*	Feels hunger always
4.	*Karapada Daha* (burning sensation in palms and soles)	Absent	Mild burning sensation	Moderate burning sensation	Severe burning sensation

Table: 2 Showing effect of *Bhandira patra vati* on subjective parameters by applying Friedman's test

Parameters	N	Mean Rank	Chi Square(x^2)	p value	Remarks
Praboota mootrata BT	32	2.70	49.980	< 0.001	Significant
Praboota mootrata 15th Day		2.13			
Praboota mootrata 3Oth Day		1.17			
Praboota mootrata BT	32	2.78	50.515	< 0.001	Significant
Praboota mootrata 15th Night		2.02			
Praboota mootrata 3Oth Night		1.20			
Avila mootrata BT	32	2.73	45.648	< 0.001	Significant
Avila mootrata 15TH DAY		1.95			
Avila mootrata 30TH DAY		1.31			
Kshudadikya BT	32	2.78	47.290	< 0.001	Significant
Kshudadikya 15TH DAY		1.89			
Kshudadikya 30TH DAY		1.33			
Karapada daha BT	32	2.73	48.639	< 0.001	Significant
Karapada daha 15TH DAY		2.05			
Karapada daha 30TH DAY		1.22			

Table: 3 Showing effect of *Bhandira patra vati* on Objective parameters by applying Paired t Test

Parameter	Mean		Paired Difference					
	BT±SD	AT± SD	Mean difference	SD	SE	't' value	'p' value	Remark
FBS	181.40	155.15	26.25	18.62	3.29	7.974	0.001	S
FUS	0.76	0.31	0.45	0.34	0.06	7.440	0.001	S
PPBS	240.84	196.95	43.88	27.89	4.93	8.899	0.001	S
PPUS	1.48	0.98	0.50	0.40	0.07	7.043	0.001	S