

CLINICAL STUDY ON CHIRABILVA (*Holoptelia integrifolia* Planch.) WITH SPECIAL REFERENCE TO ITS ROLE IN HYPERGLYCAEMIA

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ABSTRACT

All the 50 patients were registered for the study after clinical and laboratory examination as per our protocol out of 50 patients, 30 patients turned up for full follow up. All diagnosed patients were divided into three groups consisting of 10 patients each. Group A consisting of 10 patients which were treated with a standard drug i.e. oral hypoglycemic agents i.e. Gliclazide. Patients of Group B (comprising 10 patients) were treated by only trial drug (water soluble solid extract of *Chirabilva*), while group C comprising of 10 patients were already taking OHA but were found to have raised blood sugar

level, allowed to continue modern treatment in the same dose along with our trial drug. After the initial registration and basal study all patients were randomly recruited in respective trials groups and were given the treatment regularly as per the schedule. The 500 mg capsule of trial drug was prescribed in a dose of 2 capsules daily into two divided dose half an hour before major meals for a period of 3 months, they were advised to visit at monthly interval for assessment of therapeutic response.

KEYWORDS: *Chirabilva*, oral hypoglycemic agents i.e. Gliclazide. Patients.

INTRODUCTION

The disease Diabetes Mellitus (DM) is one of the gravest disease of present era and is a great challenge to the scientist of medical field, due to its gravity and perplexing complications. Now in the present era because of modified lifestyle majority of population has become prone to it and its incidence is continuously rapidly increasing. Not only the disease but its

devastating complications are a great threat to the mankind. This disorder is gradually progressive and irreversible, and when occurs remains for the rest of one's life. It roughly affects 7 to 8% of population. At any given time an equal number of cases are undiagnosed. It is responsible for significant morbidity among the affected individuals and also acquired prominent position in the list of cause of blindness and renal failure. Diabetes mellitus (Madhumeha) is a worldwide chronic disorder with prevalence rate of 0.24 – 5.5%. The rate has increased to some extent about 6% in United State of America and European Countries. In older adults prevalence rate varies extremely from 20% to 30%. There are many factors that play role in the development of this disease including environment, nutrition, infection, genetic predisposition and side effect of modern drugs. It is not only a problem of present time but Diabetes mellitus was known to ancient Indian physicians as "Madhumeha". So many herbal and animal products including several metals/minerals (incorporated with herbs) have been described for the treatment of diabetes in the ancient literature. The method of management, as composite scheme of diet control, exercise, yoga, shodhan therapy and medication have all been claimed to be of beneficial value in the literature. Special regimen of diet, including whole barley, wheat and gram flour (without removing bran) with bitter vegetables has been mentioned much helpful to diabetic patients. The ancient Indian physicians have left a great heritage especially regarding the diagnosis and treatment of diabetics. They have not only described the general syndrome of "Prameha" but have also differentiated (Diabetes insipidus), Ikshumeha (glycosuria) and Madhumeha (Diabetes mellitus) properly. Diabetics were classified in two groups – obese and thin and different therapeutic approaches regarding diet, drugs, exercise and yoga were suggested for them. They have given precise and practical approach through drug as well as diet therapy.

The selected drug Chirabilva possess Tikta, Kashaya rasa and have Pramehaghna action, therefore drug seems to be rational for the treatment of madhumeha.^[1] The entire present research work has been presented scientifically in the following way. In this research work it was tried to assess the efficacy of the drug on two major aspects i.e. subjective and objective profile. In subjective profile history taking, symptoms and physical examination as per our protocol was done. The objective profile included the assessment of result on the basis of BMI, blood sugar (fasting and post prandial) and serum cholesterol.

MATERIAL AND METHOD

All the 50 patients were registered for the study after clinical and laboratory examination as

per our protocol out of 50 patients, 30 patients turned up for full follow up. All diagnosed patients were divided into three groups consisting of 10 patients each. Group A consisting of 10 patients which were treated with a standard drug i.e. oral hypoglycemic agents i.e. Gliclazide. Patients of Group B (comprising 10 patients) were treated by only trial drug (water soluble solid extract of *Chirabilva*), while group C comprising of 10 patients were already taking OHA but were found to have raised blood sugar level, allowed to continue modern treatment in the same dose along with our trial drug. The 500 mg capsule of trial drug was prescribed in a dose of 2 capsules daily into two divided dose half an hour before major meals for a period of 3 months, they were advised to visit at monthly interval for assessment of therapeutic response.

Selection of Drug

There are many drugs available for a disease and one drug for many diseases. This is available in our Ayurvedic texts i.e. samhitas. The object of exploring samhitas is to find out the base for its various rational therapeutic applications and also to think upon its other probable use. This is evident from the pathogenesis of Madhumeha that due to the causes mentioned, the kapha, pitta and medas aggravate excessively leading to Avarana (obstruction) of Vata, due to which vata gets provoked and carries ojas to basti and produces Madhumeha.^[2] Therefore, the selection of drug was aimed to achieve possible controls over the aetiological factors and Samprapti vighatana.

Criteria for selection of the Chirabilva in Madhumeha

We found following basis on which we selected Chirabilva for this study -

1. The drug Chirabilva is Kashaya in Rasa. (Dravyagunavigyana Vol. 2, page 817). Being Kashaya rasa the drug has "Stambhana property" and supposed to alleviate "Bahumutrata".
2. The drug Chirabilva is Ruksha in guna^[3] (Dravyagunavigyana Vol. II, page 817). Being Rukshaguna the drug has potent kaphanashaka action which is desirable because "Bahudravah Shleshma Dosha Visheshah" – the kapha is the main dosha involved in causation of all the Pramehas.
3. The drug Chirbilva is included in the aragvadhadi of Sushruta Samhita (Su.Su. 38/6-7). The drug of aragvadhadi gana are used in Prameha, Kushtha, Jwara, Vamana and Kandu, reduces kapha and Visha and also purify the wound.
4. Charak has indicated Chirabilva in Lekhaniya and Bhedaniya Mahakashaya which denotes

its action of Lekhana and Bhedana which is desirable to clear the channels (Srotorodha).

5. Vagbhata has also indicated Chirbilva in Aragvadhadi, Varunadi and Asanadigana which were used in the disease of prameha.

6. Having Ushna virya it may be used for kaphavata shamana which is the root cause Madhumeha.

7. Chirabilva has Laghu guna that can alleviate the kapha and meda.

8. Vagbhata has described that Chirabilva has Rasayana properties in "Kshata Kshaya Chikitsa". This Rasayana property is useful for Krisha pramehi.^[4]

9. The drug Chirabilva described in Varunadi-gana of Susruta and Vagbhata. Drugs of Varunadi gana have been indicated for many diseases including Prameha.

Collection of Drug

The trial drug Chirabilva was collected from the Ayurvedic garden, Department of Dravyaguna, IMS, BHU, stem bark of the Chirabilva was dried in shade and cut into small pieces and then sent to Rasa Shastra Department, where ghanasatva was prepared.

Dose and duration of Treatment

According to Sharangdhar, the dose of churna is 1 karsa (i.e. 12 gms). After the decoction of chirabilva stem bark further heated and evaporated, the ghansatva is obtained.^[5]

In 25 kg of churna 5 kg of Ghansatva has been obtained. It means that 1 kg (1000 gm) churan yields 1/5 kg (200 gm) Ghansatva. It means that:

One Karsha of churna = $12 \times \frac{1}{5} = 2.4$ gm of Ghansatva.

Thus, the human dose of Chirabilva Ghansatva calculated for an average of 70 kg man is 2.4 gm per day. The duration of the treatment was planned for three months. The patients were assessed at monthly periodic period intervals.

Study setting and patients

The study was conducted at Diabetic Clinic O.P.D./I.P.D. of the -Department of Dravyaguna, S.S.Hospital, Banaras Hindu University, Varanasi.

Study population

The study recruited population of 50 diagnosed patients of Type II diabetes mellitus.

Enrolment Criteria^[6]

1. Patients of either sex and age suffering from clinical condition of Madhumeha (Type 2 DM).
2. Patients having classical presentation of DM type II like polyuria, polydipsia, polyphagia, rapid or severe loss of weight.
3. Patients having symptoms of neuropathy, and recurrent urinary infections and female patient having vulvitis.
4. Patients having associated disorders such as Hypertension, obesity, cardiac disease etc.
5. Patients having BMI > 24 kg/m²

Study Design**Pretreatment Evaluation**

- All the patients were studied at the time of registration regarding their age, sex, address, occupation, education, monthly income, life styles, and dietary habits.
- After preliminary registration, patients were subjected to detailed case history taking and physical examination as per following our protocol (Annexure 1) which included -
 - Chief complaints with severity and duration.
 - Past history
 - Family history
 - Personal history
 - Treatment history
 - Physical examination

In general examination, built, pulse, B.P. weight, BMI etc. are recorded. Systemic examination was conducted for detail check up to explore any complications of DM.

Exclusion Criteria

The patients of following conditions were excluded from this study.

1. Patients with chronic arthritis (i.e. due to regular ingestion of steroid which may induce DM).
2. Patients having other chronic diseases like tuberculosis leprosy etc.
3. Patients with diabetic Keto acidosis and having other severe complications who need emergency treatment.
4. The cases of type 1 DM.

Diagnostic Criteria of DM**Clinical diagnosis**

- Classical symptoms of polydipsia, polyuria and polyphagia.
- Sudden and excessive weight loss.

Laboratory diagnosis**Biochemical investigations**

- Fasting Blood Sugar $\geq 120\text{mg/dL}$.
- Postprandial Blood sugar $\geq 200\text{mg/dL}$.
(Consensus panels of experts from the National Diabetes Group and the WHO).
- Lipid profile, Total cholesterol, Triglycerides, LDL, HDL, VLDL were evaluated.
- Total Serum cholesterol

Desirable $< 200\text{ mg/dL}$

Border High risk $200 - 239\text{ mg/dL}$

High risk $\geq 240\text{mg/dL}$

After a confirm diagnosis of DM the patients were subjected for thorough routine examination viz.

1. Hb%, TLC, DLC, ESR
2. Blood urea, serum creatinine
3. Urine routine and microscopic

Radiological investigation

X-ray Chest-PA view was conducted to exclude any lung pathology.

ECG was conducted to exclude heart diseases.

Plan of Study**Treatment Schedule**

Out of 50 patients only 30 patients returned for the followup. These were randomized to three groups namely A, B and C having 10 patients in each.

Group A

Patients of this group were treated with a known hypoglycaemic agent i.e. gliclazide. This group is kept for comparison.

Group B

Patients of group B received test drug i.e. water soluble solid extract of Chirabilva according to the severity of diseases.

Group C

Patients of Group C were treated with a combination of known drug + our test drug.

Evaluation parameters for assessment of drug efficacy

Both subjective and objective parameters were taken for assessment. Subjective criteria of evaluation included both patient and physician assessment.

Patient assessment

On this assessment the symptomatology is classified into grades during and after treatment. The clinical symptomatology was graded into four grades (1-4) scale on the basis of severity and duration.

Grading of Classical symptoms of DM**I. Fatigue : Graph 1**

Grade:

1. Fatigue on severe exertion.
2. Fatigue occurs on moderate activity.
3. Fatigue occurs on mild or ordinary activity.
4. Fatigue occurs even at rest.

II. Polyuria : Graph 2

Grade: Frequency at night

1. 0 - 2 with normal volume
2. 3 - 4 with increased volume
3. 4 - 6 with excessive volume
4. > 6 with excessive volume

III. Polydipsia : Graph 3

Grade: Frequency in 24 hours

1. Normal
2. Once in every 3 hours and not urgent.
3. Once in every hour and urgent.
4. Twice in every hour and very urgent.

IV. Polyphagia : Frequency in 24 hours : Graph 4

Grade: Breakfast Main meals

- | | | |
|----|-------|----|
| 1. | 2 | 2 |
| 2. | 3 – 4 | 3 |
| 3. | 5 – 6 | 3 |
| 4. | > 6 | >3 |

V. Loss of Weight

Grade: Loss of Weight (Kg)

- | | |
|----|-------|
| 1. | 0 - 2 |
| 2. | 2 – 4 |
| 3. | 4 - 6 |
| 4. | > 6 |

VI. Burning and tingling sensation : Graph 5

Grade: Sensation

1. Normal, (no sensation of burning & tingling in palm & soles).
2. Sense of Burning and tingling in palm and soles of mild degree.
3. Sensation like crawling of ants all over the body & burning that disturb the patient's life.
4. Loss of sensation.

Physician assessment : Graph 6,7

1. Assessment of Quetlet's Index (Body Mass Index) BMI

$$= \text{Weight in Kg} / (\text{Height in meter})^2$$

Assessment of drug efficacy on BMI was done under two heading

- i. Effect on BMI of Sthool pramehi - (BMI-22-28kg/m²)
- ii. Effect on BMI of Krisha pramehi - (BMI-<20kg/m²)

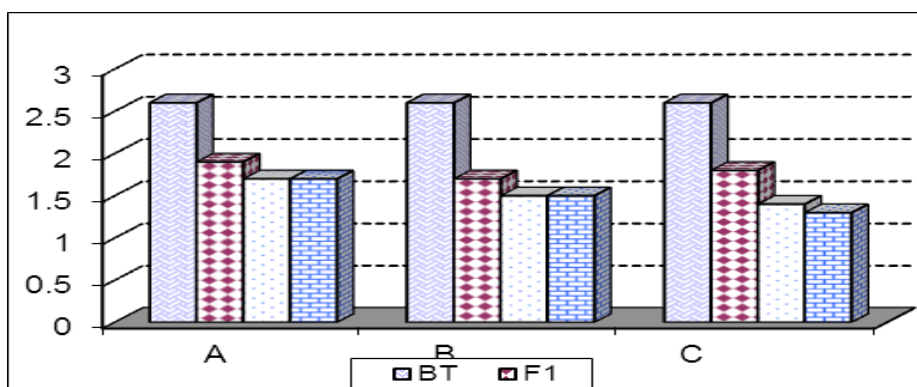
Objective Parameters**Biochemical Parameters:** Graph 8,9,10

1. Reduction in Fasting Blood Sugar
2. Reduction in Postprandial Blood Sugar level
3. Reduction in Serum Cholesterol level

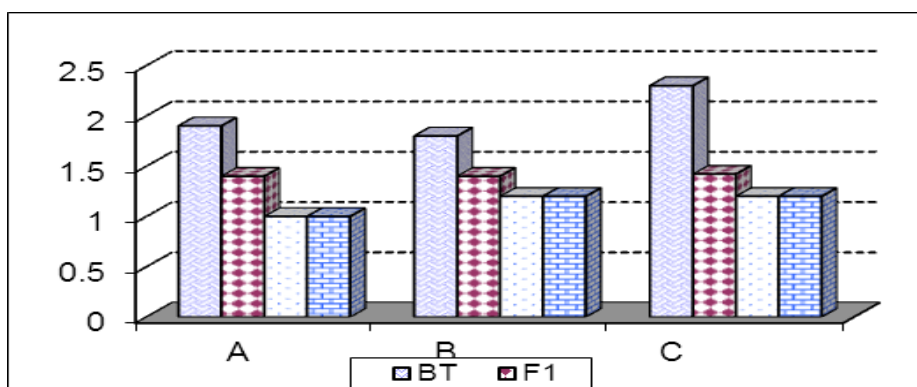
OBSERVATION AND RESULTS

The observation and results have been made in the present work under the following headings.

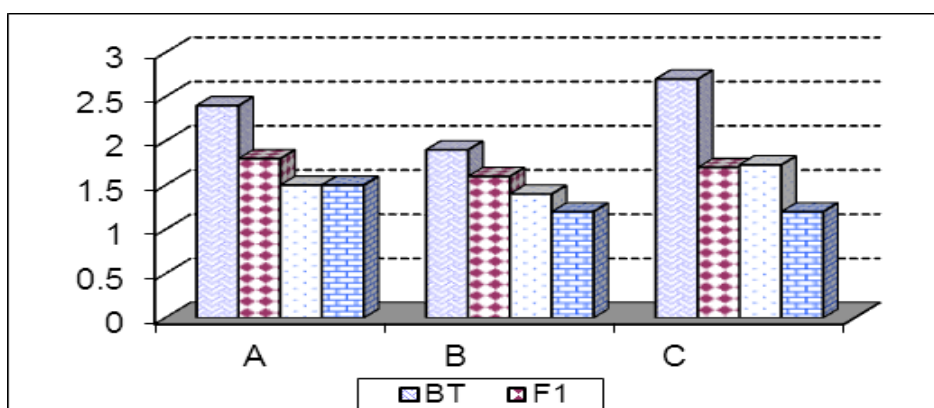
1. Demographic profile : These observations were made in 50 registered cases.
2. Clinical profile : These observation were made only among 30 cases who attended regular follow up.
3. Results of therapeutic trial.



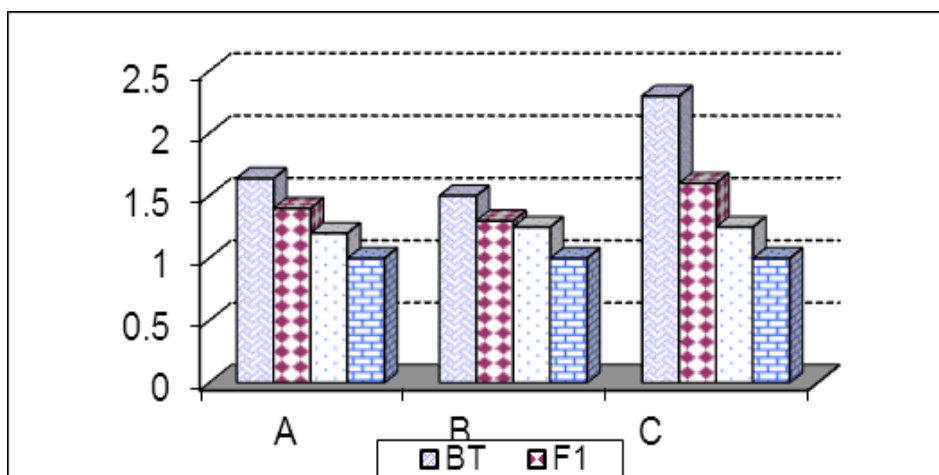
Graph 1: Shows the effect of treatment on fatigue in 30 patients



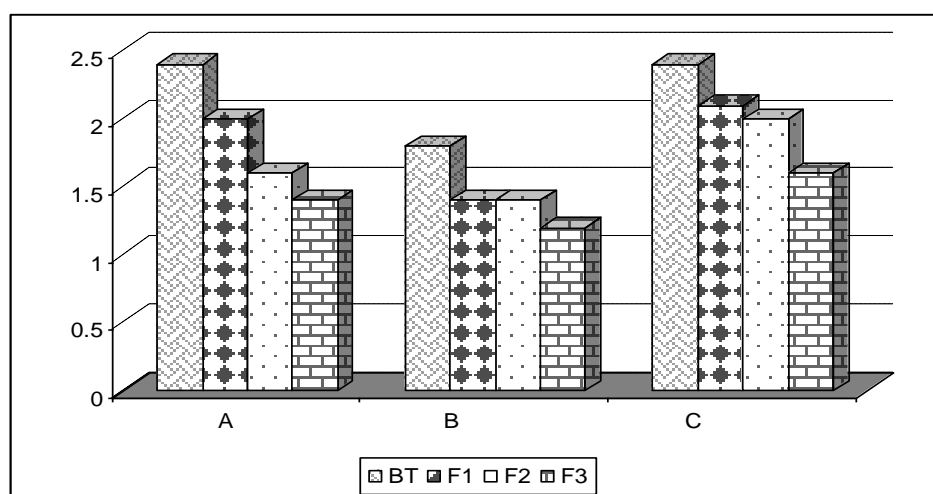
Graph 2: Shows the effect of treatment on Polyurea in 30 patients of madhumeha



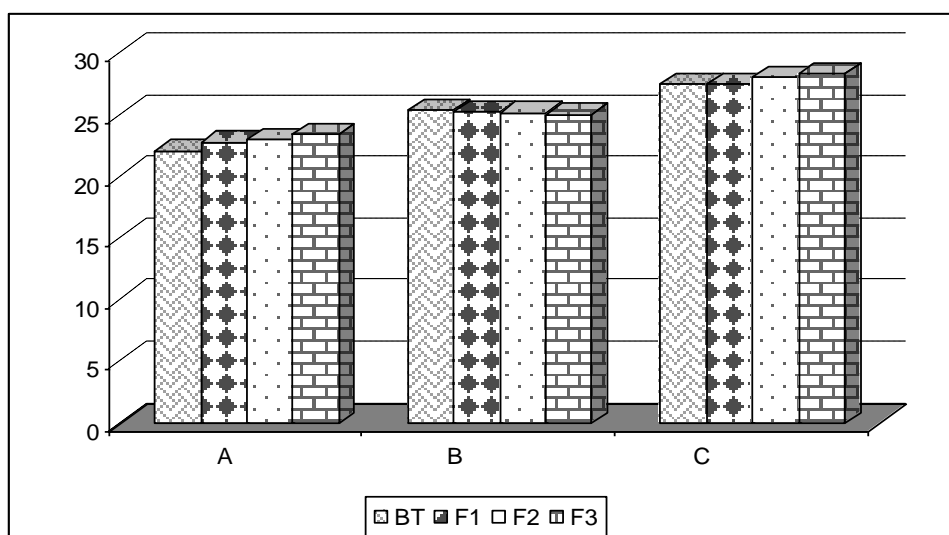
Graph 3 : Shows the effect of treatment on Polydipsia in 30 patients



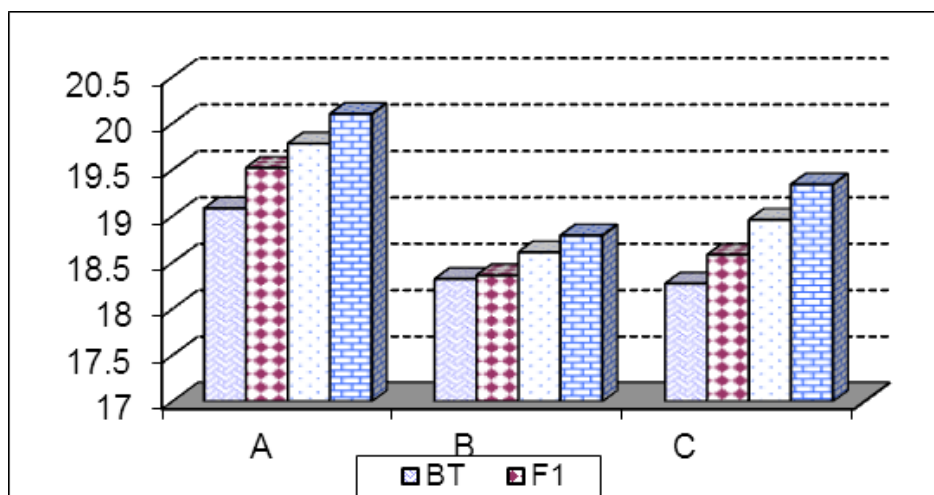
Graph 4: Shows the effect of treatment on Polyphagia in 30 patient



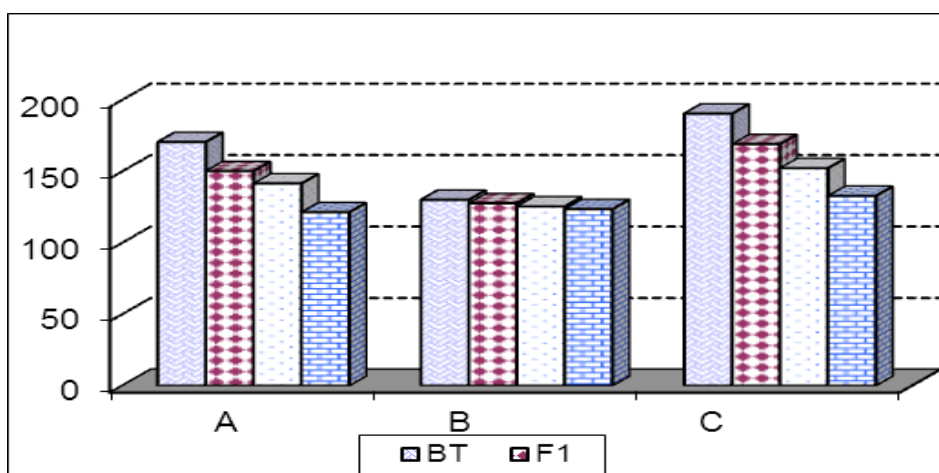
Graph 5: Shows the effect of treatment on Burning and tingling sensation in 30 patients



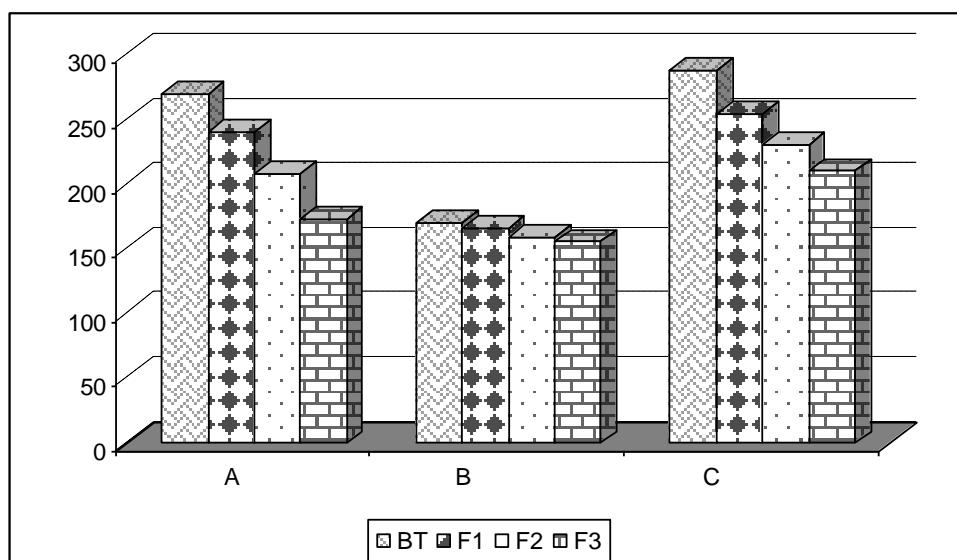
Graph 6 : Shows the effect of treatment on BMI / Sthoola Pramehi



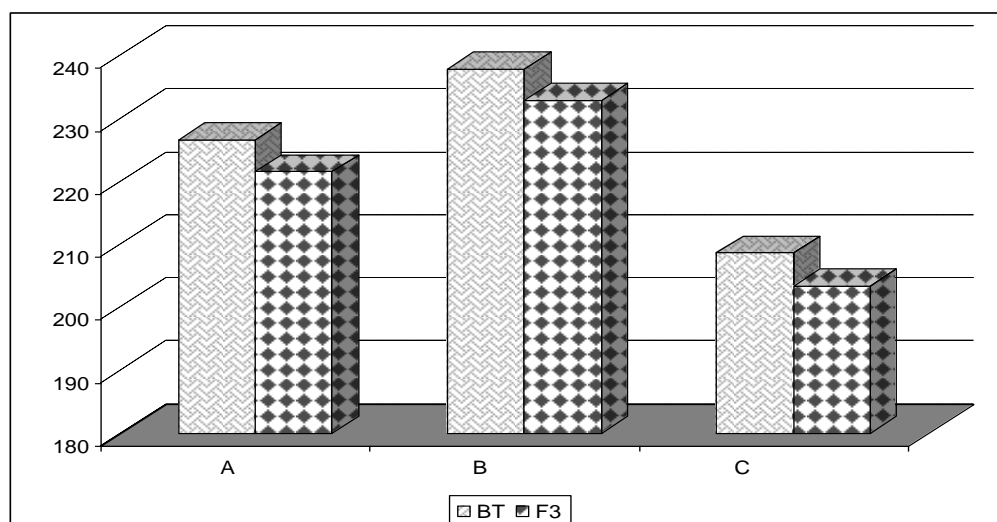
Graph 7 : Shows the effect of treatment on BMI in Krisha Pramehi



Graph 8 : Shows the effect of treatment on Fasting Blood Sugar



Graph 9 : Shows the effect of treatment on Post prandial Blood Sugar



Graph 10: Shows the effect of treatment on serum cholesterol

DISCUSSION

Prameha has been included among Mahavyadhis and it has got very close relation which rich calorie foods. Havish of yagya performed by Daksha Prajapati was eaten by some Rishi and he developed Prameha (Madhumeha i.e. Diabetes mellitus). The Prameha is of 20 types. The Madhumeha is one of them. Acharya given the name of Mahatyayika for Madhumeha because it is very difficult to treat. It originates due to Vata prakopa either by obstruction of vessels (i.e. Srotorodha) or by Dhatukshaya. In both the ways the vata prakopa is quite apparent in this particular disease. Medicinal value of plant *Chirabilva* was known since the era before Christ. References of *Chirabilva* are mentioned in Charaka Samhita, Susruta Samhita and Vagbhata providing its effect in disease Prameha. In Sushruta Samhita, *Chirabilva* is included in “Salasaradi gana”. Ingredient of Salasaradigana are said to have potent Madhumehahara action.

As mentioned in Nighantu Granthas the properties of *Chirabilva* are Tikta and Kashaya in rasa, Laghu and Ruksha in Guna. Its Vipaka is Katu and Virya is Ushna. All the properties of drug favour its action in Madhumeha. According to Acharya Charaka some drugs act by Rasa, some by virtue of Virya or Guna or Vipaka, or sometimes empowered by Prabhava. Charaka says about drug action that some drugs act by its own prabhava (i.e. Dravya Prabhava) some act by virtue of Guna (Guna prabhava) and some act jointly by virtue of both (Dravya and Guna Prabhava). After going through Samprapti of Madhumeha and after analyzing the results which was encouraging and on looking the pharmacokinetic profile of *Chirabilva* it's found that only Kasaya rasa, Laghu, Ruksha guna go in favour of the action of

Chirabilva observed in present work. After a lot of discussion we came to this conclusion that some of the actions performed by *Chirabilva* are by virtue of its 'Gunaprabhava' and others may be attributed to Dravyaprabhava. Meaning to say that *Chirabilva* acts by Dravyaguna prabhava.

As mentioned in the disease review (Ayurvedic) on the basis of Aetiopathogenesis, Madhumeha may be of two types:

1. Kshayajanya
2. Avaranajanya

According to Charaka all types of prameha are tridoshaja and primary cause of all types of Prameha are Kapha and meda. *Chirabilva* having Laghu Ruksha guna alleviates disease of Kapha and Meda. Rasa of *Chirabilva* is Kashaya which alleviates Kapha and being stambhana, it is useful in Bahumutrata.

Present work comprises of following studies:

1. Preliminary Phytochemical and pharmacological study.
2. Experimental evaluation of hypoglycemic activity of *Chirabilva*.
3. Clinical evaluation of *Chirabilva* in madhumeha.

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CONCLUSION

The drug *Chirabilva* was explored on literary, pharmacognostical and phytochemical grounds. Its rationality for use in Madhumeha was established. Clinical trials have shown satisfactory results by fulfilling all the criterion which are said to be beneficial for Diabetics. *Chirabilva* was proved to be useful, rational and harmless remedy for Madhumeha. It is to be noted that patients of only mild to moderate DM have been included in this study and the control over blood sugar level were achieved not so quickly by *Chirabilva* as compared to modern hypoglycemic drugs. However, this was a preliminary and pilot study on *Chirabilva* with special reference to its hypoglycemic activity which needs further studies for its proper pharmacological effects. After all I hope this study will be proved useful for future researches.

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