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# Clinical Efficacy of Traditional Indian Gold Containing Preparation: *Triguna Balijarita Makaradhwaja* Prepared By *Swarna Bhasma* in Type II Diabetes Mellitus (*Madhumeha)*

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**Abstract**

*Background and Objectives:* A huge number of drugs have been emphasized in Ayurveda like *Makaradhwaja* (mercurial preparation), *Guduchi Ghana* (dried extract of *Tinospora cordifolia* Linn) etc. in the treatment of *Madhumeha* (Diabetes mellitus). Nevertheless, their efficacy was not reported till date. Considering this, it is attempted to evaluate its efficacy in the patients of Type-II Diabetes Mellitus. *Methods:* 34 patients were screened for diabetes in the OPD of Ayurvedic Hospital, IPGT & RA, Gujarat Ayurved University, Jamnagar. Signs and symptoms of diabetes and history were recorded. 125 mg of *Makaradhwaja* and 125 mg of *Guduchi Ghana* with honey were administered for four weeks daily to the patient. Patients follow up was carried out for next four weeks. *Results:* Significant decrease in symptoms of diabetes and fasting and postprandial sugar level were observed ($P<0.001$) insignificant decrease in serum urea, serum creatinine, serum triglyceride and SGPT levels were observed. Minimal increase in serum cholesterol, total protein and SGOT levels were observed. *Conclusion: Makaradhwaja* at significant extent attenuated symptoms of Type-II diabetes mellitus. Both fasting and post prandial sugar levels were decreased significantly. *Makaradhwaja* has anti hyperglycemic effect as well as synergistic action with dried extract of *Tinospora cordifolia* and Honey.

**Keywords:** Diabetes Mellitus; *Guduchi Ghana*; *Kupipakwa Rasayana*; *Madhumeha*; *Makaradhwaja*.

## Introduction

Diabetes mellitus is a metabolic disorder with impaired glucose tolerance. It causes micro and micro complications like diabetic neuropathy, nephropathy, retinopathy, keto-acidosiss finally which leads to death. As per the WHO data, it will be the major cause of death in recent era. In 2012, an estimated 1.5 million deaths were directly caused by diabetes. Recently compiled data show that approximately 150 million people have diabetes mellitus worldwide, and that this number may well double by the year 2025. WHO projects that diabetes will be the 7th leading cause of death in 2030 [1]. According to the Indian Heart Association, India is the diabetes capital of the world with a projected 109 million individuals with diabetes by 2035 [2]. The disease currently affects more than 62 million Indians, which is more than 7.1% of India's adult Population [3].

Management of Diabetes mellitus primarily includes Metformin, Sulfonylureas, Thiazolidinediones, GLP-agonists, DPP-IV Inhibitors, Meglitinides, Alpha-glucosidase inhibitors. In spite of many advances, the allopathic management of diabetes is still remains unsatisfactory having common side effects like nausea, diarrhea, hypoglycemia, weight gain and swelling of the feet and ankles etc. Complications like Insulin resistance, hypersensitivity, drug intolerance, and hypoglycemic episodes make it even more important to search out safe, effective drugs [4]. Alternative and complementary system of medicines is one of new hope in this field.

This condition, Diabetes mellitus can be compared with *Madhumeha* that was referred centuries ago, in Ayurveda. Most of the Ayurveda texts explained the etiology, patho-physiology, treatment of disease

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proper and its complications in detail [5]. It was mentioned that *Madhumeha* mainly causes due to altered life style and in its management several herbal, herbo-mineral, metallic preparations were mentioned. *Guduchi* (*Tinospora cordifolia* Linn) [6] and *Makaradhwaja,* gold containing mercurial preparation [7-9] are among such formulations. Though these drugs are claimed to be beneficial in *Madhumeha,* published evidences are not available. Few works validated safety and efficacy of *Makaradhwaja* in experimental animals [10-15]. Immouno-modulatory, anti-diabetic and anti-rheumatoid effect of *Makaradhwaja* were also reported [12, 16-17]. Here in present study it was planned to evaluate clinical efficacy of *Makaradhwaja* with *Guduchi Ghana* and honey in *Madhumeha* (Diabetes Mellitus).

## Materials and Methods

### *Preparation of Drug*

*Makaradhwaja* is prepared in modified electrical furnace (Modified *Valuka Yantra*). Procedure of *Triguna Balijarita Makaradhwaja* preparation was followed. Raw materials like incinerated gold (*Swarna Bhasma*), processed mercury (*Parada*) procured from the processed *Hingula* (cinnabar) and processed sulfur (*Gandhaka*) in the ratio 1:8:24 were used for the preparation following standard operative procedure [9]. Incinerated Gold [18-19] was prepared in the department of Rasashastra and Bhaishajya Kalpana, IPGT & RA, Gujarat Ayurvedm Uniersity, Jamnagar. Cinnabar and sulfur was procured from the pharmacy of Gujarat Ayurved University Jamnagar. Cinnabar was processed and mercury was procured from it by *Nadayantra* [20]. Sulfur was processed and powdered [21]. Amalgamation of incinerated gold and Mercury was done in mortar and pestle of stone manually and then sulfur was added to it and triturated up to *Kajjali* formation. *Kajjali* was levigated with juice of flowers of *Hibiscus rosa sinensis* Linn. (*Japa*) and juice of *Aloe barbadensis* Miller. (*Kumari*) respectively for three hours. The mixture was sundried and filled in seven mud smeared cotton cloth glass bottle. This glass bottle was heated in the modified electrical muffle furnace with increasing manner of heating. The sublimed product was collected and powdered after self cooled [18]. In analytical studies, it was observed that *Makaradhwaja* is consisted of red sulfide of mercury and having an empirical formula of HgS. Inductively coupled Plasma optical emission spectrometry (ICPOES) was observed that it contains 19 ppm gold as a minor element.

*Tinospora cordifolia's* stem was collected from the herbal garden of Gujarat Ayurved University Jamnagar. The stems was crushed and cut in to small pieces. These pieces were cooked with four times of potable water ant reduced at $1/4^{th}$ of the same to prepare decoction. The decoction was sieved, cooked to semisolid consistency. The semisolid mass was dried in hot air oven at $45^0$C to prepare dry extract [22]. The dried extract was powdered and stored.

Honey was collected from the local forest of Jamnagar.

### *Patients*

Patients of either sex with fasting serum glucose >125 mmol/L or 2- h glucose >200 mmol/L from the OPD of Rasashastra & Bhaishajya Kalpana, I.P.G.T. & R.A., Gujarat Ayurved University, Jamnagar were included in to the study. Patients of Type I DM, taking insulin therapy, or serious complications such as cardiac/cerebral vascular diseases, or renal dysfunction were excluded from the study. The study was approved by the Institutional Ethics committee and all participants gave informed consent. Total 34 patients were enrolled in this study. Out of 34 patients, 30 patients completed duration of medicine where as 4patients discontinued treatment due to inconvenience of travelling of long distance (Table 1).

### *Study Design*

Patients were assigned in single blind study.

### *Administration of Drug*

Trial group received 125 mg of *Makaradhwaja* and 125 mg of dried extract if *Tinospora cordifolia* in capsules twice a day. Patients were instructed to open the capsule carefully and mix it with one teaspoon honey and advocated for licking. It was advised to take the medicine 45 min before meal. Test drug was termed as TBM (Triguna Balijarita *Makaradhwaja*).

### *Investigations*

Hematological examinations like Hb %, ESR (erythrocyte sedimentation rate), and biochemical like Blood sugar level (BSL) (Fasting and post-prandial), Lipid profile, Liver function test & Renal Function Test were carried out before and after treatment.

### *Criteria for Assessment*

The obtained results were measured according to the grades like

- Complete control of the disease;100% relief,
- Marked improvement; ≥ 75% relief to 99% relief,
- Moderate improvement; ≥ 50% up to 75% relief,
- Mild improvement; ≥ 25% up to 50%
- No improvement; < 25% relief.

*Statistical Analysis*

The obtained data were expressed as MEAN ± SEM. The data were analyzed by paired 't' test, a level of $P < 0.05$ and $P < 0.01$ were considered as statistical significant.

*Demographic Observations*

Up to one year chronicity was observed in 12.12% of the patients and 87.87% had chronicity above 1 year (Graph 1). 41% patients were female while 59% patients were male (Graph 2). Maximum patients were found to be age group 40-60 years i.e. 51.51% while 39.39% in > 60 years and 09.10% in 20-40 years (Graph 3).

*Clinical Observations*

Polyuria (*Prabhutamutrata*) was found in 100% patients whereas polyphagia (*Kshudhadhikya*) and numbness (*Kara-Pada Suptata*) were observed in 73.33% patients. 70% patients were with positive symptom of fatigue (*Daurbalya*). Polydipsia (*Trishnadhikya*) and tingling (*Kara-Pada-tala Daha*) were observed in 80 and 83.33 % patients respectively. Leg cramps (*Pindikodweshtana*) were found in 76.66 % patients respectively. Erectile dysfunction (*Klaibya*) was observed in 81.15 % male patients (Table 2).

Symptoms like polyuria, polyphagia, polydipsia, tingling, numbness, fatigue, leg cramps and erectile dysfunction were decreased significantly ($P<0.001$) (Table 2). Non significant increase in Hb%, serum protein, serum cholesterol, SGOT (Serum glutamic oxaloacetic transaminase) and alkaline phosphate (ALP) level were observed during study. Alternatively, non significant decrease were observed in ESR, serum triglyceride, HDL (High density lipoprotein), SGPT (Serum glutamic-pyruvic transaminase) and serum albumin values. Significant decrease in fasting ($P<0.01$) and postprandial blood sugar level ($P<0.001$) was observed. Blood urea (9.73%) and serum creatinine (9.06%) were decreased insignificantly (Table 3).

80.00% patients showed marked improvement and moderate improvement was observed in 16.67% patients. 03.33% patients found mild improvement on overall effect of therapy whereas know one showed complete control of disease (Graph 4).

No any adverse drug reaction or any untoward effects were observed during the trial. All the patients were allopathic medicines like metformin , glimipride etc. Pateints instructed to continue the allopathic medicines with test drug. No any withdrawal of allopathic medicines was observed after treatment. All the patients were previously diagnosed, not a single patient of freshly diagnosed was enrolled during study.

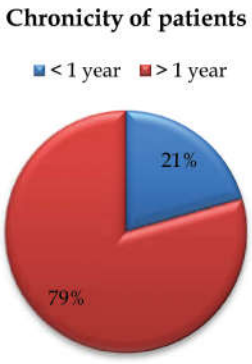


**Fig. 1:** Chronicity of disease wise distribution of 34 patients

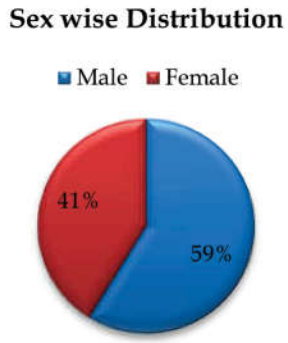


**Fig. 2:** Sex wise distribution of 34 patients

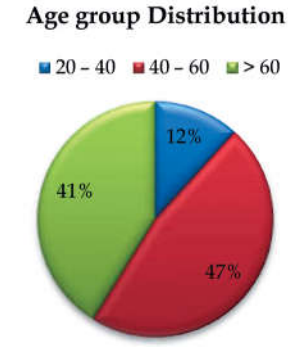


**Fig. 3:** Age wise distribution of 34 patients

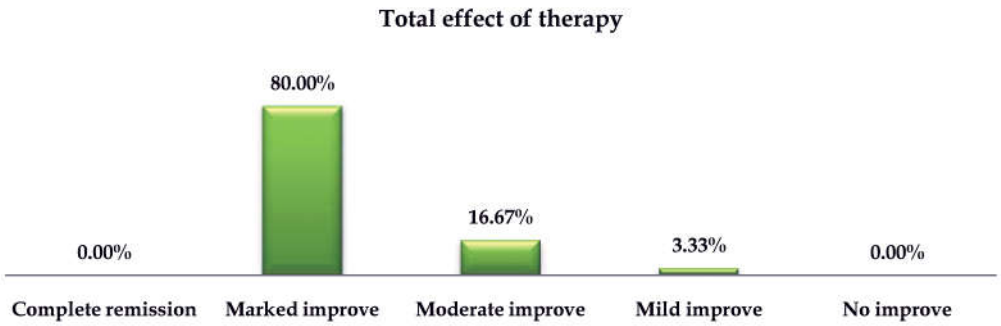


**Fig. 4:** Overall effect of therapy

**Table 1:** Distribution of 34 patients

| Total No. Patients enrolled | Completed patients | Discontinued patients |
|---|---|---|
| 34 | 30 | 4 |

**Table 2:** Effect of *triguna balijarita makaradhwaja* on cardinal symptoms, in the patients of Type II diabetes mellitus

| Symptom | N | % | Mean ± SEM | | | % change | 't' |
|---|---|---|---|---|---|---|---|
| | | | B.T. | A.T. | Change | | |
| Polyuria | (n=30) | 100.00 | 1.77±0.08 | 0.7±0.09 | 1.07±0.09 | 60.83↓ | 11.22** |
| Polyphagia | (n=22) | 73.33 | 1.41±0.09 | 0.34±0.09 | 1.10±0.10 | 78.05↓ | 10.60** |
| Polydipsia | (n=24) | 80.00 | 1.33±0.09 | 0.17±0.08 | 1.17±0.13 | 87.50↓ | 8.98** |
| Tingling | (n=25) | 83.33 | 1.48±0.10 | 0.24±0.08 | 1.24±0.09 | 83.78↓ | 14.22** |
| Numbness | (n=22) | 73.33 | 1.41±0.11 | 0.19±0.80 | 1.23±0.11 | 87.09↓ | 10.89** |
| Fatigue | (n=21) | 70.00 | 1.23±0.12 | 0.33±0.11 | 0.90±0.12 | 73.07↓ | 7.69** |
| Leg Cramps | (n=23) | 76.66 | 1.39±1.12 | 0.35±0.11 | 1.04±0.11 | 75.00↓ | 8.85** |
| Erectile Dysfunction | (n=13) | 81.15 | 1.84±0.22 | 023±0.12 | 1.58±0.18 | 83.33↓ | 8.33** |

* $p$ <0.01, ** $p$ <0.001, ↓= Decrease, ↑= Increase, n = Number of patients
B.T. = Before Treatment, A.T. =After Treatment.

**Table 3:** Effect of *triguna balijarita makaradhwaja* on hematological & biochemical parameters in the patients of type II diabetes mellitus

| Parameter | Mean ± SEM | | | % change | 't' |
|---|---|---|---|---|---|
| | B.T. | A.T. | Change | | |
| Hb% | 11.72±0.27 | 11.78±0.27 | 0.06±0.06 | 0.54↑ | 1.07 |
| ESR | 30.06±4.48 | 28.53±4.66 | 1.53±2.62 | 5.09↓ | 0.59 |
| BSL-Fasting | 214.11±15.63 | 181.70±14.05 | 32.4±13.82 | 15.13↓ | 2.34* |
| BSL Postprandial | 268±16.34 | 226.20±19.36 | 41.8±14.32 | 15.60↓ | 2.92** |
| Serum Cholesterol | 189.5±7.17 | 196.13±6.67 | 6.66±5.59 | 3.48↑ | 1.18 |
| Serum Triglyceride | 181.76±19.44 | 177.1±19.28 | 4.67±12.01 | 2.057↓ | 0.39 |
| Serum HDL | 50.3±2.43 | 50.07±1.74 | 0.23±3.28 | 0.46↓ | 0.07 |
| SGOT | 22.77±1.44 | 23.3±1.20 | 0.54±1.43 | 2.34↑ | 0.37 |
| SGPT | 23.3±1.99 | 21.5±1.68 | 1.8±1.5 | 7.72↓ | 1.18 |
| ALP | 71.77±2.80 | 75.73±4.57 | 3.97±3.69 | 5.52↑ | 1.07 |
| Blood Urea | 27.73±1.47 | 25.03±1.43 | 2.7±1.49 | 9.73↓ | 1.81 |
| Sr. Creatinine | 1.10±0.03 | 1.01±0.03 | 0.1±0.03 | 9.06↓ | 3.87 |
| Sr. Protein | 7.47±0.12 | 7.50±0.12 | 0.02±0.10 | 0.31↑ | 0.22 |
| Sr. Albumin | 4.22±0.05 | 4.20±0.04 | 0.01±0.05 | 0.39↓ | 0.33 |

* $p$ <0.01, ** $p$ <0.001, ↓= Decrease, ↑= Increase, n = Number of patients.
B.T. = Before Treatment, A.T. =After Treatment.

## Discussion

Maximum number of patients were from age group of 40-60 years. As per demographic evidences quoted by WHO it was mentioned that Type II diabetes mellitus diagnosed more after the forty ages. In the present study male patient of diabetes were more than female patients.

Significant decrease in subjective parameters might be due to rejuvenation effect of *Makaradhwaja*.

Decrease in fatigue and leg cramps may be inferred to increased energy levels in treated patients that might be due to antioxidant property of *Makaradhwaja*. Aphrodisiac property of *Makaradhwaja* appears to pacify erectile dysfunction. . Significant improvement observed in tingling sensation and numbness reveals that the drug has a role in diabetic neuropathy.

The improvement in the symptom polyphagia might be due to increase in energy levels of patients by controlling hyperglycemia, which reduced excessive hunger. Osmotic diuresiss caused by excess glucose may be reduced due to reduction in hyperglycemia may shown decrease in Polyurea [23]. As polyurea and ploydipsia are interlinked to each other, reduction in symptom polyurea might be reduced polydipsia [24].

Significant decrease in both fasting and postprandial sugar shows specific anti-diabetic action of *Makaradhwaja*. It might be due to insulinotrophic effect or biguanides type effect of test drug. Experimental study furthermore supports this action [17]. Exact pharmacological evidence is not known. Previous study reported that dried extract of *Tinspora cordifolia* and honey has insignificant results in diabetes mellitus [25]. So the results observed in the present study may be attributed to the *Makaradhwaja*.

Non significant decrease in blood urea was found may be due to increased metabolism of protein in liver. Breakdown of proteins results in the formation of ammonia which is very toxic and is immediately converted in to urea in liver and excreted through kidney in the form of urea. The decrease in blood urea level denotes decreased catabolism of proteins that which means increased glucose uptake for energy production which is very much helpful for the diabetic patient. It also implies increased functioning ability of liver as well as kidney. Insignificant increase in serum protein level was also observed. Decrease in Serum creatinine level may rise with increased GFR (Glomerular Filtration Rate) which finally protects kidneys from nephropathy. 80.00% patients showed marked improvement, it shows *Triguna Balijarita Makaradhwaja* having specific action on Type II diabetes mellitus. It might be possible that *Makaradhwaja* having synergistic action on diabetes with dried extract of Tinospora cordifolia and honey.

## Conclusion

*Makaradhwaja* at significant extent attenuated symptoms of diabetes mellitus. Both fasting and post prandial sugar levels were decreased significantly. *Makaradhwaja* declined Blood urea and serum creatinine levels. No any untoward effect was observed during the course of study. *Makaradhwaja* has anti hyperglycemic effect as well as synergistic action with dried extract of Tinospora cordifolia and Honey.

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