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Research Article

An open-labeled RCT of *Triguna* and *Shadguna Makaradhwaja* - Ayurvedic Herbo-mineral formulations on *Madhumeha* (type II Diabetes Mellitus)

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Abstract

Makaradhwaja (Au:Hg:S) is *Pramehagna* (anti-diabetic) according to *Rasatarangini* (Classical Rasashastra text), to assess the efficacy of the test drugs in the *Madhumeha* (type II Diabetes mellitus) the study was designed. Three groups 1. *Guduchi Ghana* (GG-Control-Gr. A), **2.** *Triguna* (Au:Hg:S=1:8:24) and 3. *Shadguna* (Au:Hg:S=1:8:48) *Makaradhwaja* (TM+GG-Gr. B & SM+GG-Gr. C) were prepared by *Rasatantrasara Siddha Prayoga Sangraha* and *Bhaishajya Ratnavali* and were subjected for an open-labeled randomized control clinical trial (RCT) at the outpatient department of *Rasashastra* & *Bhaishajya Kalpana*, IPGT & RA, GAU, Jamnagar, India. (IEC No. PGT/7/Ethics/2009-10/2157/24/09/2009). A dose of 250 mg capsule twice a day; before a meal with a quantity of sufficient honey as a vehicle was given for 28 days with the follow-up of 6 weeks to 153 patients; before-after investigations viz. blood sugar fasting and postprandial, serum triglycerides, serum cholesterol, serum calcium, etc. were carried out. Statistical analysis was done with unpaired 't', ANOVA, and Dunnett's 't' tests. In results, TM group was shown statistically highly significant over GG group in decreasing *Kshudhadhikya* (polyphagia) i.e. 66.26%. The average fasting blood glucose was reduced by 10.13mg/dl, 19.14 mg/dl, 18.03 mg/dl, and post-prandial glucose by 15.58, 25.46, and 29.05 mg/dl in GG, TM, and SM respectively. TM and SM were found to be more effective than GG. Both the groups showed significant to a highly significant decrease in subjective as well as objective parameters as compared to the GG group. Amongst all; SM was slightly more effective than the TM.

Keywords: *Madhumeha,* Immunomodulatory, Antidiabetic, *Makaradhwaja,* RCT

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Introduction

Several health advocacy organizations, including WHO, have acknowledged diabetes mellitus as a global epidemic that is on the rise (1).

WHO has estimated that diabetes will be one of the world's leading causes of death and disability in the next quarter century (2). It is a chronic metabolic syndrome that affects many people worldwide. The International Diabetes Federation (IDF) has estimated that 451 million adults live with diabetes worldwide in 2017 which is projected to reach 693 million by 2045 if no effective prevention methods are adopted. The disease initially thought to be one affecting people of developed countries having calorie surplus diets is now showing signs of surpassing this boundary and is being increasingly seen in developing countries. The countries with the largest numbers of adults with diabetes aged 20 –79 years in 2021 are China, India, and Pakistan according to IDF. The diagnosed cases are just the tip of the iceberg. It is also estimated that nearly 57% of adults with diabetes are undiagnosed in India, which is approximately 43.9 million. The prevalence of diabetes in India has risen from 7.1% in 2009 to 8.9% in 2019 (3) and is higher in men than women, but there are more women with diabetes than men (4).

Antidiabetic activity of *Triguna Makaradhwaja* (Herbo mineral Kupipakva medicine Au:Hg:S=1:8:24) has been proven (5) and *Makaradhwaja* is a well-established immunomodulatory drug (6). *Shadaguna Makaradhwaja* (Herbo mineral Kupipakva medicine Au:Hg:S=1:8:48) is considered antidiabetic in classics. As the quantity of sulfur varies in the manufacturing of *Makaradhwaja* the properties enhance and the name of the product also differs viz. Samagun when equal quality of sulfur is used, Dwigun when twice sulfur that of mercury is digested, and so forth (7). *Gandhaka Jarana* (The process of digestion of excess of sulfur in mercury): it has been claimed that *Parada* (Hg) with the process of *Gandhaka Jarana,* can cure all the diseases. (8,9), so it must be treated with *Gandhaka* (sulfur) to make it highly effective pharmacologically and therapeutically. Here *Makaradhwaja* was prepared using three and six times *Gandhaka* (sulfur) than that of *Parada* (mercury) i.e. *Thriguna* (TM) (7) and *Shadaguna Balijarita Makaradhwaja* (SM)(10) and hence to evaluate their

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efficacy in diabetes; especially in type II diabetes mellitus; a randomized clinical trial was planned with *Guduchi Ghana* (dried aqueous extract of *Tinospora quordifolia*) (GG) as a control drug which is prescribed in fevers, diabetes, dyspepsia, jaundice, urinary problems, skin diseases, chronic diarrhea, and dysentery(11).

To evaluate the efficacy of *Guduchi Ghana* Group-A (GG), *Triguna Balijarita Makaradhwaja* prepared by *Ashtasamskarita Parada* with *Guduchi Ghana*- Gr. B (TM+GG) and *Shadaguna Balijarita Makaradhwaja* prepared by *Ashtasamskarita Parada* with *Guduchi Ghana*-Gr. C (SM+GG), on *Madhumeha* (type II Diabetes mellitus).

Materials and methods

Place: Pharmacy & Dept. of Rasa Shastra & Bhaishajya Kalpana, Gujarat Ayurveda University, Jamnagar.

Ethical clearance: Permission from the clinical ethics committee has been taken with the ethical clearance no. PGT/7/Ethics/ 2009-10/2157/24/09/2009.

Experimental design: Randomized clinical trial.

Description of subjects/ No. of patients enrolled/completed the study: A total of 162 patients were enrolled; of type II diabetes mellitus; in which 153 patients completed the study of 28 days with a follow-up of 6 weeks and 9 patients left the study against medical advice. The expected number of patients enrolled in each group is 40. A randomized control trial of three test drugs viz. control drug *Guduchi Ghana* (Gr.A), *Guduchi Ghana* (12) with *Triguna Makaradhwaja* (Gr. B), and *Shadaguna Makaradhwaja* (13) with *Guduchi Ghana* (Gr. C) was carried out.

Inclusion criteria: Classical symptomatology of *Madhumeha* (Diabetes Mellitus Type II) also those who were taking allopathic medicine however their blood sugar was not controlled. Age group between 30 – 75 years, which were fulfilling diagnostic Criteria; Standard criteria of National Diabetes Data Group and W.H.O. for DM was adopted viz. (Adopted by American Diabetic Association) Symptoms of Diabetes + Random B. Glucose ³ 200 mg/dl or Fasting blood glucose ³ 126 mg/dl or Two hours blood glucose ³ 200 mg/dl (during an oral glucose tolerance test)

Exclusion criteria: All patients with diabetes mellitus receiving insulin. Patients having chronic complications of diabetes mellitus viz. micro vascular: retinopathy, neuropathy & nephropathy. Macrovascular: coronary artery disease, peripheral vascular disease, and cerebrovascular disease.

Detailed about medicine and manufacturing process: All the raw drugs used in the formulation were procured and authenticated by the Dept. of Pharmacy Gujarat Ayurved University, Jamnagar.

Triguna Makaradhwaja and *Shadaguna Makaradhwaja* (14) were prepared using *Shuddha Swarna* (processed gold), *Ashtasamskarita Parada* (Eight specific processes for the purification and potentiating mercury), and *Gandhaka* (Sulphur) in the proportion of 1:8:24 and 1:8:48 using *Bhavana dravyas* (levigating media) as; *Rakta Karpasa Pushpa* (flowers of *Gossypium arboretum* Linn.) and *Kumari Swarasa* (expressed juice of *Aloe barbadensis* Mill.) by following the classical guidelines with the *Kupipakva* method using electric muffle furnace (EMF) with the help of gradual heating pattern in 18 hours (for TM) and 36 hours (for SM) (15), in the department of *Rasashastra* and *Bhaishajya Kalpana* of IPGT & RA.

Guduchi Ghana (16); (GG – Dried aqueous extract of *Tinospora cordifolia*) used as adjuvant; was prepared by crushing fresh stem pieces of *Guduchi* [*Tinospora cardifolia* (Willd.) Miers ex Hook.f.] Honey used as the vehicle was procured from the local market.

Posology: The capsule of test drugs *Triguna Makaradhwaja* (TM), *Shadaguna Makaradhwaja* (SM), and the control *Guduchi Ghana* (GG) were administered in the dose of 2 *Ratti* (250 mg) (1 capsule) twice a day for 28 days orally with the follow up of 42 days with *Mamajjaka Ghana Vati* (17,18) 500 mg twice and *Vijyayasaradi Kwatha* (19) 10 ml BD which were prepared in Dept of Pharmacy, Gujarat Ayurved University Jamnagar (20).

Grouping of patients

Table 1: Showing drug and dose of the respective groups

Group	GG (mg)	TM (mg)	SM (mg)	Total dose (mg/ capsule)
A	250	--	--	250
B	232.5	17.5	--	250
C	232.5	--	17.5	250

GG = Control Group of Guduchi Ghana, B-TM = Triguna Makaradhwaja + Guduchi Ghana, C-SM = Shadaguna Makaradhwaja + Guduchi Ghana.

Direction and diet: The drug should be taken 30 min before taking food. Diet is predominantly with restricted carbohydrates.

Investigations: Routine Haematological Examinations**:** Hb%, TLC, DLC, and ESR will be done to rule out any other pathological condition. Biochemical Examinations: Blood Sugar: Fasting and post-prandial. Lipid profile: Serum Cholesterols. Triglyceride, Serum HDL, Blood urea, and Serum Creatinine: To assess the functional status of the kidney. Urine Examinations: Routine and microscopic examination with fasting urine sugar in all the patients before and after treatment.

Criteria of assessment: Improvement in the signs and symptoms of the disease as per Ayurvedic texts (21) and investigations conducted before and after treatment. The changes observed in the signs and symptoms were assessed by adopting a suitable scoring pattern and the objective signs by using appropriate clinical tools. For the assessment of the effect of the therapy following chief complaints and biochemical parameters were selected; *Prabutamutrata* (polyurea), *Avilamutrata* (sticky micturation), *Trushadhikyata* (polydipsia), *Klaibyata* (loss of libido), *Karapadasuptata* (numbness in soles of palms and legs), *Daurbalyata* (weakness), *Pindikodweshtana* (cramps in calf muscles), *Shramapratiti* (exertion), *Kshudhadhikyata* (polyphegia), *Karapadataladaha* (Burning soles of palms and legs), Fasting blood sugar, Fasting urine sugar, post-prandial blood sugar.

Table 2: Assessment Criteria and Grading of the Results

1	***Prabhuta Mutrata* (Polyuria)**		
	Frequency during the day	Frequency at night	Grade
A	3-5 times	0-1 times	0
B	6-8 times	2-3 times	1
C	9-11 times	4-5 times	2
D	>11times	> 5 times	3

2	***Aavila Mutrata* (Turbidity)**	
A	Crystal clear fluid	0
B	Faintly cloudy/smoky/hazy with slight turbidity	1
C	Turbidity is present, but the newsprint is readable with difficulty through the tube	2
D	Turbidity present & newsprint is not readable	3
3	***Trushadhikyata* (polydipsia) Quantity of water intake per day**	
A	Feels thirsty 7-9 times/24 hours or 1-2 liters	0
B	Feels thirsty 9-11 times /24 hours or 2 liters	1
C	Feels thirsty 11-13 times/24 hours or 3-4 liters	2
D	Feels thirsty >13 times/24 hours or >4 liters	3
4	***Klaibyata* (loss of libido)**	
A	Can perform the act with comfort	0
B	Have occasional difficulty with penile erection	1
C	Have frequent difficulty with penile erection	2
D	No penile erection at all	3
5	***Karapada Suptata* (numbness in the soles of the palms and legs)**	
A	Absent	0
B	Not continuous and occasionally present	1
C	Moderate and constantly present	2
D	Severe and hampers daily activities	3
6	***Daurbalya* (Debility)**	
A	Can do routine work/exercise.	0
B	Can do moderate exercise/routine work.	1
C	Can do mild exercise/less work with difficulty.	2
D	Cannot do even mild exercise/slight work.	3
7	***Pindikodweshtana* (cramps in calf muscles)**	
A	No cramps	0
B	1–2 times cramps in the calf muscle per week	1
C	3-5 times cramp in calf muscles per week	2
D	Cramp in the calf muscles daily	3
8	***Shramapratiti* (exertion)**	
A	No exertion	0
B	Feels slightly exerted at the end of the day	1
C	Feels exerted even with routine work	2
D	Feels exerted always	3
9	***Kshudhaadhikya* (Polyphagia)**	
A	Feels hungry at the next *Annakala (Meal time)* only	0
B	Feels hungry once in between the *Annakala*	1
C	Feels hungry twice in between *Annakala*	2
D	Feels hungry always	3
10	***Karapadataladaha* (Burning soles of palms and legs)**	
A	Absent	0
B	Not continuous and occasionally present	1
C	Moderate and constantly present	2
D	Severe and hampers daily activities	3
11	**Fasting Blood Sugar**	**Grade**
A	<110	0
B	110-126	1
C	127-170	2
D	171-220	3
12	**Post-Prandial Blood Sugar**	**Grade**
A	<180	0
B	181-230	1
C	231-280	2
D	281-300	3

Table 3: Chief complaints were assessed by grading them as below

Sr. No.	Chief Complaints	Improvement in %	Grade
1	Control of the complaint	100% relief	4
2	Marked improvement in complain	≥ 75% relief to 99% relief	3
3	Moderate improvement in complain	≥ 50% up to 74% relief	2
4	Mild improvement in complaint	≥ 25% up to 49% relief	1
5	No improvement	< 25% relief	0

The mean of each subjective parameter in the sample population was calculated before and after treatment using the above grading system.

Assessment of the overall effect of the therapy: 100 points were divided as 50 for subjective criteria, and 50 for objective criteria (25 for Blood Sugar Level-Fasting and 25 for Blood Sugar Level-Post Prandial). The result obtained from individual patients was categorized into 5 grades, control of the disease 100% relief, marked improvement ≥ 75% relief to 99% relief, moderate improvement ≥ 50% up to 74% relief, mild improvement ≥ 25% up to 49% relief and no improvement < 25% relief.

Statistical Analysis: The obtained data was analyzed statistically. The values were expressed as MEAN ± SEM. The data were analyzed by paired 't' test and a comparison of three test drugs was analyzed by unpaired 't' test, and one-way ANOVA and Dunnet's t test, a level of $P<0.05$ and $P<0.01$ was considered as statistically significant and highly significant respectively.

Results & Discussion

Classics of *Rasashastra* have emphasized *Pramehaghna* (antidiabetic (22, 23) property of *Makaradhwaja* as *Makaradhwaja* is a *Rasayana* (24) (rejuvenator), it is a proven immune-modulatory (25, 26) drug that helps in increasing the quality of life.

In Ayurveda, type 2 DM is correlated with *Madhumeha* which is *Tridosha* dominant disease (27, 28).

The study was a randomized open-label trial in which a statistically highly significant decrease was found in all symptoms in both *TM, SM,* and *GG* treated groups except with *Pindikodhweshtana* (cramps in calf muscles), and *Klaibya* (loss of libido), where TM and GG treated groups were not able to show significant improvement and the changes in above two symptoms were statistically non-significant proving SM more effective of three (29).

Table 4: Consolidated statement related to the effect of test drugs (% relief) on signs and symptoms of individual group

Sr. No.	Sign & Symptoms	Group	Mean Score		Statistical details of effect of test drug on signs and symptoms				
			B.T.	A.T.	% Relief	SD (±)	SE (±)	t'	P
1	*Prabhuta Mutrata* (Polyurea)	A-GG (n=45)	1.89	1.11	41.18¯	0.56	0.083	9.32**	<0.001
		B-TM (n=48)	1.875	0.917	51.11¯	0.62	0.089	10.75**	<0.001
		C-SM (n=46)	1.934	0.739	61.797¯	0.654	0.096	12.40**	<0.001
2	*Avila Mutrata* (Turbid Urine)	A-GG (n=43)	1.93	1.21	37.35¯	0.63	0.096	7.51**	<0.001
		B-TM(n=46)	1.98	1.07	46.15¯	0.59	0.087	10.5**	<0.001
		C-SM (n=46)	2.022	0.869	56.989¯	0.63	0.093	12.38**	<0.001
3	*Kshudhadhikya* (Polyphagia)	A-GG (n=42)	2.071	1.33	35.63¯	0.59	0.09	8.15**	<0.001
		B-TM (n=44)	2.14	1.23	57.45¯	0.57	0.085	14.41**	<0.001
		C-SM (n=44)	2.39	1.023	57.14¯	0.685	0.10	13.20**	<0.001
4	*Trishnadhikya* (Polydipsia)	A-GG (n=45)	1.8	1.378	23.46¯	0.657	0.098	4.31**	<0.001
		B-TM (n=49)	1.88	1.12	40.22¯	0.596	0.085	8.87**	<0.001
		C-SM (n=48)	1.94	0.958	**50.54¯**	0.635	0.092	10.68**	<0.001
5	*Kara-Pada-Tala Daha* (Burning palm and feet sole)	A-GG (n=44)	1.91	1.341	29.76¯	0.625	0.094	6.031**	<0.001
		B-TM (n=47)	1.957	1.106	43.478¯	0.589	0.086	9.91**	<0.001
		C-SM (n=45)	2.04	0.889	**56.52¯**	0.7057	0.105	10.98**	<0.001
6	*Kara-Pada Suptata* (Numbness of palm and sole)	A-GG (n=43)	1.977	1.44	27.06¯	0.592	0.090	5.929	<0.001**
		B-TM (n=46)	1.978	1.217	38.46¯	0.4313	0.064	11.96	<0.001**
		C-SM (n=47)	2.022	0.915	**54.737¯**	0.634	0.092	11.971	<0.001**
7	*Atisweda* (Excess Sweating)	A-GG (n=46)	2	1.41	29.35¯	0.541	0.079	7.36	<0.001**
		B-TM (n=50)	1.94	1.14	41.24¯	0.64	0.09	8.854	<0.001**
		C-SM (n=47)	2.04	0.94	**53.92¯**	0.71	0.1	11	<0.001**
8	*Galatalu-shosha* (Dryness of throat)	A-GG (n=41)	1.78	1.22	31.51¯	0.67	0.11	5.34**	<0.001
		B-TM (n=44)	1.79	1.023	43.08¯	0.605	0.09	8.475**	<0.001
		C-SM (n=42)	1.83	0.881	51.99¯	0.623	0.096	9.909**	<0.001
9	*Daurbalya* (Weakness)	A-GG (n=44)	1.82	1.182	35¯	0.61	0.092	6.88**	<0.001
		B-TM (n=47)	1.915	1.043	45.56¯	0.54	0.078	11.15**	<0.001
		C-SM (n=47)	1.96	0.85	**56.52¯**	0.67	0.097	11.37**	<0.001
10	*Shrama* (Tiredness)	A-GG (n=42)	1.857	1.33	28.21¯	0.552	0.545	0.96	>0.05
		B-TM (n=46)	1.869	1.087	41.86¯	0.513	0.076	10.35**	<0.001
		C-SM (n=45)	1.955	0.8	**59.09¯**	0.706	0.105	10.98**	<0.001
11	*Pindikodweshtana* (Cramps in calf muscles)	A-GG (n=43)	1.77	1.16	34.21↓	0.62	0.095	6.369**	<0.001
		B-TM (n=46)	1.848	1.04	41.86↓	0.582	0.086	9.375**	<0.001
		C-SM (n=46)	1.869	0.85	**88.42↓**	0.715	0.105	9.697**	<0.001
12	*Klaibya* (Loss of libido)	A-GG (n=4)	1.5	1.75	16.67↑	0.5	0.433	0.577	>0.05
		B-TM (n=4)	1.75	1.25	28.57↓	0.577	0.288	0.5	>0.05
		C-SM (n=6)	1.5	0.83	65.248↓	0.516	0.211	3.16*	<0.05

¯ = Decrease, = Increase, * = P<0.01, ** = P<0.001

Comparing the effect of the test drug on chief complaints SM and TM were found highly significant statistically over the GG-treated group. SM has the best results in polydipsia, burning of palm and soles, numbness of hands and feet, excessive sweating, weakness, tiredness, and camp muscles showcasing its overall effectiveness in chief complaints.

Table 5: Consolidated statement related to the effect of test drugs (% relief) prepared on significant biochemical parameters of individual groups

Sr. No.	Parameters	Groups	Mean		Statistical details of the effect of test drug on significant				
			BT	AT	% Relief	SD (±)	SE (±)	t'	P
1	BSL-F	A-GG (DF=48)	176.94	159.02	10.13↓	41.71	6.02	2.98*	<0.01
		B-TM (DF=52)	194.23	157.06	19.14↓	40.17	5.57	6.67**	<0.001
		C-SM (DF=53)	177.58	145.56	**18.03↓**	30.81	4.23	**7.57****	<0.001

2	BSL-PP	A-GG (DF=48)	247.21	208.69	15.58↓	79.46	11.47	3.36*	<0.01
		B-TM (DF=52)	283.25	211.13	25.46↓	55.70	7.72	9.33**	<0.001
		C-SM (DF=53)	266.08	188.77	**29.05**↓	56.49	7.76	**9.96****	<0.001
3	S. cholesterol	A-GG (DF=48)	204.46	198.19	15.58↓	79.46	11.47	3.36*	<0.01
		B-TM (DF=52)	209.35	196.61	6.08↓	28.47	3.95	3.22*	<0.01
		C-SM (DF=53)	205.34	192.36	6.32↓	41.84	5.75	2.26*	<0.05
4	S. Triglyceride	A-GG (DF=48)	140.73	132.65	5.74↓	6.93	5.60	1.44	>0.05
		B-TM (DF=52)	151.73	145.94	3.81↓	39.30	5.45	1.06	>0.05
		C-SM (DF=53)	162.19	141.24	15.36↓	63.88	8.77	2.84*	<0.01
5	HDL	A-GG (DF=48)	43.60	41.54	4.73↑	14.53	2.098	0.98	>0.05
		B-TM (DF=52)	43.27	42.5	1.78↑	10.67	1.48	0.52	>0.05
		C-SM (DF=53)	40.53	42.79	5.59↑	7.49	1.03	2.20*	<0.05
6	Total Protein	A-GG (DF=48)	7.55	6.96	7.92↑	2.19	0.32	1.89	>0.05
		B-TM (DF=52)	7.21	6.92	4.11↑	1.29	0.18	1.65	>0.05
		C-SM (DF=53)	7.39	6.81	7.49↑	1.59	0.22	2.53*	<0.05
7	S. Calcium	A-GG (DF=48)	9.34	9.49	1.69↑	0.43	0.06	2.52*	<0.01
		B-TM (DF=52)	9.37	9.54	1.85↑	0.41	0.06	3.01*	<0.01
		C-SM (DF=53)	9.34	9.49	1.69↑	0.43	0.06	2.52*	<0.01

¯ = Decrease, = Increase, * = P<0.01, ** = P<0.001

Fasting and post-prandial blood sugar were significantly reduced in both TM, SM, and GG-treated groups. This implies an antihyperglycemic effect more in SM group as number implicate.

Table No. 3: Effect of therapy of SM in comparison to GG on significant chief complaints

Sr. No.	Parameters	Effect of therapy of SM in comparison to GG				
		Mean ± SEM in change		% change (C-A)/A*100	t' value	p value
		SM-C	GG-A	SM-C	SM-C	SM-C
1	*Prabhuta Mutrata* (DF=89)	1.196±0.096	0.78±0.08	53.73↓	3.272*	<0.01
2	*Avila Mutrata* (DF=87)	1.15±0.093	0.72±0.096	59.78↓	3.22*	<0.01
3	*Kshudhadhikya* (DF=84)	1.36±0.103	0.74±0.09	84.82↓	**4.54****	<0.001
4	*Trishnadhikya*(DF=91)	0.98±0.092	0.42±0.098	131.99↓	**4.16****	<0.001
5	*Kara-Padatala Daha* (DF=87)	1.156±0.105	0.57±0.09	103.52↓	**4.15****	<0.001
6	*Kara-pada Supttata* (DF=88)	1.196±0.096	0.78±0.08	53.73↓	3.272*	<0.01
7	*Atisweda* (DF=94)	1.1±0.1	0.59±0.08	87.39↓	**3.97****	<0.001
8	*Gala-Talu- shosha* (DF=81)	0.95±0.096	0.56±0.11	69.69↓	2.75*	<0.01
9	*Daurbalya*(DF=89)	1.10±0.097	0.64±0.09	73.89↓	**3.49****	<0.001
10	*Shrama* (*Pratiti*) (DF=86)	1.16±0.10	0.52±0.09	120.61↓	**4.63****	<0.001
11	*Pindikodhweshtana* (DF=87)	1.02±0.10	0.61±0.09	68.93↓	2.93*	<0.01

*< .01 – Significant & **< .001 – Highly Significant, ¯ = Decrease.

It can be concluded from the table that there was a significant decrease in the chief complaints in SM treated group in comparison to the control, especially in polyurea, turbid urination, dryness of the throat, and cramps in muscles explaining the *Rasayana* (rejuvenator) property of *Shadaguna Makaradhwaja* helping in improving the quality of life in Type II diabetic patients.

Table No. 4: Showing the effect of TM on significant chief complaints in comparison to GG:

Sr. No.	Parameters	Effect of therapy of TM in comparison to GG				
		Mean ± SEM in change		% change (C-A)/ A*100	t' value	p value
		TM-B	GG-A	TM-B	TM- B	TM- B
1	*Kshudhadhikya* (DF=84)	1.23±0.09	0.74±0.09	66.26↓	**3.94****	<0.001
2	*Trishnadhikya* (DF=92)	0.755±0.09	0.422±0.098	78.91↓	2.58*	<0.05
3	*Kara-Padatala Daha* (DF=89)	0.85±0.09	0.57±0.09	49.82↓	2.22*	<0.05
4	*Kara-Pada Suptata* (DF=87)	0.76	0.54	42.24↓	2.7*	<0.05
5	*Shrama (Pratiti)* (DF=86)	0.78±0.08	0.52±0.09	49.43↓	2.28*	<0.05

*< .01 – Significant & **< .001 – Highly Significant, ¯ = Decrease.

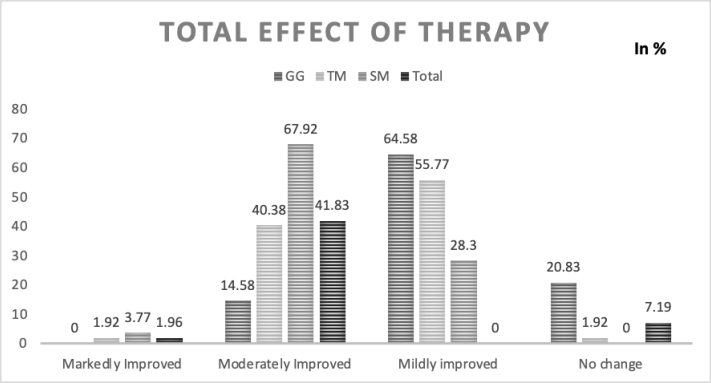
Table 4 explains that *Triguna Makaradhwaja* has a very significant decrease in excess hunger showing the special effect on Agni (Digestive fire) in comparison to control *Guduchi Ghana.*

Table 5: Showing the effect of SM & TM drugs on significant biochemical parameters in comparison to GG

Sr. No.	Parameters	Effect of therapy of SM-C in comparison to G -A				
		Mean ± SEM in change	% change (C-A)/A*100	t' value	p value	Mean ± SEM in change
		SM-C	GG-A	SM-C	SM-C	SM-C
1	BSL-PP(DF=99)	77.30±7.76	38.52±11.47	100.68↓	2.847*	<0.01
2	Alkaline phosphates (DF=99)	-2.698± 1.83	2.69±1.52	200.37↑	2.24*	<0.05
3	Serum Calcium (DF=99)	0.10±0.07	-0.16±0.06	164.56↑	2.648*	<0.01
Sr. No.	**Parameters**	**Effect of therapy of TM-B in comparison to GG-A**				
		Mean ± SEM in change	**% change (C-A)/A *100**	**t' value**	**p value**	**Mean ± SEM in change**
		TM	**GG-A**	**TM-B**	**TM-B**	**TM-B**
1	Blood S-F(DF=98)	37.17±5.57	17.92±6.02	107.47↓	2.35*	<0.05
2	BLO S-PP(DF=98)	72.11±7.73	38.52±11.47	87.21↓	2.46*	<0.05
3	Total RBC(DF=98)	0.05±0.03	-0.11±0.05	140.79↑	2.713*	<0.05

The difference between control and test drugs treated groups by ANOVA test (Table No.5) demonstrating *Shadaguna Makaradhwaja* has a significant decrease in Blood sugar pos-prandial and a significant increase in alkaline phosphatase and serum calcium. Whereas *Triguna Makaradhwaja* reduces both fasting and post-prandial blood sugar with an increase in total RBC. Retarating the fact that both *Shadaguna* and *Triguna Makaradhwaja* have antihyperglycemic effects with positive effects on calcium and RBC values betterment (30).

Chart 1: Total effect of therapy



The chart denotes markedly improvement was observed in 1.96 % of patients. Moderate improvement was observed in 41.83 % of patients. 49.2 % of patients showed mild improvement while 7.19 % of patients showed no change.

Out of 162 enrolled patients, 153 patients completed the study of *Madhumeha* (Diabetes mellitus type II), patients were maximum from the age group 46-60 years i.e. 66.67% while 12.34 % in > 60 years and 20.99% in 30-45 years as type 2 diabetes, conventionally considered a disease of middle and older age (31). Maximum numbers of patients (53.1%) were males. This observation correlates with the modern textual observation (Oliver) where the sex-wise incidence of DM is mentioned (32).

The average fasting blood glucose was reduced by 10.13mg/dl, 19.14 mg/dl, and 18.03 mg/dl and an average decrease in postprandial glucose was 15.58, 25.46, and 29.05 mg/dl in GG, TM and SM respectively. It may be concluded that both *Triguna* and *Shadaguna Makaradhwaja* with third GG have antihyperglycemic effects as well as synergistic action with oral hypoglycemic agents. But in mutual comparison, the positive results turn more in favor of *Shadaguna Makaradhwaja* as *Balijarana* increases the disease-curing property of the drug, and also in ICPOES maximum amount of Gold had been directed in SM sample i.e. 663.14 in comparison to TM i.e. 7.2976 which is the very well know *Rasayana,* immuno-modulatory and antidiabetic drug (33).

Blood urea level was moderately decreased in all three drug-treated groups. Though the decrease was within normal limits, it is a good sign from the patient as a breakdown of proteins results in the formation of ammonia which is very toxic and is immediately converted into urea in the liver and excreted through the kidney in the form of urea. The decrease in blood urea level denotes decreased catabolism of proteins which means increased glucose uptake for energy production which is very helpful for the diabetic patient. It also implies increased functioning ability of the liver as well as kidney so the chances of renal damage can be ruled out (34).

Conclusion

Herbo-mineral drug *Triguna Makaradhwaja* (TM) and *Shadaguna Makaradhwaja* (SM) are both *Madhumehahara (antidiabetic)*, among them *Shadaguna Makaradhwja* (SM) is better. Control drug *Guduchi Ghana* also showed a *Madhumehahara* (antidiabetic) effect. The effect implied indirectly that the process of *Gandhaka Jarana* improves the therapeutic efficacy of the drug concerning *Madhumeha* (Type II diabetes mellitus). Further clinical trials with larger sample sizes; are needed in the current scenario.

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