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Synergistic Antidiabetic Potential of *Machilus macrantha* Bark and *Eulophia herbacea* Leaf Mucilages

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Keywords: Gulmavu (*Machilus macrantha* Nees), Kukudkan (Salep), *Eulophia herbacea* Lindl, anti-diabetic activity.

ABSTRACT

The present study was conducted to investigate the synergistic anti-diabetic potential of Gulmavu (*Machilus macrantha* Nees), Kukulkan (Salep), *Eulophia herbacea* Lindl. together synergistically. The various dose for both the drugs is selected for investigation of anti-diabetic activity. The Pharmacological evaluation of both herbs are carried out by bioassay involving experimental animals, Albino Wistar male rats and diabetes was induced by them by i.p injection of streptozocin 60mg/kg body weight. Then both of our drugs were fed to them in 1:1 ratio (per oral route) and as a reference standard, Gliclazide (8mg/kg) is used. Blood glucose levels are monitored at different intervals to examine the blood glucose level by using standard electronic glucometer and Glucose estimation strips. Combination dose of both herbs (100mg+100mg) shows significant anti-diabetic potential in the synergistic way rather than the individual.

INTRODUCTION

"Diabetes mellitus is a group of syndromes characterized by hyperglycemia altered metabolism of lipids, carbohydrates and proteins and an increased risk of complications from vascular disease" [(1)].

The name 'diabetes' which means 'to run through' and 'mellitus' means sweet or with a taste of honey. Diabetes mellitus is the most common endocrine disorder affecting 16 million individuals in the United States and as many as 200 million worldwide [(2)]. In the present era, diabetes mellitus is affecting around 2-3% of the total population worldwide. As per ancient literature, more than 800 plants are reported to have antidiabetic properties. Ethno pharmacological surveys indicate that more than 1200 plants are used in the hypoglycemic activity. Various herbs such as *Azadarachta indica*, *Curcuma longa*, *Eugenia jambolana*, etc[(3)].

Various drugs are used to prevent, diagnose, treat, or to cure many diseases or disorder such a Glipizide belongs to the novel class of oral hypoglycemic drug. Their principal action is a

β-cell stimulating insulin secretion and then reducing plasma glucose. Metformin belongs to biguanide class of oral hypoglycemic drug. They lower blood glucose level by increasing glucose uptake and utilization in skeletal muscle. It causes gluconeogenesis and also reduces low density and very low-density lipoproteins. The combination of Glipizide and Metformin is used to treat the high blood sugar levels. The limitations of currently available oral hypoglycemic agents either in terms of efficacy/safety coupled with the emergence of the disease into a global epidemic have encouraged a concerted effort to discover drugs that can manage type 2 diabetes along with type 1 diabetes more efficiently[(4)].

When it comes to the plants used in this research work, both *Machilus macrantha* Nees and *Eulophia herbacea* Lindl do have numerous ethnic pharmacological applications including anti-diarrheal, anticolic ulcer, stimulant, anti-anxiety, etc activities[(5)]. An extensive literature survey from all scientific sources revealed that Gulmavu (*Machilus macrantha* Nees) and Kukudkan (Salep), *Eulophia herbacea* Lindl may have anti-diabetic activity. This research is just an attempt to provide an evidence to their usefulness in the management of diabetes mellitus.

MATERIAL AND METHODS

Collection & Authentication

1- Gulmavu - *Machilus macrantha* Nees.

Gulmavu is a plant obtained from fresh as well as dried aerial parts as well as the bark of *Machilus macrantha* Nees. It is a tree which is known for its application in bulk formation of Essence sticks on a commercial basis [6]. Gulmavu was obtained from Rye wood park premises in May 2014 with due permission of Regional Forest Officer as it is a protected species. Only fallen matured pieces were allowed to be collected.

Prof. Dr. D. A. Patil, Professor & HOD, Department of Botany, S. S. V. P. S. Arts, Science College, Dhule did the confirmation of the plant. The authentication of the plant was done by comparing the morphological features (leaf arrangement, fruit, and seed morphology). The herbarium of the plant has been deposited at Registered Botanist, Department of Botany, S. S. V. P. S. College of Arts and Science, Dhule.

Fig. 1: Herbarium of Gulmavu (*Machilus macrantha* Nees)

2- *Eulophia herbacea* Lindl

Collection &Authentication

Kukudkan/ SalepMisri plant was collected from Toranmaal Tehsil of Nandurbar District in August 2014 as the plant germinates only after one or two heavy rain falls. The species *Eulophia herbacea* Lindl (Family: Orchidaceae) is labeled as an endangered species [7].

Prof. Dr. D.K. Patil, Professor & HOD, Department of Botany, S.S.V.P.S. Arts, Science College, Dhule did the confirmation of the plant. The authentication of the plant was done by comparing the morphological features (leaf arrangement, fruit, and seed morphology). The

herbarium of the plant has been deposited at Registered Botanist, Department of Botany, S. S. V. P. S. College of Arts and Science, Dhule.

Fig 2: Herbarium of Kukudkan (*Eulophia herbacea* Lindl.)

Extraction of mucilage:

Machilus macrantha Nees. the bark was first of all pulverized to the fine powder after shade drying. The powder is then subjected to the mucilage extraction by using warm water for three (03) hours. After which it was kept aside for two (02) hours. The extract was squeezed through a muslin cloth. Th filtrate collected was slowly added to acetone along the sidewall of the container which resulted in precipitation of mucilage. Mucilage was later separated and made moisture free by successive precipitation using ethanol. At the end, it was freeze dried and stored in desiccators [8].

For *Eulophia herbacea* Lindl. leaves same procedure was followed in order to obtain moisture free mucilage content. The brief data of both drugs is as follows.

Physical Characteristics:

Table 1: *Machilus macrantha* bark mucilage

Sl. No.	Name of the Extract	Nature	Color	Odor	Taste	Quantity in gms (for 4 kg bark powder)	Percentage yield
4.	*Machilus macrantha* mucilage	Dried mucilage powder	Off white	Characteristic	Mucilaginous	51 gm	1.275%

Table 2: *Eulophia herbacea* bark mucilage

Sl. No.	Name of the Extract	Nature	Color	Odor	Taste	Quantity in gms (for 4 kg bark powder)	Percentage yield
4.	*Eulophia herbacea* mucilage	Dried mucilage powder	Pale yellow	Characteristic	Mucilaginous	51.8 gm	1.85%

Pharmacological evaluation:

The Pharmacological evaluation of both herbs is carried out by using wistar albino male rats which weighing around 250gm, the **s**tudy comprised of five groups in which each group comprised of 5 animals.

Ad libitum diet for a month prior to the study with the provision of 12X12 dark and light cycles. Diabetes was induced by i.p. injection of Streptozotocin 60mg/kg body weight. The mortality rate was high at first instance killing 9 out of first 12 animals.

Then orally our drug has been fed (per oral route) and as a reference standard Gliclazide (8mg) is used then by drawing blood which used for checking blood glucose level.

Blood samples were drawn from the tail tip of the rat at weekly intervals till the end of study (i.e. 2 weeks). Fasting blood glucose estimation was done on day 1, 7, and 14 of the study. Blood glucose estimation can be done by one-touch electronic glucometer using glucose test strips [(9)].

1) Drug1, drug 2(100 mg/kg)

Group I-Normal group

Group II-Vehicle treated group (STZ 60 mg/kg i.p) one time

Group III-Drug 1(100 mg/kg p.o)

Group IV-Drug 2(100 mg/kg p.o)

Table 3: Group I-Normal group

Sr. No.	0th day	7th day	14th day
1	120 mg/dl	122 mg/dl	118.11 mg/dl
2	100.12 mg/dl	105.2 mg/dl	109.30 mg/dl
3	140.3 mg/dl	135 mg/dl	141 mg/dl
4	120 .2mg/dl	130 mg/dl	125.25 mg/dl
5	131.3 mg/dl	133 mg/dl	130 mg/dl
	122.4±6.733	125±5.432	124.7±5.36

Table 4: Group II-Vehicle treated group (STZ 60 mg/kg i.p)

Sr. No.	0th day	7th day	14th day
1	333 mg/dl	344 mg/dl	338 mg/dl
2	366 mg/dl	369 mg/dl	375.5 mg/dl
3	350mg/dl	360mg/dl	378mg/dl
4	342mg/dl	349 mg/dl	352 mg/dl
5	408 mg/dl	400 mg/dl	419 mg/dl
	359.8±13.22	364.4±9.903	372.5±13.81

Table 5: Group III-STZ (60 mg/kg i.p) Drug 1(100 mg/kg p.o)

Sr. No.	0th day	7th day	14th day
1	366mg/dl	360 mg/dl	358 mg/dl
2	350 mg/dl	330 mg/dl	319 mg/dl
3	350mg/dl	341mg/dl	325mg/dl
4	342mg/dl	333 mg/dl	325 mg/dl
5	408 mg/dl	400 mg/dl	483 mg/dl
	339.4±14.69	352.8±12.91	362±31.02

Table 6: Group IV- STZ (60 mg/kg i.p) Drug 2(100 mg/kg p.o)

Sr. No.	0th day	7th day	14th day
1	307mg/dl	300 mg/dl	293mg/dl
2	338 mg/dl	330 mg/dl	300 mg/dl
3	369mg/dl	353mg/dl	333mg/dl
4	376mg/dl	369 mg/dl	350 mg/dl
5	307 mg/dl	300mg/dl	287 mg/dl
	363.2±11.86	330.4±13.87	312.6±12.27

Group I-Normal group

Group II-Vehicle treated group (STZ 60 mg/kg i.p) one time

Group III-Drug 1(200 mg/kg p.o)

Group IV- Drug 2(200 mg/kg p.o)

Group V – combination (100 mg Drug 1 + 100 mg Drug 2)

Table 7: Group I-Normal group

Sr. No.	0th day	7th day	14th day
1	120 mg/dl	122 mg/dl	118.11 mg/dl
2	100.12 mg/dl	105.2 mg/dl	109.30 mg/dl
3	140.3 mg/dl	135 mg/dl	141 mg/dl
4	120 .2mg/dl	130 mg/dl	125.25 mg/dl
5	131.3 mg/dl	133 mg/dl	130 mg/dl
	122.4±6.733	125±5.432	124.7±5.36

Table 8: Group II-Vehicle treated group (STZ 60 mg/kg i.p)

Sr. No.	0th day	7th day	14th day
1	333 mg/dl	344 mg/dl	338 mg/dl
2	366 mg/dl	369 mg/dl	375.5 mg/dl
3	350mg/dl	360mg/dl	378mg/dl
4	342mg/dl	349 mg/dl	352 mg/dl
5	408 mg/dl	400 mg/dl	419 mg/dl
		364.4±9.903	372.5±13.81

Table 9: Group III-STZ (60 mg/kg i.p) Drug 1(200 mg/kg p.o)

Sr. No.	0th day	7th day	14th day
1	366mg/dl	316mg/dl	228 mg/dl
2	325 mg/dl	300 mg/dl	264 mg/dl
3	308mg/dl	275mg/dl	214mg/dl
4	375mg/dl	350 mg/dl	278 mg/dl
5	350 mg/dl	290 mg/dl	280 mg/dl
	344.8±12.52	306.2±12.82	252.8±13.46

Table 10: Group IV- STZ (60 mg/kg i.p) Drug 2(200 mg/kg p.o)

Sr. No.	0th day	7th day	14th day
1	366mg/dl	358 mg/dl	278mg/dl
2	333 mg/dl	325 mg/dl	250 mg/dl
3	316mg/dl	391mg/dl	221mg/dl
4	325mg/dl	250 mg/dl	207 mg/dl
5	305 mg/dl	285mg/dl	225 mg/dl
	329±10.36	321.8±25.12	236.2±12.54

Table 11: Group V – combination (100 mg Drug 1 + 100 mg Drug 2)

Sr. No.	0^{th} day	7^{th} day	14^{th} day
1	360mg/dl	308 mg/dl	228mg/dl
2	329 mg/dl	311 mg/dl	221 mg/dl
3	309mg/dl	375mg/dl	220mg/dl
4	313mg/dl	242 mg/dl	201 mg/dl
5	305 mg/dl	285mg/dl	225 mg/dl
	323±11.1	304.2±25.32	219.2±07.6

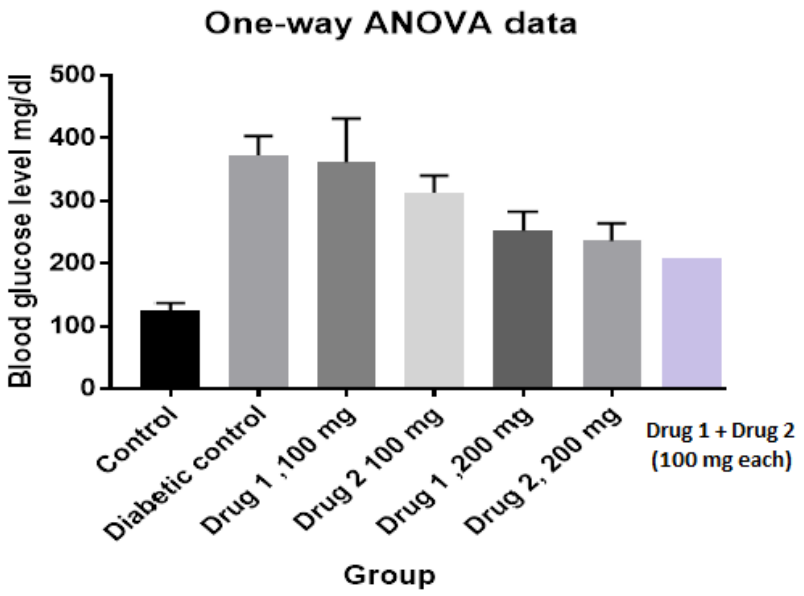

Fig. 3: Statistical data (Antidiabetic activity)

RESULT AND DISCUSSION

In light of the results, our study indicates that mucilage extracts of *Machilus macrantha* Nees. And *Eulophia herbacea* Lindl.have antidiabetic activity individually as well as synergistically in Streptozotocin-induced diabetic rats. It is found that mucilage from *Machilus macrantha* at a dose (200 mg/kg) is having more or less similar antidiabetic potential when compared with mucilage from *Eulophia herbacea*. But when both mucilage extracts are clubbed together (in 1:1 ratio), after 14 days of treatment. The study reveals that though it has the moderate approach towards lowering of blood glucose level when compared with the Standard Gliclazide (8 mg/ kg) the results were obtained only as an individual drug

initially. Later on, both drugs are used as the combination (100 mg each) to make a moderate effect a significant one.

CONCLUSION

The above-said combination is found to have significant anti-diabetic potential in a synergistic way rather than an individual. One thing can be done in order to further potentiate the effect of this combination that we can use repetition of dosing's in order to achieve an aggravated hypoglycemic response.

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