

Withania Coagulans in Management of Diabetes Mellitus

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Abstract: *Diabetes mellitus, a progressively increasing metabolic and endocrinal disorder and a combined effect of changed diet, life style and generation of non nutrient toxic product in the food and drinks due to increased misuse of fertilizers, chemicals, hormones and adulterants.*

These days, a disease of comfort and luxury is widely affecting the people who even craving for their lively hood, usually precipitated by alcoholism and stress.

The changed present scenario of diabetes mellitus in the era of advanced diagnostic facilities the patients with >500mg plasma sugar remain conscious and present their history of illness himself whether earlier at this level patient usually became comatose or presents with various consequent sequel.

The most commonly prescribed therapeutic regime remain either Oral hypoglycemic or insulin supplementation which in turn affects the patient's psyche and stress predisposes for rise in blood glucose and its sequel.

Majority prescription used to impose burden rather to modify the continuing diet, clinician usually change the brand, which usually yields with diabetic sequel.

Thus with consideration of bio regulating body metabolism and scavenge free radical from Beta cells of pancreas and increase hepatic utilization of absorbed glucose, an indigenous herb Withania coagulans fruit extract in dose of 5 fruits with warm water morning and evening been assessed and achieved normoglycemic state in 6 weeks of therapy, lipid bio regulation, spared the continuing OHA or Insulin without any adversity and any alteration in hematologic, hepato-renal functions.

These effects are attributed to-

It increases cellular sensitivity, Insulin binding and glucose uptake, scavenges free radicals from Beta cells of pancreas and modulate Insulin secretion improve metabolism, reduces hypothalamic irritation, promote and bio regulate insulin production in pancreas and improve resting energy expenditure.

1. INTRODUCTION

Changing dietary status, increasing non dietary constituents in the routinely used food and drinks, and changing life style predisposes for progressively increasing incidence of metabolic and endocrinal disorders. Though available advanced diagnostic methods prompts better research treatment planning, but declining nutritional status predisposes for declined immune protection, rising economical burden

resulting in mental stress. Thus combination of non dietary constituents and stress load primarily increasing the incidence of diabetes mellitus, its consequent sequel and drug dependency.

In spite of availability of various oral hypoglycemic molecules, non insure bio regulation of blood sugar and check diabetic sequel.

Withania coagulans fruit having established role as hypoglycemic in rat (1,2) been evaluated as an adjuvant with continuing oral hypoglycemic, Insulin and dietary restriction in old cases and dietary restriction only in fresh cases of diabetes mellitus to adjudge its hypoglycemic effect and safety profile.

2. MATERIALS & METHODS

Patients of Diabetes mellitus (both old and new) attending centre for metabolic & endocrinal disease, RA.Hospital & Research Centre, Warisaliganj (Nawada) were considered for evaluation of *Withania coagulans* fruit as an adjuvant in bio regulation of blood sugar level in the body, as an adjuvant with continuing anti diabetics in old cases of Diabetes mellitus.

2.1. Who Criteria for Establishing a Case of Diabetes Mellitus

- Fasting plasma glucose > 7 mmol/L Or 126mg/dl
- Plasma glucose after 2 hours of 75 gm glucose load : >11.1 mmmol/L Or 200mg/dl
- Manifestation of hyperglycemia with random plasma glucose 11.1mmol/L Or 200mg/dl
- Glycosylated HbA1C >48

All the selected patients were interrogated for their dietary status, drug therapy and its schedule, outcome, weight of the patient, blood pressure, diabetic sequel and investigated for blood sugar level, both fasting, PP, random, urine sugar, lipid profile, hepatic, renal and hematological status along with its neurophysiology. Patients with blood sugar >500mg/dl been also evaluated for their cardiac function with ECG tracing

Each patients were given *Withania coagulans* fruit watery extract as an adjuvant as –In old cases:

Continue the continuing drug (OHA Or Insulin supplementation Or both) with 5 *Withania coagulans* fruit watery extract in the early morning and bed time

In freshly detected new cases:

Dietary control with watery extract of 5 fruits of *Withania coagulans* at the early morning and at bed time



Commonly known in the country as -

Bengal – Asvagandha

Bombay - Kaknaj

Gwalior - Asgandha

Panjab - Khamjaria, Khamjira, Panir

Sindhi - Punirjafota, Punirband

Persian - Kaknajehindi, Punirbad

Arabic - Javzulmizaja, Kaknajehindi

Canares - Asvagandhi

Telgu - Panneru-gadda

Urdu - Hab kaknaj

Characteriostic feature:

A rigid grey- tomentose undershrub 0.3-0.9 m. high, branches terete, clothed with dense grey or yellowish white tomentum. Leaves : 2.5-5.7 by 1-2.2 cm., lanceolate-oblong, obtuse, entire, clothed with a persistent not easily detachable greyish tomentum, of a uniform colour on both sides, thick, more or less rugose, base acute, running down into an often obscure petiole; petiole 6 mm. long but often indistinct. Flowers : Dioecious, in axillary clusters; pedicles 0-6mm. long, deflexed, slender. Calyx 6 mm. long, campanulate, clothed with fine stellate grey tomentum; teeth triangular, 2.5 mm. long. Corolla 8 mm. long, stellately mealy outside, divided about 1/3 the way down; lobes ovate-oblong, subacute. Male flowers: Stamens about level with the top of the corolla- tube; fillaments 2 mm. long, glabrous; anthers 3-4 mm. long. Ovary ovoid, without style or stigma. Female flowers: Stamens scarcely reaching ½ way up the corolla-tube; filaments about 0.85 mm. long; anthers smaller than in the male flowers, sterile. Ovary ovoid, glabrous; style glabrous; stigma mushroom- shaped, 2-lamellate. Fruits : Berry 6-8 mm. diam., globose, smooth, closely girt by the enlarged membranous calyx which is scurfy pubescent outside. Seeds 2.5-3 mm. diam., somewhat ear-shaped, glabrous. Seeds : 2.5-3mm diam., dark brown, ear-shaped, glabrous; Flowering period: from January to April and berries ripen during January to May. The natural regeneration is from seed.

Each selected patients were primarily made aware regarding the treatment modules and taken consent for their inclusion in the proposed study and given a follow up card to asses self-

- Any manifestations suggestive of hypoglycemia
- Self asses urine for the presence of glucose and protein in the urine with Glucostix
- Any manifestation suggestive of allergy or untoward effect of *Withania coagulans* i.e.- Nausea, vomiting, abdominal cramp, lose motion, respiratory discomfort, any other parameters observed.
- Each patients were asked to seek advise on 24 hours help line number for any queries.

On each visit at the centre every 7th day, Blood sugar (both fasting and PP), urine analysis and in old cases having hypoglycemic manifestation or decline in blood sugar level ,continuing anti diabetic drug been gradually tapered down.

In case of Insulin therapy after reducing the Insulin dose, Patients were put on Oral hypoglycemic with adjuvant to maintain the normo glycemic state.

Dietary intake and other physical measures were strictly maintained. To adjudge circadian variation of blood glucose level in patients whose blood sugar (F) >200mg were provided with Glucostix and patients with fasting blood sugar <200mg, Glucometer with strips to repeat the blood sugar assessment before breakfast, lunch and dinner.

Patients hematological, hepatic, renal and lipid profile were repeated on every 30th day to adjudge the effect of adjuvant and asses safety profile Or effect of *Withania coagulans* on hemato, hepato, renal and lipid profile .

3. OBSERVATIONS

Among the selected patients 157(40.25%) were old diabetics non responsive to the continuing anti diabetic drugs and 233 (59.75%) were freshly detected cases of diabetes mellitus

Patients were of age group 30-80 yrs and majority(57.7%)were of age 40-60 yrs though 12.05% were of 70-80 yrs,male:female composition of the selected patients was 245:145 while among the old and freshly detected cases were 97:60 and 148:85 respectively.

4. TABLE & LEGENDS

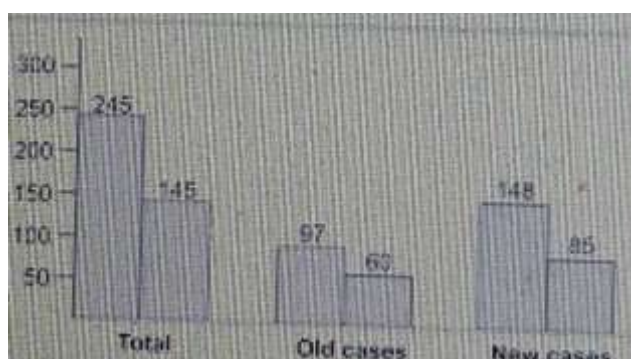
(Table -I , Bar diagram and Pie diagram)

TableI. *distribution of patients as per their age, sex and disease status*

| Age group (in yrs) | Number of patients | | | | Total |
|-----------------------|--------------------|-----------|-----------|-----------|------------|
| | Newly detected | | Old Cases | | |
| | Male | Female | Male | Female | |
| 30-40 | 20 | 12 | 15 | 08 | 055 |
| 40-50 | 40 | 20 | 25 | 15 | 100 |
| 50-60 | 50 | 26 | 30 | 19 | 125 |
| 60-70 | 20 | 17 | 15 | 11 | 063 |
| 70-80 | 18 | 10 | 12 | 07 | 047 |
| Total | 148 | 85 | 97 | 60 | 390 |

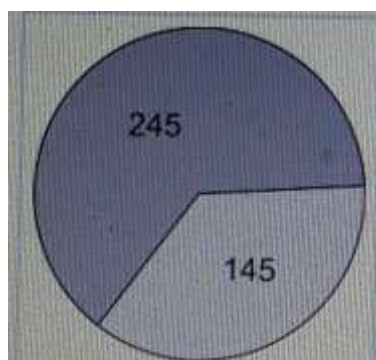
Selected patients irrespective of their therapeutic status 30(7.6%) shows blood sugar between 200-250mg while 10(2.5%) cases were with blood sugar >500mg %,majority (240/61.5%) cases were with blood sugar 300-400 mg % . (Table II)

TableII. *Bar diagram showing male :female composition*



Out of all 84 cases were presenting with hypertension (mean pressure >120mm Hg) while rest other were non hypertensive, though among old cases73(46.5%) had hypercholesterolemia.(Table III)

TableIII. *Pie diagram showing disease wise composition*



No selected cases had any altered hematological ,hepatic or renal function alteration, ECG pattern of all the selected cases were within normal limit.

As per dietary status of the patients 164(42%) and 226(58%)were taking vegetarian and non vegetarian diet respectively.(Table - Bar diagram)

Among old cases 10(6.3%) patients were on purely diet restriction while 16(10.1%) were taking Insulin and 18(11.4%) combination of multiple hypoglycemic and Insulin,45(28.6%) cases were on only Metformin and 55 (35%) on Glipizide .(Table IV)

TableIV. Showing distribution of patients as per their blood sugar level.

| Blood Sugar (in mg%) | Number of patients | | |
|-------------------------|--------------------|--------|-------|
| | Male | Female | Total |
| 200-250 | 25 | 05 | 30 |
| 250-300 | 50 | 40 | 90 |
| 300-350 | 50 | 30 | 80 |
| 350-400 | 45 | 25 | 70 |
| 400-450 | 40 | 25 | 65 |
| 450-500 | 30 | 15 | 45 |
| >500 | 05 | 05 | 10 |

During therapy on 1st week 35(9%) patients had fasting blood sugar <100mg and by 6th week 361(92.6%) shows fasting blood sugar <100mg.

After 4th week of therapy 388 (99.5%) patients show fasting blood sugar <120mg and on 6th week post prandial blood sugar in 337(86.5%) <150mg and in all 390 cases <160mg.

(Table V and VI)

TableV. Distribution of patients as per average blood pressure

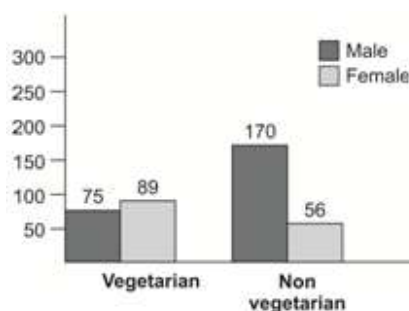
| Average blood pressure (in mm Hg) | Number of patients | | | |
|--------------------------------------|------------------------|--------|-----------|--------|
| | Fresh (newly detected) | | Old cases | |
| | Male | Female | Male | Female |
| <90 | 02 | 01 | 05 | 02 |
| 90-100 | 03 | 01 | 04 | 01 |
| 100-110 | 77 | 42 | 31 | 23 |
| 110-120 | 42 | 32 | 21 | 18 |
| >120 | 24 | 09 | 35 | 16 |

TableVI. Distribution of old patients as per their therapeutic status

| Therapeutic s | Number of patients | | |
|-------------------------|--------------------|--------|-------|
| | Male | Female | Total |
| Diet | 06 | 04 | 10 |
| Metformin | 30 | 15 | 45 |
| Glipizide | 36 | 19 | 55 |
| Combination drug | 12 | 06 | 18 |
| Insulin | 07 | 09 | 16 |
| Other oral hypoglycemic | 06 | 07 | 13 |

In addition majority show decline in serum cholesterol and bio regulate lipid profile. No patients had any hemato,hepato and renal function alteration. (Table VII)

TableVII. Bar diagram showing distribution of patients as per their dietary status



5. CONCLUSION

Withania coagulans fruit extract orally early morning and evening at bed time as an adjuvant with continuing anti diabetics in old cases and with OHA in fresh cases progressively established normoglycemic level both fasting and pp and spared the dose of continuing anti diabetic drug and patients taking insulin become completely free of insulin prick.

It also bioregulated lipid profile, alleviated diabetic complication and reduced the dose of OHA without any alteration in hemato, hepatic and renal function.

6. DISCUSSION

Diabetes mellitus, a manifestation of altered metabolism is progressively increasing due to declining nutrients in food and drinks, increasing non nutrient constituents of the diet due to progressively increasing use of fertilizers, chemicals, pesticides and adulterants. In addition drugs in vogue i.e.- either supplementation of insulin or activate Beta cell secretion, but non bio regulate metabolic function i.e.- metabolism and transformation of glucose which results in circadian variation of blood glucose level.

In the context use of *Withania coagulans* fruit extract in early morning and at bed time either alone or with continuing OHA or with Insulin bio regulate blood sugar both fasting and PP in 6 weeks in majority cases and also bioregulate lipid profile without any hemato -hepato -renal adversity.

This clinical achievement of *Withania coagulans* can be explained as (3,4 -

Active ingredients of the *Withania coagulans* fruit extract not only activate Insulin receptor sensitivity but also revitalize Beta cells for Insulin secretion, In addition also bio regulate glucose utilization by hepatic parenchyma i.e.- glucose to glycogen, also bio regulate lipid metabolism, thus *Withania coagulans* fruit watery extract not only bio regulate glucose utilization, its metabolism and lipid metabolism, maintains HDL/LDL ratio to check diabetic sequel but also –

- makes the cells more sensitive to Insulin binding and glucose uptake,
- improves metabolism by scavenging free radicals in Beta cells for modulated insulin secretion.
- Relieves hypothalamic irritation thus promotes and bio regulate insulin production by pancreas
- Improves resting energy expenditure.

TableVIII. Shows status of fasting blood sugar during therapy

| Fasting blood sugar (in mg%) | 1 st week | 2 nd week | 3 rd week | 4 th week | 6 th week |
|---------------------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| ----- --- | | | | | |
| <100 | 35 | 194 | 224 | 317 | 361 |
| 100-110 | 84 | 84 | 133 | 65 | 27 |
| 110-120 | 120 | 80 | 14 | 06 | 02 |
| 120-130 | 70 | 28 | 16 | 02 | - |
| 130-140 | 35 | 04 | 03 | - | - |
| 140-150 | 30 | - | - | - | - |
| 150-160 | 10 | - | - | - | - |
| 160-170 | 04 | - | - | - | - |
| >170 | 02 | - | - | - | - |

TableIX. Distribution of patients as per post prandial blood sugar during therapy

| PP Blood sugar (in mg) | 1 st week | 2 nd week | 3 rd week | 4 th week | 6 th week |
|------------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| ----- --- | | | | | |
| <150 | 35 | 52 | 156 | 199 | 337 |
| 150-160 | 16 | 90 | 102 | 138 | 53 |
| 160-170 | 80 | 140 | 68 | 45 | - |

| | | | | | |
|---------|----|----|----|----|---|
| 170-180 | 79 | 68 | 79 | 08 | - |
| 180-190 | 50 | 37 | 11 | - | - |
| 190-200 | 35 | 03 | - | - | - |
| 200-210 | 42 | - | - | - | - |
| 210-220 | 19 | - | - | - | - |
| 220-230 | 11 | - | - | - | - |
| 230-240 | 10 | - | - | - | - |
| 240-250 | 07 | - | - | - | - |
| >250 | 06 | - | - | - | - |

TableX. Distribution of patients as per their basic and post therapy biological values.

| Biological parameters | | Number of patients | | | |
|---------------------------|------|--------------------|--------------|--------|--------------|
| ----- | | | | | |
| ---- | | Male | | Female | |
| --- | | ----- | | | |
| | | Basic | Post therapy | Basic | Post therapy |
| ----- | | | | | |
| -- | | | | | |
| Hepatic parameter: | | | | | |
| Serum bilirubin : | | | | | |
| < 1mg | | 242 | 245 | 145 | 145 |
| >1mg | | 003 | - | - | - |
| SGOT: | | | | | |
| <35 IU | | 244 | 245 | 145 | 145 |
| >35IU | | 001 | - | - | - |
| SGPT: | | | | | |
| <35 IU | | 244 | 245 | 145 | 145 |
| >35 IU | | 001 | - | - | - |
| HbsAg: | | | | | |
| Positive | None | None | | None | None |
| Negative | | 245 | 245 | 145 | 145 |
| Renal parameter: | | | | | |
| Blood urea | | | | | |
| <20mg/dl | | 240 | 245 | 143 | 145 |
| >20 mg/dl | | 005 | - | 002 | - |
| Serum creatinine | | | | | |
| < 1.5mg/dl | | 244 | 245 | 145 | 145 |
| >1.5mg/dl | | 001 | - | - | - |
| Urine: | | | | | |
| Albumin | | | | | |
| Present | 001 | - | | - | - |
| Absent | | 244 | 245 | 145 | 145 |
| Ketone | | | | | |
| Present | 004 | - | | 003 | - |
| Absent | | 241 | 245 | 142 | 145 |
| Sugar: | | | | | |
| Present | 245 | - | | 145 | - |
| Absent | | - | 245 | - | 145 |
| Crystal: | | | | | |
| Present | 004 | - | | 002 | - |

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| Absent | 241 | 245 | 143 | 145 |
|--------------------------|-----|-----|-----|-----|
| Hematological: | | | | |
| Hemoglobin | | | | |
| <19gm/dl | 195 | - | 138 | - |
| >10gm/dl | 050 | 245 | 007 | 145 |
| Lipid profile: | | | | |
| Serum cholesterol | | | | |
| <200mg/dl | 130 | 244 | 080 | 145 |
| .200mg/dl | 115 | 001 | 065 | - |
| HDL | | | | |
| <60mg/dl | 115 | - | 065 | - |
| >60mg/dl | 130 | 245 | 080 | 145 |
| LDL | | | | |
| < 60mg/dl | 130 | 245 | 080 | 145 |
| >60mg/dl | 115 | - | 065 | - |
| ECG : | | | | |
| Normal | 245 | 245 | 145 | 145 |

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