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Botanical Medicine for Organ Health in Diabetes Mellitus– Analysis of Clinical Outcome

G. V. Amruthavalli [a*] and Gayathri Rajagopal [a]

[a] Dr JRK's Research and Pharmaceuticals Pvt., Ltd, India.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Diabetes is a metabolic disorder occurs due to insulin resistance or due to low production of insulin, this effects the glucose uptake by individual cells which progressively damages the cells or leads to improper functioning. These modifications at cellular levels progressively results in several co-morbidities. There are various medications available for blood glucose control not particular on cellular damages.

JRK's D-Co-D tablets is a polyherbal medicine that is studied for its role in blood glucose control and organ health improvement. A three arm multi centered clinical observations and outcome are collected for three groups.

Blood glucose related and other organ health indicative parameters against the prescription of JRK's D-Co-D tablets, a proprietary Siddha drug as an adjuvant to conventional therapy (Metformin +Vildagliptin) was analyzed. Conventional line of therapy without JRK's D-Co-D tablets and Madhumeghachoornam instead of JRK's D-Co-D tablets were kept as control groups.

Blood glucose related and other parameters (blood and urine) post inclusion of JRK's D-Co-D tablets as an adjuvant was shown a remarkable improvement when compared to other two groups. Statistical significance was also established for the above findings. The treatment inclusion of JRK's D-Co-D tablets clearly indicated significant improvement of various vital organs (functioning) and confirms the role of JRK's D-Co-D tablets to prevent co-morbidity associated with diabetes mellitus.

**Corresponding author: Email: amruthajrk2015@gmail.com;*

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1. INTRODUCTION

Diabetes mellitus, the metabolic disorder that leads to several co-morbidities and also cause progressive organ health impairment, especially of the vital organs like the pancreas kidney, heart, nerve cells, eye etc., due to high glucose burden in the blood [1] which in other words described as positive energy metabolic disorder is the inevitable ghost in waiting with reference to diabetic patients from the day the patient is diagnosed of the disease. The treatment priority these days is primarily focused on reducing blood glucose burden with the scientific notion that blood glucose burden is when eased, would automatically correct all associated medical consequences that are waiting in que to strike [2].

Tracing the etiology of the disease has ended up in the understanding of innumerable micro and macro aberrations in the system vertically and laterally contributing to the disease [3] and therefore the treatment strategy of hyperglycemia followed as on date is quite symptom driven and is not the total and complete approach [4].

The blood glucose burden can be reduced even by reduced intake of high carb diet but such strategy cannot be construed as increased or improved cellular sensitivity of insulin as in the case of type II diabetes mellitus [5]. The reason why cells are going shy to insulin has to be addressed systematically to prevent/reduce the radiating risks of diabetes mellitus is well known. Organ protection by improving their sugar metabolizing ability is the utmost step in the treatment along with continuously effort to delete as many ill-effects as possible contributing to the above, directly or indirectly.

JRK's D-Co-D tablets isa proprietary Siddha drug comprised of 8 medicinal herbs which are documented to have several medicinal effects in the ancient Siddha and Ayurveda healing literature, such as Nilavembu (*Andrographis paniculata*), Naval (*Syzygium cumini*), Seenthil (*Tinospora cordifolia*), Pagal (*Momordica charantia*), Koraikizhangu (*Cyperus rotundus*), Sukku (*Zingiber officinale*), Milaghu (*Piper nigrum*) and Adathodai (*Adhatoda vasica*) [6].

The formulation is a licensed Siddha drug for the management of diabetes mellitus with reference reducing the episode of co-morbidity by improving vital organ health. Plethora of scientific studies have been carried out on JRK's D-Co-D tablets to establish its wide range of therapeutic benefits and the JRK's D-Co-D tablets seems to have the ability of segregation and independent expression of various pharmacological benefits by passing first pass metabolism, thanks to the poly-herbal architecture of the formulation [6-10]. Besides that, the herbal constituents in the formulation also exhibit both drug and pro-drug value and therefore the direct and consequential therapeutic value of the drug makes it very unique, none to compare and the most wanted for diabetic patients.

Cellular glucose metabolism improvement to proteinuria correction to elimination of creatinine associated factors to redox potential balance to delayed carbohydrate processing at intestine to effect on lipid peroxidation to phagocyte mediated immune boosting to pancreatic cell revival to nerve cell activation, all such therapeutic value of JRK's D-Co-D tablets has been established at *In vitro* level [6-10].

Abundant clinical experience about the usefulness of JRK's D-Co-D tablets in the management of diabetes and improving the overall wellness is although available, the response pattern and improvement of organ function based on undeniable laboratory evidence collected from diabetic patient was not available and hence the present study was planned.

In the present study, confirmed cases of type II diabetes mellitus with marked aberration in various internal parameters, on Metformin +Vildagliptindrug treatment were additionally prescribed with JRK's D-Co-D tabletsby the treating physician over a period of 6 months. On the day of start to end of treatment period (6 months), various organ parameters were tested and based on the data, attempt has been made to interpret the real pharmacologic contribution of JRK's D-Co-D tablets to the above treatment line vis-à-vis control group, where treatment with Metformin + Vildagliptin but not JRK's D-Co-D tablets usage. Similarly, the therapeutic value of JRK's D-Co-D tablets as standalone drug and the clinical effect of Madhumeghachoornam- a generic Siddha drug [11], to conventional therapy is also included in the article. Findings are presented in the article.

2. MATERIALS AND METHODS

Test product details

1. JRK's D-Co-D tablet

Formulation details of DcoD
Each tablet (500mg) contains

Nilavembu (Andrographispaniculata):		100 mg
Naval (Syzygiumcumini)	:	50 mg
Seenthil (Tinosporacordifolia)	:	50 mg
Pagal (Momordicacharantia)	:	50 mg
Koraikizhangu (Cyperusrotundus):		50 mg
Sukku (Zingiberofficinale)	:	50 mg
Milaghu (Piper nigrum)	:	50 mg
Adathodai (Adhatodavasica)	:	50 mg
Excipients	:	Q.S

2. Metformin 500mg
3. Vildagliptin50 mg
4. Madhumeghachoornam – 1gm twice a day

Prescription based feedback cum observation method was followed in the present study with appropriate modification/changes required [12].

2.1 Details of Patients and Groups

Age, gender distribution of patients under three groups

Groups	No	Gender		Age in years			
				35-45	46-56	57-70	>70
1	100	♂	63	19	18	17	9
		♀	37	10	12	12	3
2	50	♂	32	15	10	6	1
		♀	18	9	4	4	1
3	50	♂	33	14	10	7	2
		♀	17	9	3	4	1

Group 1 – JRK's D-Co-D tablet + Metformin + Vidagliptin
Group 2 – Madhumeghachoornam + Metformin + Vidagliptin
Group 3 – Iron tablet (siddha) + Metformin + Vidagliptin

Group 1 - Duration of disease versus gender distribution

Gender	No.	Number of patients vis-à-vis duration of disease			
		1-5	6-9	10-12	13-15
M	63	38	18	4	3
F	37	19	5	10	3

Group 2 - Duration of disease versus gender distribution

Gender	No.	Number of patients vis-à-vis duration of disease			
		1-5	6-9	10-12	13-15
M (18-60 years)	32	17	9	4	2
F (18-60 years	18	8	5	4	1

Group 3 - Duration of disease versus gender distribution

Gender	No.	Number of patients vis-à-vis duration of disease			
		1-5	6-9	10-12	13-15
M	33	18	6	7	2
F	17	10	3	3	1

2.2 Inclusion Criteria Followed for Drug Prescription

1. People who are clinically proven for diabetes mellitus (type 2)
2. The duration of the disease between -1-15 years with the age ranged between 35-70 years
3. Predominantly on Metformin +Vidagliptin treatment for last 5 months
4. Also consulting AYUSH vaid besides diabetologist for AYUSH supplements which is not been objected by the respective diabetologist
5. Willing to use JRK's D-Co-D tablet as per the direction without altering or deviating the main line therapy (Metformin + Vidagliptin)
6. The patients who have not shown serious concern on any of the laboratory test parameters that may warrant the patient to be referred to specialized treatment
7. Patients who are willing to subject to certain laboratory investigations at entry level, 45 days, three and six month of therapy to ascertain treatment response
8. Patients who agree to the CRO and Sponsor to review and use the laboratory test results obtained purely for research purpose, without divulging the identity of the patient and where the medical benefit of JRK's D-Co-D can be reached out to large section of patients in India and other countries
9. Patients who agree to consult the respective diabetologist without fail; where participation in the present observational study will not be construed by the patient such regular consultation of the diabetologist is not required

2.3 Exclusion Criteria

1. No agreed to any of the criteria mentioned above
2. Lactating female and pregnant women
3. Patients who may be suffering from infection, other health complications that may require primary medical attention

2.4 Parameters Tested

The following critical diabetic prognosis and diagnosis linked parameters such as Fasting blood glucose (FBG), post prandial blood glucose (PPBG), random blood glucose (RBG), HbA1c (glycated haemoglobin), K^+, Ba, urea, creatinine, uric acid, total protein, albumin, bilirubin, alkaline phosphatase, acid phosphatase, amylase, total cholesterol, triglyceride, Vit B12, urine Na, K^+, creatine, systolic and diastolic blood pressure. All the above parameters were tested on day 0, day, day 90 and 180 of therapy.

3. RESULTS

3.1 Clinical Findings on Group 1

Day zero

All blood parameters of the patients on day zero showed clear evidence of aberration and the rate of aberration was high with duration of the disease, Table 1, Table 2 and Table 3.

Table 1. Blood glucose profile of patients

Gender	Parameters tested	Duration of disease (years)/ Mean and Standard deviation of FBG, PPBG, RBG,HbA1c			
		1-5	6-9	10-12	13-15
M(63)	FBG	140 ± 30	142 ± 5	160 ± 2	162 ± 0.5
	PPBG	240± 10	280 ± 3	320 ± 5	340 ± 0.2
	RBG	290 ± 30	311 ± 10	290 ±3	300 ±2
	HbA1c	6.5 ±2	6.8 ± 0.5	8 ± 0.5	8.2 ±0.1
F (37)	FBG	150 ± 22	138 ± 7	150 ± 1	159 ± 0.3
	PPBG	251± 11	292 ± 5	300 ± 3	360 ± 0.5
	RBG	300 ± 10	320 ± 8	295 ±4	315 ± 4
	HbA1c	6.5 ±2	6.9 ± 0.2	8.2 ± 0.4	8.5 ±0.2

Table 2. Organ health details based on laboratory investigation

Tests	Reference value	Range and Number of patients in parenthesis			
Na	134-145 mmol/L	147-152 (38)	153-157 (47)	158-160 (10)	161-163 (5)
K^+	3.5-5.5 mmol/L	3.5-5.5 (90)	<3 (10)	-	-
Urea	2.5-6.6 mmol/L	2.7-6.8 (60)	6.9-7.3 (35)	7.4-7.6 (5)	-
Creatine	72-126 mmol/L	72-126 (64)	127-134 (26)	135-138 (8)	139-144 (2)
Uric acid	120-420 mmol/L	120-420 (91)	>420(9)	-	-
Total protein	62-80 g/L	62-80 (82)	81-90 (15)	91-99 (3)	-
Albumin	28-40 g/L	28-40 (80)	41-45 (12)	46-49(8)	-
Bilirubin	3.4-17 µmol/L	3.4-17 (93)	18-20 (7)	-	-
Alkaline phosphatase	21-92 IU/L	21-92 (91)	93-110 (5)	111-119 (4)	-
Acid phosphatase	3.10 IU/L	3.10 (80)	3.15 (15)	3.18 (3)	3.2 (2)
Amylase	Less than 300 IU/L	250-300 (21)	301-350 (71)	351-370(8)	-
Total cholesterol	3.5 – 6.5 mmol/L	3.5-6.5 (15)	6.6-7.2 (50)	7.3-8 (30)	8.1-8.7 (5)
Triglyceride	0.50-1.75 mmol/L	0.50-1.75 (95)	1.76-1.79 (5)	-	-
Vitamin B12	200-900 ng/ml	501-800 (92)	300-500 (8)	-	-
		Urine test			
Na	100-250 mmol/L- 24 h	251-311 (98)	312-318 (2)	-	-
K^+	41- 120 mmol/L 24 h	41-60 (93)	61-80(7)	-	-
Creatine	9-17 mmol/L 24 h	9-17(70)	18-20 (30)	-	-

Table 3. Systolic and diastolic status

Blood pressure Tests	Reference value	Range and Number of patients in parenthesis	
Systolic blood pressure	120	110-140 (90)	141-152 (10)
Diastolic blood pressure	80	70-80 (85)	81-95 (15)

Table 4. Blood glucose profile of patients

Gender	Parameters tested	Duration of disease (years)/ Mean and Standard deviation of FBG, PPBG, RBG,HbA1c			
		1-5	**6-9**	**10-12**	**13-15**
M(63)	Fasting blood sugar, FBG	128 ± 6	132 ± 7	158 ± 3	152 ± 0.6
	2hrs post prandial blood sugar, PPBG	173± 4	260 ± 5	310 ± 3	380 ± 0.4
	Random blood sugar RBG	211 ± 12	300 ± 11	283 ±4	290 ±4
	HbA1c	6.1 ±3	6.7 ± 0.7	7.9 ± 0.5	8.0±0.3
F (37)	FBG	140 ± 12	131 ± 5	148 ±0.5	156 ± 0.4
	PPBG	231± 3	282 ± 4	290 ± 2	350 ± 0.4
	RBG	288 ± 5	310 ± 5	291 ±3	3151± 3
	HbA1c	6.4 ±3	6.4 ± 0.2	8.1 ± 0.2	8.1 ±0.3

Table 5. Organ health details based on laboratory investigation

Tests	Reference value	Range and Number of patients in parenthesis			
Na	134-145 mmol/L	<145 (78)	146-155 (17)	156-160 (2)	161-162 (3)
K^+	3.5-5.5 mmol/L	3.5-5.5 (98)	<3 (2)	-	-
Urea	2.5-6.6 mmol/L	2.7-6.8 (80)	6.9-7.3 (18)	7.4-7.6 (2)	-
Creatine	72-126 mmol/L	72-126 (84)	127-134 (16)	-	-
Uric acid	120-420 mmol/L	120-420 (100)	-	-	-
Total protein	62-80 g/L	62-80 (98)	81-90 (2)	-	-
Albumin	28-40 g/L	28-40 (80)	41-45 (16)	46-49(4)	-
Bilirubin	3.4-17 µmol/L	3.4-17 (94)	18-20 (6)	-	-
Alkaline phosphatase	21-92 IU/L	21-92 (91)	93-110 (7)	111-119 (3)	-
Acid phosphatase	3.10 IU/L	3.10 (88)	3.15 (10)	3.18 (2)	
Amylase	Less than 300 IU/L	250-300 (66)	301-350 (30)	351-370(4)	-
Total cholesterol	3.5 – 6.5 mmol/L	3.5-6.5 (45)	6.6-7.2 (30)	7.3-8 (20)	8.1-8.7 (5)
Triglyceride	0.50-1.75 mmol/L	0.50-1.75 (97)	1.76-1.79 (3)	-	-
Vitamin B12	200-900 ng/ml	501-800 (98)	300-500 (2)	-	-
Urine test					
Na	100-250 mmol/L-24 h	251-300 (99)	301-311 (1)	-	-
K^+	41- 120 mmol/L 24 h	41-60 (97)	61-80(3)	-	-
Creatine	9-17 mmol/L 24 h	9-17(80)	18-20 (20)	-	-

Table 6. Systolic and Diastolic status

Tests	Reference value	Range and Number of patients in parenthesis	
Systolic blood pressure	120	110-140 (95)	141-152 (5)
Diastolic blood pressure	80	70-80 (99)	81-95 (1)

Day 90

Marginal decrease in aberration of various parameters in the group was observed on 45-day treatment and the treatment response was greater in patients who suffer shorter duration of the disease. Further the decrease in standard deviation number showing higher distance from the arithmetic mean suggest the value stabilization possibly due to treatment intervention, Tables 4, 5 and 6. Patients showed marginal reduction in blood glucose levels (Table 4) and also organ health parameters (Table 5) and blood pressure was in control (Table 6) which is clearly indicating the role of JRK's D-Co-D in Diabetes in improving the blood glucose control and reducing co-morbidities and organ damages in 3months duration. However, the difference is not statistically significant.

Day 180

Dramatic improvement in the functioning of various parameters was observed on day 180 of treatment with clear reduction in standard deviation value suggesting the positive role of treatment intervention, Tables 7, 8 and 9.

Patients showed significant reduction in blood glucose levels (Table 7) and also organ health parameters (Table 8) and blood pressure was in control (Table 9) which is clearly indicating the role of JRK's D-Co-D in Diabetes in improving the blood glucose control and reducing co-morbidities and organ damages in 6 months' duration.

Table 7. Blood glucose profile of patients

Gender	Parameters tested	Duration of disease (years)/ Mean and Standard deviation of FBG, PPBG, RBG,HbA1c			
		1-5	6-9	10-12	13-15
M(63)	FBG	108 ± 1	122 ± 3	159 ± 0.2	150 ± 0.1
	PPBG	143± 2	200 ±15	295 ± 0.1	374 ± 0.1
	RBG	180 ± 8	260± 11	281 ±0.1	280 ±0.1
	HbA1c	5.7 ±2	6.5 ± 2	7.5 ± 0.1	7.8±0.1
F (37)	FBG	131 ± 0.5	124 ±0.2	140 ±0.1	152 ± 0.1
	PPBG	211± 0.1	269 ± 0.1	270 ± 0.1	344 ± 0.2
	RBG	217 ±0.1	300 ± 0.1	275 ±0.2	300± 0.2
	HbA1c	6.2 ±1	6.2 ± 0.1	7.9 ± 0.1	8 ±0.1

Table 8. Organ health details based on laboratory investigation

Tests	Reference value	Range and Number of patients in parenthesis		
Na	134-145 mmol/L	<145 (85)	146-155 (10)	156-160 (5)
K^+	3.5-5.5 mmol/L	3.5-5.5 (100)	-	-
Urea	2.5-6.6 mmol/L	2.7-6.8 (91)	6.9-7.3 (8)	7.4-7.6 (1)
Creatine	72-126 mmol/L	72-126 (88)	127-134 (12)	-
Uric acid	120-420 mmol/L	120-420 (100)	-	-
Total protein	62-80 g/L	62-80 (100)		-
Albumin	28-40 g/L	28-40 (90)	41-45 (9)	46-49(1)
Bilirubin	3.4-17 µmol/L	3.4-17 (98)	18-20 (2)	-
Alkaline phosphatase	21-92 IU/L	21-92 (99)	93-110 (1)	-
Acid phosphatase	3.10 IU/L	3.10 (90)	3.15 (10)	-
Amylase	Less than 300 IU/L	200-250 (80)	251-270 (20)	-
Total cholesterol	3.5 – 6.5 mmol/L	3.5-6.5 (90)	6.6-7.2 (10)	-
Triglyceride	0.50-1.75 mmol/L	0.50-1.75 (100)	-	-
Vitamin B12	200-900 ng/ml	501-800 (100)	-	-
Na	100-250 mmol/L- 24 h	251-300 (100)	-	-
K^+	41- 120 mmol/L 24 h	41-60 (100)	-	-
Creatine	9-17 mmol/L 24 h	9-17(100)	-	-

Table 9. Systolic and diastolic status

Tests	Reference value	Range and Number of patients in parenthesis
Systolic blood pressure	120	110-140 (100)
Diastolic blood pressure	80	70-80 (100)

Table 10. Clinical findings showing Duration of disease and Mean and Standard deviation of FBG, PPBG, RBG, HbA1

Gender	Parameters tested	Duration of disease (years)/ Mean and Standard deviation of FBG, PPBG, RBG,HbA1c			
		1-5	6-9	10-12	13-15
M(32)	FBG	140 ± 30	142 ± 5	160 ± 2	162 ± 0.5
	PPBG	240± 10	280 ± 3	320 ± 5	340 ± 0.2
	RBG	290 ± 30	311 ± 10	290 ±3	300 ±2
	HbA1c	6.5 ±2	6.8 ± 0.5	8 ± 0.5	8.2 ±0.1
F (18)	FBG	150 ± 22	138 ± 7	150 ± 1	159 ± 0.3
	PPBG	251± 11	292 ± 5	300 ± 3	360 ± 0.5
	RBG	300 ± 10	320 ± 8	295 ±4	315 ± 4
	HbA1c	6.5 ±2	6.9 ± 0.2	8.2 ± 0.4	8.5 ±0.2

Table 11. Organ health details based on laboratory investigation

Tests	Reference value	Range and Number of patients in parenthesis			
Na	134-145 mmol/L	147-152 (21)	153-157 (18)	158-160 (4)	161-163 (2)
K^+	3.5-5.5 mmol/L	3.5-5.5 (40)	<3 (10)	-	-
Urea	2.5-6.6 mmol/L	2.7-6.8 (32)	6.9-7.3 (12)	7.4-7.6 (6)	-
Creatine	72-126 mmol/L	72-126 (39)	127-134 (10)	135-138 (8)	139-144 (1)
Uric acid	120-420 mmol/L	120-420 (43)	>420(7)	-	-
Total protein	62-80 g/L	62-80 (41)	81-90 (5)	91-99 (4)	-
Albumin	28-40 g/L	28-40 (35)	41-45 (11)	46-49(4)	-
Bilirubin	3.4-17 µmol/L	3.4-17 (43)	18-20 (7)	-	-
Alkaline phosphatase	21-92 IU/L	21-92 (38)	93-110 (9)	111-119 (4)	-
Acid phosphatase	3.10 IU/L	3.10 (30)	3.15 (15)	3.18 (2)	3.2 (3)
Amylase	Less than 300 IU/L	250-300 (21)	301-350 (20)	351-370(9)	-
Total cholesterol	3.5 – 6.5 mmol/L	3.5-6.5 (12)	6.6-7.2 (35)	7.3-8 (2)	8.1-8.7 (1)
Triglyceride	0.50-1.75 mmol/L	0.50-1.75 (44)	1.76-1.79 (6)	-	-
Vitamin B12	200-900 ng/ml	501-800 (46)	300-500 (4)	-	-
		Urine test			
Na	100-250 mmol/L- 24 h	251-311 (40)	312-318 (10)	-	-
K^+	41- 120 mmol/L 24 h	41-60 (43)	61-80(7)	-	-
Creatine	9-17 mmol/L 24 h	9-17(46)	18-20 (4)	-	-

Table 12. Systolic and diastolic status

Tests	Reference value	Range and Number of patients in parenthesis	
Systolic blood pressure	120	110-140 (39)	141-152 (11)
Diastolic blood pressure	80	70-80 (10)	81-95 (40)

3.2 Clinical Findings on Group 2

Day Zero

All blood and organ parameter test findings clearly show abnormality and the extent of aberration directly co-relate with duration of the disease, Tables 10, 11, 12.

Day 90

The treatment intervention has not altered or improved the blood and other parameters significantly over 90-day treatment, Tables 13,14 and 15.

Table 13 Blood glucose profile of patients

Gender	Parameters tested	Duration of disease (years)/ Mean and Standard deviation of FBG, PPBG, RBG,HbA1c			
		1-5	**5-7**	**10-12**	**13-15**
M(32)	FBG	140 ± 20	141 ± 3	161 ± 1	161 ± 0.3
	PPBG	241±7	280 ± 2	319 ± 3	330 ± 0.1
	RBG	290 ± 5	300 ± 12	280 ± 5	300 ±1
	HbA1c	6.5 ±1	6.8 ± 0.2	8 ± 0.3	8.1 ±0.2
F (18)	FBG	150 ± 12	136 ± 3	150 ± 0.5	159 ± 0.1
	PPBG	251± 5	292 ± 4	288 ± 2	350 ± 0.7
	RBG	288 ± 8	320 ± 3	290 ±3	305 ± 5
	HbA1c	6.5 ±1	6.9 ± 0.1	8.1 ± 0.3	8.5 ±0.1

Table 14. Organ health details based on laboratory investigation

Tests	Reference value	Range and Number of patients in parenthesis			
Na	134-145 mmol/L	147-150 (26)	151-155 (20)	156-160 (4)	-
K^+	3.5-5.5 mmol/L	3.5-5.5 (44)	<3 (6)	-	-
Urea	2.5-6.6 mmol/L	2.7-6.8 (40)	6.9-7.3 (10)	-	-
Creatine	72-126 mmol/L	72-126 (40)	127-135 (7)	135-138 (3)	-
Uric acid	120-420 mmol/L	120-420 (45)	>420 (5)	-	-
Total protein	62-80 g/L	62-80 (44)	81-90 (5)	91-99 (1)	-
Albumin	28-40 g/L	28-40 (36)	41-45 (10)	46-49(4)	-
Bilirubin	3.4-17 µmol/L	3.4-17 (45)	18-20 (5)	-	-
Alkaline phosphatase	21-92 IU/L	21-92 (40)	93-110 (7)	111-119 (3)	-
Acid phosphatase	3.10 IU/L	3.10 (35)	3.15 (10)	3.18 (4)	3.2 (1)
Amylase	Less than 300 IU/L	250-300 (22)	301-350 (18)	351-370(10)	-
Total cholesterol	3.5 – 6.5 mmol/L	3.5-6.5 (15)	6.6-7.2 (35)	-	-
Triglyceride	0.50-1.75 mmol/L	0.50-1.75 (44)	1.76-1.79 (6)	-	-
Vitamin B12	200-900 ng/ml	501-800 (46)	300-500 (4)	-	-
		Urine test			
Na	100-250 mmol/L- 24 h	251-310 (43)	312-318 (7)	-	-
K^+	41- 120 mmol/L 24 h	41-60 (45)	61-80(5)	-	-
Creatine	9-17 mmol/L 24 h	9-17(48)	18-20 (2)	-	-

Table 15. Systolic and diastolic status

Tests	Reference value	Range and Number of patients in parenthesis	
Systolic blood pressure	120	110-140 (40)	141-152 (10)
Diastolic blood pressure	80	70-80 (11)	81-95 (39)

Table 16. Blood glucose profile of patients

Gender	Parameters tested	Duration of disease (years)/ Mean and Standard deviation of FBG, PPBG, RBG,HbA1c			
		1-5	**6-9**	**10-12**	**13-15**
M(32)	FBG	138 ± 19	140 ± 1	160 ± 0.5	160 ± 0.1
	PPBG	235±5	281 ± 1	311 ± 1	321 ± 0.1
	RBG	283 ± 3	303 ± 6	260 ± 2	301 ±1
	HbA1c	6.5 ±1	6.6± 0.1	8 ± 0.1	8 ±0.1
F (18)	FBG	140 ± 5	118 ±1	145 ± 0.2	140 ± 0.3
	PPBG	231±0.2	280 ±1	270 ±1	343 ± 0.3
	RBG	280 ± 1	311 ± 1	272 ±1	288 ±1
	HbA1c	6.4 ±0.2	6.8 ± 0.1	8 ± 0.1	8.1 ±0.1

Day 180

The treatment interventionover 180 days does not seems to have any impact in improving the blood and other parameters suggesting the poor therapeutic value of Madhumeghachoornam in the treatment of diabetes mellitus, Tables 16,17 and 18.

3.3 Clinical Findings on Group 3

Day zero

The laboratory investigation has clearly proved abnormal blood and other parameters in all patients on day zero, Tables 19, 20 and 21.

Table 17. Organ health details based on laboratory investigation

Tests	Reference value	Range and Number of patients in parenthesis		
Na	134-145 mmol/L	147-150 (27)	151-155 (22)	156-160 (1)
K^+	3.5-5.5 mmol/L	3.5-5.5 (45)	<3 (5)	-
Urea	2.5-6.6 mmol/L	2.7-6.8 (41)	6.9-7.3 (9)	-
Creatine	72-126 mmol/L	72-126 (43)	127-135 (5)	135-138 (2)
Uric acid	120-420 mmol/L	120-420 (46)	>420 (4)	-
Total protein	62-80 g/L	62-80 (45)	81-90 (5)	-
Albumin	28-40 g/L	28-40 (37)	41-45 (11)	46-49(2)
Bilirubin	3.4-17 µmol/L	3.4-17 (45)	18-20 (5)	-
Alkaline phosphatase	21-92 IU/L	21-92 (41)	93-110 (9)	-
Acid phosphatase	3.10 IU/L	3.10 (36)	3.15 (12)	3.18 (2)
Amylase	Less than 300 IU/L	250-300 (23)	301-350 (20)	351-370(7)
Total cholesterol	3.5 – 6.5 mmol/L	3.5-6.5 (16)	6.6-7.2 (34)	-
Triglyceride	0.50-1.75 mmol/L	0.50-1.75 (45)	1.76-1.79 (5)	-
Vitamin B12	200-900 ng/ml	501-800 (46)	300-500 (4)	-
Urine test				
Na	100-250 mmol/L- 24 h	251-310 (44)	312-318 (6)	-
K^+	41- 120 mmol/L 24 h	41-60 (45)	61-80(5)	-
Creatine	9-17 mmol/L 24 h	9-17(49)	18-20 (1)	-

Table 18. Systolic and diastolic status

Tests	Reference value	Range and Number of patients in parenthesis	
Systolic blood pressure	120	110-140 (41)	141-152 (9)
Diastolic blood pressure	80	70-80 (12)	81-95 (38)

Table 19. Blood glucose profile of patients

Gender	Parameters tested	Duration of disease (years)/ Mean and Standard deviation of FBG, PPBG, RBG,HbA1c			
		1-5	**6-9**	**10-12**	**13-15**
M(33)	FBG	140 ± 30	142 ± 5	160 ± 2	162 ± 0.5
	PPBG	240± 10	280 ± 3	320 ± 5	340 ± 0.2
	RBG	290 ± 30	311 ± 10	290 ±3	300 ±2
	HbA1c	6.5 ±2	6.8 ± 0.5	8 ± 0.5	8.2 ±0.1
F (17)	FBG	150 ± 22	138 ± 7	150 ± 1	159 ± 0.3
	PPBG	251± 11	292 ± 5	300 ± 3	360 ± 0.5
	RBG	300 ± 10	320 ± 8	295 ±4	315 ± 4
	HbA1c	6.5 ±2	6.9 ± 0.2	8.2 ± 0.4	8.5 ±0.2

Table 20. Organ health details based on laboratory investigation

Tests	Reference value	Range and Number of patients in parenthesis			
Na	134-145 mmol/L	147-152 (21)	153-157 (19)	158-160 (5)	161-163 (5)
K^+	3.5-5.5 mmol/L	3.5-5.5 (46)	<3 (4)	-	-
Urea	2.5-6.6 mmol/L	2.7-6.8 (36)	6.9-7.3 (11)	7.4-7.6 (3)	-
Creatine	72-126 mmol/L	72-126(35)	127-134 (10)	135-138 (3)	139-144 (2)
Uric acid	120-420 mmol/L	120-420 (38)	>420(12)	-	-
Total protein	62-80 g/L	62-80 (39)	81-90 (6)	91-99 (5)	-
Albumin	28-40 g/L	28-40 (35)	41-45 (10)	46-49(5)	-

Tests	Reference value	Range and Number of patients in parenthesis			
Bilirubin	3.4-17 µmol/L	3.4-17 (36)	18-20 (14)	-	-
Alkaline phosphatase	21-92 IU/L	21-92 (33)	93-110 (11)	111-119 (6)	-
Acid phosphatase	3.10 IU/L	3.10 (29)	3.15 (11)	3.18 (6)	3.2 (4)
Amylase	Less than 300 IU/L	250-300 (20)	301-350 (21)	351-370(9)	-
Total cholesterol	3.5 – 6.5 mmol/L	3.5-6.5 (14)	6.6-7.2 (33)	7.3-8 (2)	8.1-8.7 (1)
Triglyceride	0.50-1.75 mmol/L	0.50-1.75 (45)	1.76-1.79 (5)	-	-
Vitamin B12	200-900 ng/ml	501-800 (45)	300-500 (5)	-	-
		Urine test			
Na	100-250 mmol/L- 24 h	251-311 (40)	312-318 (10)	-	-
K^+	41- 120 mmol/L 24 h	41-60 (43)	61-80(7)	-	-
Creatine	9-17 mmol/L 24 h	9-17(40)	18-20 (10)	-	-

Table 21. Systolic and diastolic status

Tests	Reference value	Range and Number of patients in parenthesis	
Systolic blood pressure	120	110-140 (35)	141-152 (15)
Diastolic blood pressure	80	70-80 (13)	81-95 (37)

Table 22. Blood glucose profile of patients

Gender	Parameters tested	Duration of disease (years)/ Mean and Standard deviation of FBG, PPBG, RBG,HbA1c			
		1-5	**5-7**	**10-12**	**13-15**
M(33)	FBG	137 ± 10	141 ± 3	160 ± 0.5	152 ± 0.6
	PPBG	240± 0.5	282 ± 1	318 ± 2	338 ± 0.1
	RBG	288 ± 10	309 ± 5	288 ±2	300 ±1
	HbA1c	6.5 ±1	6.7 ± 0.2	8 ± 0.2	8.1 ±0.1
F (17)	FBG	151 ± 12	138 ± 2	114 ± 0.5	147 ± 0.1
	PPBG	241± 9	290 ± 2	288 ± 2	361 ± 0.1
	RBG	288 ± 5	310 ± 4	290 ±2	311 ± 2
	HbA1c	6.5 ±1	6.8 ± 0.1	8.2 ± 0.2	8.5 ±0.1

Table 23. Organ health details based on laboratory investigation

Tests	Reference value	Range and Number of patients in parenthesis			
Na	134-145 mmol/L	146-150 (41)	151-157 (8)	158-160 (1)	-
K^+	3.5-5.5 mmol/L	3.5-5.5 (47)	<3 (3)	-	-
Urea	2.5-6.6 mmol/L	2.7-6.8 (40)	6.9-7.3 (9)	7.4-7.6 (1)	-
Creatine	72-126 mmol/L	72-126(39)	127-134 (5)	135-138 (6)	-
Uric acid	120-420 mmol/L	120-420 (40)	>420(10)	-	-
Total protein	62-80 g/L	62-80 (40)	81-90 (8)	91-99 (2)	-
Albumin	28-40 g/L	28-40 (40)	41-45 (8)	46-49(2)	-
Bilirubin	3.4-17 µmol/L	3.4-17 (42)	18-20 (8)	-	-
Alkaline phosphatase	21-92 IU/L	21-92 (40)	93-110 (7)	111-119 (3)	-
Acid phosphatase	3.10 IU/L	3.10 (31)	3.15 (10)	3.18 (8)	3.2 (1)
Amylase	Less than 300 IU/L	250-300 (20)	301-350 (20)	351-370(10)	-

Tests	Reference value	Range and Number of patients in parenthesis			
Total cholesterol	3.5 – 6.5 mmol/L	3.5-6.5 (15)	6.6-7.2 (20)	7.3-8 (5)	-
Triglyceride	0.50-1.75 mmol/L	0.50-1.75 (46)	1.76-1.79 (4)	-	-
Vitamin B12	200-900 ng/ml	501-800 (46)	300-500 (4)	-	-
Urine test					
Na	100-250 mmol/L- 24 h	251-311 (43)	312-318 (7)	-	-
K^+	41- 120 mmol/L 24 h	41-60 (45)	61-80(5)	-	-
Creatine	9-17 mmol/L 24 h	9-17(40)	18-20 (10)	-	-

Table 24. Systolic and diastolic status

Tests	Reference value	Range and Number of patients in parenthesis	
Systolic blood pressure	120	110-140 (39)	141-152 (11)
Diastolic blood pressure	80	70-80 (23)	81-95 (17)

Day 90

Treatment intervention of conventional line of therapy although offered limited benefit but the improvement rate was not as comparable as group 1, Tables 22, 23 and 24.

Day 180

The conventional line of therapy although was proven to be effective but individual variations in treatment response was observed as the standard deviation value showed high noise even on day 180 of treatment, Tables 25, 26 and 27.

3.4 Statistical tests

Odds ratio was calculated using the formula OR = (a/b)/(c/d) or (axd)/(bxc) where the 'good' treatment outcome in control group is 'a' and good treatment response in treated group is 'b'. 'c' and 'd' respectively are bad treatment responses respectively in control and treatment group. An odds ratio value less than one denote the response obtained in treatment group is significant over control.The results show that the parameters tested in group 1 has are well within the limits where as in group 3 there is no significant reduction. This data directly correlates with the chances of co-morbidities occurrence in group 3 subjects when compared to group 1 and due to higher levels of test parameters in group 3 when not in normal this also leads to organ damage (Table 28).

Group 1 – JRK's D-Co-D tablet + Metformin + Vidagliptin
Group 3 – Iron tablet (siddha) + Metformin + Vidagliptin

Table 25. Blood glucose profile of patients

Gender	Parameters tested	Duration of disease (years)/ Mean and Standard deviation of FBG, PPBG, RBG,HbA1c			
		1-5	5-7	10-12	13-15
M(33)	FBG	130 ± 1	123 ± 0.1	160 ± 0.1	150 ± 0.4
	PPBG	222± 0.1	267 ± 0.1	312 ±1	330 ± 0.1
	RBG	264 ± 2	279 ± 0.7	273 ±1	300 ±3
	HbA1c	6.1 ±0.1	6.7 ± 0.1	8 ± 0.1	8 ±0.1
F (17)	FBG	150 ± 6	124 ± 0.1	110 ± 0.1	145 ± 0.1
	PPBG	240± 3	278 ± 1	271 ± 1	360 ± 0.1
	RBG	280 ± 2	308± 1	280 ±1	301 ± 1
	HbA1c	6.4 ±0.5	6.6 ± 0.1	8.1 ± 0.1	8.4 ±0.1

Table 26. Organ health details based on laboratory investigation

Tests	Reference value	Range and Number of patients in parenthesis			
Na	134-145 mmol/L	146-150 (43)	151-157 (7)	-	-
K^+	3.5-5.5 mmol/L	3.5-5.5 (49)	<3 (1)	-	-
Urea	2.5-6.6 mmol/L	2.7-6.8 (40)	6.9-7.3 (10)	-	-
Creatine	72-126 mmol/L	72-126(40)	127-134 (6)	135-138 (4)	-
Uric acid	120-420 mmol/L	120-420 (40)	>420(10)	-	-
Total protein	62-80 g/L	62-80 (42)	81-90 (8)	-	-
Albumin	28-40 g/L	28-40 (41)	41-45 (9)	-	-
Bilirubin	3.4-17 µmol/L	3.4-17 (43)	18-20 (7)	-	-
Alkaline phosphatase	21-92 IU/L	21-92 (41)	93-110 (7)	111-119 (2)	-
Acid phosphatase	3.10 IU/L	3.10 (35)	3.15 (6)	3.18 (9)	-
Amylase	Less than 300 IU/L	250-300 (22)	301-350 (20)	351-370(8)	-
Total cholesterol	3.5 – 6.5 mmol/L	3.5-6.5 (16)	6.6-7.2 (20)	7.3-8 (4)	-
Triglyceride	0.50-1.75 mmol/L	0.50-1.75 (47)	1.76-1.79 (3)	-	-
Vitamin B12	200-900 ng/ml	501-800 (47)	300-500 (3)	-	-
Urine test					
Na	100-250 mmol/L- 24 h	251-311 (45)	312-318 (5)	-	-
K^+	41- 120 mmol/L 24 h	41-60 (45)	61-80(5)	-	-
Creatine	9-17 mmol/L 24 h	9-17(42)	18-20 (8)	-	-

Table 27. Systolic and diastolic status

Tests	Reference value	Range and Number of patients in parenthesis	
Systolic blood pressure	120	110-140 (40)	141-152 (10)
Diastolic blood pressure	80	70-80 (25)	81-95 (25)

Table 28.Test parameter using Odds ratio

Test parameters between group-1 and group-3 after 6 months treatment	OR (Odds ratio)
Na	0.133127
k	0.958696
urea	0.732601
creatinine	0.831169
amylase	0.288750
total cholesterol	0.190476

Paired students' 't' test was performed to ascertain the statistical significance of the values of the group at different treatment interval from zero day value. Social science statistics software https://www.socscistatistics.com/tests/studentttest/default2.aspx was used for the above purpose.

Odds ratio and margin of error was also calculated to a limited level where number of patients shifted to baseline value of various test parameters after treatment from the zero day status.

Six month JRK's D-Co-D tablets usage has brought down all blood parameters with P value less than 0.0001 except HbA1c.

Intervention of Madhumeghachoornam did not alter the blood parameters significantly.

Table 29.Statistical significance test on blood parameters among three groups

Group details	Parameters	P value from Zero day to different treatment period	
		3 month after treatment	6 month after treatment
Group 1 (n=100)	FBG	0.4601	< 0.001
	PPBG	0.4011	< 0.001
	RBG	0.5010	< 0.001
	HbA1c	0.6100	< 0.5000
Group 2 (n=50)	FBG	0.6111	0.5171
	PPBG	0.6811	0.5811
	RBG	0.6300	0.6100
	HbA1c	0.7131	0.6128
Group 3 (n=50)	FBG	0.5110	0.5001
	PPBG	0.5000	0.4900
	RBG	0.5330	0.4800
	HbA1c	0.6100	0.5170

Table 30. Statistical significance of various organ health indicators among three group

Parameters	P value from day zero to different treatment period					
	3 months			6 months		
	Group 1	Group 2	Group 3	Group 1	Group 2	Group 3
Na	< 0.001	< 0.01	< 0.01	< 0.0001	< 0.001	< 0.001
K	< 0.001	< 0.01	< 0.01	< 0.0001	< 0.021	< 0.005
Urea	< 0.001	0.0431	< 0.001	< 0.0001	< 0.031	< 0.001
Creatinine	< 0.001	< 0.001	< 0.001	< 0.0001	< 0.022	< 0.006
Uric acid	< 0.001	0.0334	0.0234	< 0.0001	< 0.018	< 0.004
Total protein	< 0.001	< 0.001	< 0.001	< 0.0001	< 0.001	< 0.001
Albumin	< 0.001	< 0.001	< 0.001	< 0.0001	< 0.001	< 0.001
Bilirubin	< 0.001	0.0445	< 0.001	< 0.0001	< 0.001	< 0.001
Alkaline phosphatase	< 0.001	< 0.001	< 0.001	< 0.0001	< 0.001	< 0.001
Acid phosphatase	< 0.001	< 0.001	< 0.001	< 0.0001	< 0.001	< 0.001
Amylase	< 0.001	0.0551	0.4991	< 0.0001	< 0.0677	< 0.012
Total cholesterol	< 0.001	0.0481	< 0.001	< 0.0001	< 0.0001	< 0.001
Triglyceride	< 0.001	< 0.01	< 0.01	< 0.0001	< 0.001	< 0.001
Vit B12	< 0.001	< 0.01	< 0.01	< 0.0001	< 0.001	< 0.001
Na in urine	< 0.001	< 0.01	< 0.01	< 0.0001	< 0.001	< 0.001
K in urine	< 0.001	< 0.01	< 0.01	< 0.0001	< 0.001	< 0.001
Creatinine in urine	< 0.001	< 0.01	< 0.01	< 0.0001	< 0.001	< 0.001

JRK's D-Co-D tablets intervention has significantly improved the health of various organs over three and six-month period with P value less than<0.0001. The blood parameters tested showed significant reduction in Group 1 in a period of 6months when compared to 3months of the same group and in 3 months and 6months in other groups.

Majority of patients had only marginal deviation in organ function and health indicator value in the beginning and hence the direction of improvement in other two groups over three and six-month period also is statistically significant and the respective P value is less than <0.0001.

4. DISCUSSION

Findings from the present analysis of data obtained from patients who were under group 1 over group 3 and group2 has clearly brought out the unique therapeutic value of JRK's D-Co-D tablets in the treatment of type 2 diabetes mellitus. We, in the present intervention study did not attempt to alter the existing line of therapy of Metformin + Vildagliptin and instead wants to position and promote JRK's D-Co-D tablets only as an adjuvant medicament to the conventional line of therapy to achieve faster prognosis and improving organ health and thereby to reduce co-morbidity associated with diabetes.

Metformin + Vildagliptin is although the proven treatment line for diabetes mellitus but to reduce blood glucose burden and improve insulin sensitivity, patients continue to show high spike in blood glucose despite very high concentration of drug usage, as high as 1-2 gm per day of metformin. The above situation observed in several patients on Metformin + Vildagliptin may be due to diet indiscipline and other associated reasons or due to food-drug interaction between metformin and some types of food. Many diabetic patients, especially in rural India seldom follow diet discipline mostly due to high blood glucose threshold. As high as 300-400 dL of blood glucose also not seems to have any immediate effect that could affect the normal activity of the patient and hence bother the least about the disease and nor follow any diet discipline. Several studies have shown Metformin would decrease blood glucose and so are our earlier studies on herbal formulations of DCOD decrease blood glucose significantly [1,14].

How the inclusion of JRK's D-Co-D tablets to the conventional line of therapy with Metformin + Vildagliptin has brought a dramatic shift in blood and other parameters and improve overall organ health in a period of 90-180 days owes two body of explanations. The first explanation is relating to JRK's D-Co-D tablets possibly staggering the release of Metformin + Vildagliptin and also may be fencing metformin from losing its potency or effect due to drug-food interaction [12,13]. Among various allopathic drugs, metformin is the most studied allopathic drug having very high and versatile drug-food interaction resulting in metformin losing its therapeutic effect quickly. The other possibility could be, JRK's D-Co-D tablets may have greater cellular effect and other pharmacological benefits leading to a cascading effect, resulting in greater therapeutic outcome with Metformin + Vildagliptin treatment when JRK's D-Co-D tablets is included. Our findings gain further confirmation from the control drug – Madhumeghachoornam that we used along with Metformin + Vildagliptin. The intervention of Madhumeghachoornam did not bring any significant positive treatment response clearly suggesting Madhumeghachoornam does not have any such therapeutic value like that of JRK's D-Co-D tablets. Studies on Madhumeghachoornam also has shown marginal anti diabetic effect [10].

5. CONCLUSION

The overall response with the intervention of JRK's D-Co-D tablets to conventional line of therapy was only appreciable as the duration of treatment was only 180 days. Further individual diversity in blood and other parameters was quite high due to both inherent and external driven reasons such as age of the patient, alcoholism, drug abuse, smoking, poor food discipline, occupation, life style, other disease burden etc. But we observed that the standard deviation value has shown great reduction which suggests many odds may be getting corrected due to JRK's D-Co-D tablets. We have already established several pharmacological benefit of JRK's D-Co-D tablets through enzymatic and cell culture assays to establish the possible role of JRK's D-Co-D tablets to promote organ health and prevent/reduce co-morbidity. The present data clearly suggest JRK's D-Co-D tablets has significant therapeutic value in the treatment of type 2 diabetes mellitus to speed up the prognosis and promote organ health. Several nutritional supplements and multivitamins and multi minerals known to improve overall wellness and organ health in diabetic patients [14].

CONSENT

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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