Hypoglycaemic and hypolipidaemic activities of a polyherbal formulation in streptozotocine – nicotinamide induced type 2 diabetes mellitus rats

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International Diabetes Federation (2011) recently reported that the prevalence of diabetes mellitus is dramatically increasing worldwide. It has been estimated that 366 million people of world population have diabetes in 2011; by 2030 this will have risen to 552 million. Globally, 85% of all people who remain undiagnosed diabetes are in low and middle-income countries (International Diabetes Federation, 2011). A national study on Sri Lankan subjects aged over 20 years indicated a 20-30% population prevalence of dysglycaemia incluing Type 2 diabetes mellitus (T2DM) caused by insulin resistance in adults (Katulanda et al., 2008).[2] Physical inactivity, raised body mass index (BMI) and central obesity along with urban living are strongly associated with the increased risk of dysglycaemia. In the presence of substantial failure in long term management of hyperglycaemia and its complications with existing synthetic drugs, the scientists are focusing on natural resources to develop alternative drugs and strategies for

better management of hyperglycaemia and its complications. The main objective of the present study was to evaluate the effect of short term administration of a decoction of novel polyherbal formulation on serum glucose and lipid levels of "streptozotocine-nicotinamide induced hyperglycaemic condition of type 2 diabetes mellitus rat model" and compare them with the effects of two conventional antidiabetic drugs viz. Glibenclamide and Metformin on experimental rat model.

Two months old male Wistar albino rats (200-250g) were used in this experiment. After acclimatization for two weeks, normal rats were kept fasting for 16 hours and single intraperitonial injection of streptozotocin at a dose of 50mg/kg body weight was given after the intraperitoneal administration of nicotinamide at a dose of 250mg/kg body weight (Masiello et al, 1998). Fasting serum glucose levels were estimated to determine the induction of diabetes and rats showing elevated fasting serum glucose level > 250mg/dl were selected for the study and randomly divided into four groups consisting of 10 rats per each group.

The decoction of the novel polyherbal formulation was orally administered to the rats of decoction group at a dose of 10.8 ml/kg/day, whereas Glibenclamide (600µg/kg/day) and Metformin (270mg/kg/day) were orally administerd to the respective two positive

control groups and the placebo group was given comparable volume (10.8 ml/kg/day) of distilled water for 14 consecutive days. Blood samples were drawn at 14 days of drugs administration for determination of serum serum glucose levels and serum lipid levels.

All rats were normoglycaemic and normolipidaemic before the induction of type 2 diabetes mellitus. After induction of type 2 diabetes mellitus all groups showed elevated fasting serum glucose concentrations of greater than 250mg/dl. Before the initiation of treatment, fasting serum glucose concentration of placebo control group and $D_{2(8\rightarrow0.5)}$ decoction group were 266.0±2.6 and 273.9±3.7 mg/dl respectively while rats assigned for glibenclamide group and metformin group showed 267.2±3.6 and 281.7±6.1mg/dl of fasting serum glucose levels respectively. After 14 days treatment, the $D_{2(8\rightarrow0.5)}$ decoction group and two positive control groups showed statistically significant decrease in serum glucose levels compared to the placebo control group. The decoction group showed 47% decrease in fasting serum glucose level in comparison the that of control group whereas the Glibenclamide group and Metformin group showed 64% and 32% decrease in the same parameter. All groups showed significant decrease in serum glucose levels after oral administration of 50% glucose solution (Table 1)

Before the commencement of treatments, all groups showed no significant difference in serum total cholesterol, triglyceride, HDL, LDL and VLDL levels. After 14 days treatment, the $D_{2\ (8\rightarrow0.5)}$ decoction and other two positive control groups showed statistically significant decrease in fasting serum total cholesterol, triglyceride, LDL and VLDL levels and a significant increase in HDL level compared to those of placebo control group. When compared with the

serum lipid parameters of all groups before the initiation of treatment, placebo control group showed 37.1% increase in serum total cholesterol level while the $D_{2(8\rightarrow0.5)}$ decoction, Glibenclamide and Metformin groups showed 35.5%, 15.3% and 12.7% decrease in the same parameter. Further, the placebo control group showed 14.5% increased level of fasting serum triglyceride level (327.0±8.7mg/dl) after completion of 14 days of the experiment compared to the pretreatment level of triglyceride of placebo control group (285.5±13.2mg/dl). Fasting serum triglyceride level of $D_{2(8\rightarrow0.5)}$ decoction, Glibenclamide and Metformin groups were 174.8±8.2, 184.6±9.6 and 183.2±9.3mg/dl showed 44.2%, 36.5% and 42.7% decrease in serum triglyceride level compared to pretreatment level of triglyceride. $D_{2(8\rightarrow0.5)}$ decoction group showed 10.7% increase in serum HDL level (22.6±0.6mg/dl) in contrast to the depletion of same parameter by 29.6% in placebo control group (14.5±0.7 mg/dl) compared with the pretreatment levels of serum HDL of placebo control group (20.6±0.9 mg/dl) and $D_{2(8\rightarrow0.5)}$ decoction group (20.4±0.4 mg/dl).The serum LDL level of placebo control group was 85.2±4.0mg/dl and it was a 102.8% increase where as $D_{2\ (8\rightarrow0.5)}$ decoction group showed 38.6% decrease in serum LDL level (31.1±2.6mg/dl) compared to the pretreatment level of serum LDL of $D_{2(8\rightarrow0.5)}$ decoction group (50.7±6.7mg/dl) (Table 2).

According to the results observed, it could be concluded that the selected decoction of polyherbal formulation was effective in decreasing the serum glucose levels and lipid levels except to the increase in serum HDL levels of experimentally induced type 2 diabetic rat model. Further, the results of present study provide scientific background for further studies on the effect and efficacy of

the polyherbal formulation in the management of type 2 diabetic patients.

Table 1: Serum glucose levels of streptozotocine-nicotinamide induced type 2 diabetes mellitus rats after 14 days of treatment with $D_{2(8\rightarrow0.5)}$ decoction of polyherbal formulation, Glibenclamide and Metformin

Treatment	Serum Glucose Levels (Mean ±SEM - mg/dl)			
	0h	1h	2h	3h
Dist Water	293.9±3.0[a]	463.6±10.9[a]	526.5±8.2[a]	443.7±17.3[a]
Decoction	156.0±11.6[c]	199.2±12.3[c]	283.5±5.5[c]	194.9±7.6[c]
Glibenclamide	105.1±4.5[d]	194.6±11.7[c]	246.0±6.5[d]	168.8±5.3[c]
Metformine	197.9±8.9[b]	304.1±26.1[b]	440.6±15.5[b]	388.7±9.4[b]

In a column data are presented as Mean ±SEM of ten rats. For each time period, data indicated by different superscript letters are significantly different from each other(ANOVA; Tukey's test: $p<0.05$)

Table 2: Serum lipid levels of streptozotocine-nicotinamide induced Type 2 Diabetes Mellitus rats after 14 days of treatment with decoction of polyherbal formulation, Glibenclamide and Metformin

Treatment	Serum Lipid Levels (Mean ±SEM - mg/dl)				
	Total Cholesterol	Triglyceride	HDL	LDL	VLDL
Dist Water	165.1±3.6[a]	327.0±8.7[a]	14.5±0.7[b]	85.2±4.0[a]	65.4±1.7[a]

Decoction	88.6±2.6^{c}	174.8±8.2^{b}	22.6±0.6^{a}	31.1±2.6^{c}	35.0±1.6^{b}
Glibenclamide	116.6±3.0^{b}	184.6±9.6^{b}	19.0±0.7^{a}	60.6±2.9^{b}	36.9±1.9^{b}
Metformine	124.4±5.4^{b}	183.2±9.3^{b}	20.4±1.0^{a}	67.4±4.9^{b}	36.6±1.9^{b}

In a column data are presented as Mean ±SEM of ten rats. For each time period, data indicated by different superscript letters are significantly different from each other (ANOVA; Tukey's test: p<0.05)

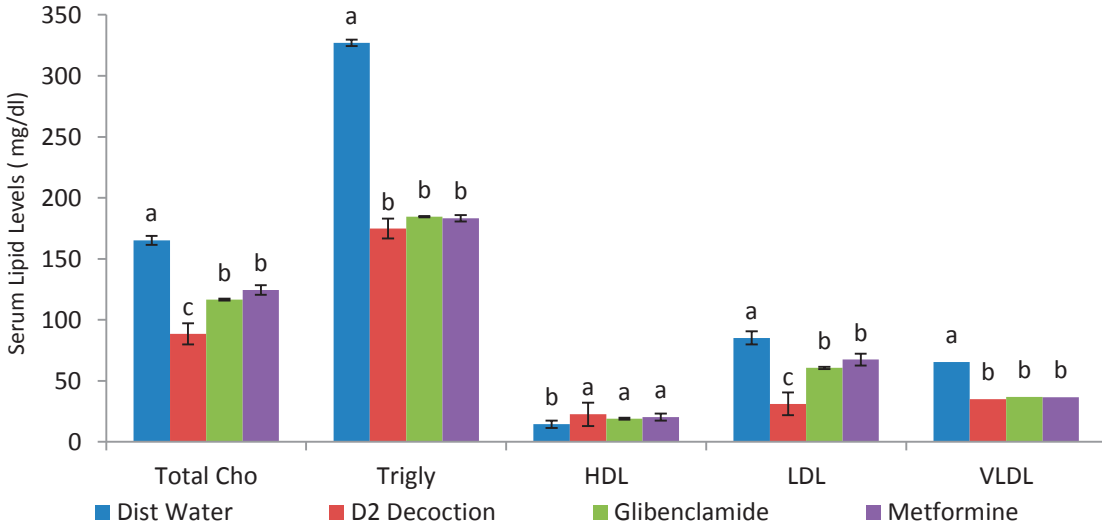

Figure 1: Serum lipid levels of streptozotocine-nicotinamide induced type 2 diabetes mellitus rats after 14days treatment of decoction of polyherbal formulation, Glibenclamide and Metformin *(Each bar represent the Mean ±SEM of ten rats. For each parameter, the bars indicated by different letters are significantly different from each other (ANOVA: p <0.05; Tukey's test: p<0.05).*

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