

**Efficacy of a novel formulation of medicinal plants in
managing experimentally induced hyperglycaemic and
hyperlipidaemic conditions in rat models**



Waliwita Angoda Liyanage Chandrasiri
(Reg No: FGS/01/01/07/2006/01)

Thesis submitted to the
Faculty of Graduate Studies, University of Kelaniya, Kelaniya, Sri Lanka
as a requirement for the degree of
Doctor of Philosophy

ප්‍රකාශන අංකය:	939
විෂය අංකය:	

February, 2014

ABSTRACT

Efficacy of a novel formulation of medicinal plants in managing experimentally induced hyperglycaemic and hyperlipidaemic conditions in rat models

Hyperglycaemia and hyperlipidaemia are two major pathophysiological conditions of Diabetes Mellitus. The present study was undertaken to investigate the effectiveness of decoction of a novel formulation consisting of 10 medicinal plant materials viz. fruits of *Terminalia chebula*, *Terminalia bellirica* & *Emblica officinalis*, seeds of *Eugenia jambolana* & *Nigella sativa*, stems of *Salacia reticulata* & *Coccinia indica*, rhizomes of *Curcuma longa* & *Picrorhiza kurroa* and bulbs of *Allium sativum* in managing hyperglycaemic and hyperlipidaemic conditions using six different experimental rat models which included normal healthy rats, hyperlipidaemic rats as well as drug induced Type I and Type II Diabetic rats.

In normal healthy rats, short term (14 days) and long term (90 days) oral administration (10.8 ml/kg body weight/day) of three different strengths of the decoction (D_1 (8→1), D_2 (8→0.5) and D_3 (8→0.25)) corresponding to 2.7g, 5.4g and 10.8g of the initial plant materials of mixture per dose respectively showed dose dependent effects on serum glucose and lipids levels. Although long term administration of both D_2 (8→0.5) and D_3 (8→0.25) decoctions induced significant decreases in serum glucose and lipid levels, only D_2 (8→0.5) decoction was evaluated further in dietary or/drug induced experimental rat models along with placebo and relevant conventional allopathic drugs due to the time and resource limitation. Potential side effects of the

treatments were assessed based on key hepatic enzymes and creatinine in the serum, haematological profile and histology of liver, kidney and pancreas in the rat models.

In diet induced hyperlipidaemic rats, short term and long term administration of $D_{2(8 \rightarrow 0.5)}$ decoction caused a significantly greater serum glucose, triglyceride and VLDL lowering effects compared to that of Simvastatin and Fenofibrate whereas both Simvastatin and Fenofibrate showed greater effects in decreasing serum total cholesterol and LDL levels. The two drugs and the decoction showed comparable increase in HDL in long term administration.

In alloxan induced type 1 diabetic rat model, serum glucose lowering effect of long term administration of $D_{2(8 \rightarrow 0.5)}$ decoction, Glibenclamide and Metformin followed the order: $D_{2(8 \rightarrow 0.5)} \approx$ Glibenclamide $>$ Metformin whereas the lipid lowering effects of the decoction and the two drugs were similar. In the streptozotocine-nicotinamide induced type 2 diabetic rat model, $D_{2(8 \rightarrow 0.5)}$ decoction administration induced similar glucose lowering and lipid lowering effects.

In both type 1 and type 2 diabetic rat models complicated with hyperlipidaemia, long term administration of $D_{2(8 \rightarrow 0.5)}$ decoction and Glibenclamide showed a greater decrease in serum glucose levels compared to Simvastatin. The $D_{2(8 \rightarrow 0.5)}$ decoction caused a greater decrease in serum total cholesterol and LDL levels compared to Glibenclamide whereas Simvastatin showed the highest lipid lowering effects in both short term and long term administration of the treatments.

In different experimental rat models examined, long term administration of $D_{2(8 \rightarrow 0.5)}$ decoction exhibited significant decreases in fasting serum glucose (31-66%), total cholesterol (24-60%), triglycerides (27-59%), LDL(43-80%) and VLDL(29-59%) levels and significant increase in HDL (9-66%) levels. In the rat models treated with decoction and conventional drugs, recovery of dietary induced liver steatosis conditions were observed where as experimentally induced pancreatic damage was not restored. Adverse effects of long term administration of the $D_{2(8 \rightarrow 0.5)}$ decoction were not found in relation to the haematological profile, key hepatic enzymes, & creatinine in the serum and histological structure of the tested organs.

In conclusion, long term oral administration of the $D_{2(8 \rightarrow 0.5)}$ decoction is effective in reducing hyperglycaemic and hyperlipidaemic conditions without causing adverse side effects in different experimental rat models. Hence the novel polyherbal formulation could be recommended for further evaluations especially genotoxicity and clinical efficacy.