International Journal of Diabetes Mellitus (2015) 3, 45–50

Diabetes Science International

International Journal of Diabetes Mellitus

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www.sciencedirect.com

ORIGINAL ARTICLE

Hypoglycemic and hypolipidemic effect of Allopolyherbal formulations in streptozotocin induced diabetes mellitus in rats

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Received 19 October 2010; accepted 11 January 2011

KEYWORDS

Streptozotocin (STZ);
Hypoglycemia;
Gliclazide;
Polyherbal formulation (PH);
Allopolyherbal formulation (APH)

Abstract *Aim of the study:* In the present study, we examined and compared the effect of Polyherbal (PH), Allopolyherbal-A (APH-A), Allopolyherbal-B (APH-B), and Allopolyherbal-C (APH-C) formulations on hyperglycemia, lipid profile, renal, and hepatic function in streptozotocin (STZ) induced diabetes mellitus in rats.

Materials and methods: The hypoglycemic activity (along with other parameters) of Polyherbal and Allopolyherbal formulations was investigated in STZ induced diabetes in rats. Polyherbal (PH) (3.63 g/kg body wt.); Allopolyherbal-A (APH-A) [(5 mg Gliclazide + 1.81 g PH)/kg body wt.]; Allopolyherbal-B (APH-B) [(4 mg Gliclazide + 2.17 g of PH)/kg body wt.]; Allopolyherbal-C (APH-C) [(2 mg of Gliclazide + 2.904 g of PH)/kg body wt.], and Gliclazide (10 mg/kg body wt.) were administered once a day, orally by gavages for 21 days.

Blood glucose levels were measured on 0, 7, 14, and 21 days of the study; total cholesterol, triglycerides, LDL, VLDL, HDL, serum creatinine, SGOT, and SGPT were estimated on 21st day.

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1877-5934
doi:10.1016/j.ijdm.2011.01.005

Production and hosting by Elsevier

Results: Gliclazide, Polyherbal (PH), Allopolyherbal-A (APH-A), Allopolyherbal-B (APH-B), and Allopolyherbal-C (APH-C) formulations treated rats showed significant ($P < 0.01$) decrease in blood glucose, total cholesterol, triglycerides, LDL, VLDL, serum creatinine, SGOT, and SGPT level, along with significant increase in HDL.

Conclusions: Present findings provide experimental evidence that the combination of allopathic hypoglycemic drugs with hypoglycemic Polyherbal formulations provides effective and rapid glycemic control and can also minimize the cardiovascular risk factors of type II diabetes mellitus.

1. Introduction

Diabetes mellitus is characterized by hyperglycemia, hypercholesterolemia, and hypertriglyceridemia, resulting from defects in insulin secretion or reduced sensitivity of the tissue to insulin (insulin resistance) and/or combination of both [1]. The worldwide survey reported that the diabetes is affecting nearly 10% of the population [2]. It is the third leading cause of death (after heart disease and cancer) in many developed countries.

It is a serious endocrine syndrome with poor metabolic control and responsible for increased risk of cardiovascular diseases including atherosclerosis, renal failure, blindness or diabetic cataract worldwide [3,4]. Therapeutic options for diabetes are diet, exercise, oral hypoglycemic drugs, and insulin therapy.

Treatment with oral hypoglycemic agents is associated with side effects related to pharmacokinetic properties, secondary failure rates, hypoglycemia, gastrointestinal disturbances, skin reactions, hematological disorders, and rise in hepatic enzyme level.

Management of diabetes without dyslipidemia and side effects is still a challenge to the medical community. For thousands of years plants and their derivatives are being used for treatment of diabetes mellitus. Although, herbal medicines have long been used effectively in treating diseases throughout the world and frequently considered to be less toxic and free from side effects as compared to synthetic ones [1,3]. The combination of allopathic and herbal drugs can help to overcome the resistance to insulin and oral hypoglycemic therapy in case of uncontrolled diabetes mellitus. The side effects, dyslipidemias and dose of allopathic drugs can be reduced by their use in combination with herbal drugs. One of the examples of such Allopolyherbal formulation is therapeutic approach by combination of 4-hydroxyisoleucine and pioglitazone and combined therapy of 4-hydroxyisoleucine and glyburide [5].

Streptozotocin (STZ) is a naturally occurring nitrosourea product of *Streptomyces achromogenes*. Usually, the intraperitoneal injection of a single dose (60 mg/kg body weight) of it exerts direct toxicity on β cells resulting in necrosis within 48–72 h and causes hyperglycemia.

In the present study, leaves and fruit pulp of *Aegle marmelos*, leaf pulp of *Aloe barbadensis*, leaves of *Azadirachta indica*, and seeds of *Trigonella foenum graecum* in Polyherbal (PH) and in combination with Gliclazide as Allopolyherbal-A (APH-A), Allopolyherbal-B (APH-B), and Allopolyherbal-C (APH-C) formulations were used to investigate their effect on blood glucose, lipid profile, serum creatinine, SGOT, and SGPT in rat model of STZ induced diabetes mellitus.

A comparison was made with the Gliclazide, a standard drug used in treatment of diabetes mellitus [6]. Gliclazide is a sulphonylurea drug which stimulates insulin secretion through the beta cell sulphonylurea receptor, and possibly through a direct effect on intracellular calcium transport. It specifically improves the abnormal first phase insulin release in type II diabetes, and also has an effect on the second phase. It is extensively metabolised, and renal clearance accounts for only 4% of total drug clearance. This pattern of insulin release is thought to explain the lower incidence of hypoglycemic episodes and weight gain compared with some other sulphonylureas. There is also a reduction in hepatic glucose production and improvement in glucose clearance, without changes in insulin receptors. This suggests a possible post-receptor effect on insulin action, perhaps by stimulation of hepatic fructose-2,6-bisphosphatase and muscle glycogen synthase. Gliclazide reduces platelet adhesion, aggregation, and hyperactivity and increases fibrinolysis. These actions, thought to be independent of its hypoglycemic activity, may make Gliclazide useful in halting the progression of diabetic microangiopathy [7].

The medicinal uses of plants used in study can be summarized as follows [8]:

Plant name	Family	Uses
A. marmelos	Rutaceae	Stomachic, antimicrobial, antidiarrhoeal, digestive, astringent, spasmolytic, hypoglycemic
A. barbadensis	Liliaceae	Purgative, topically emollient, anti-inflammatory, antimicrobial, hypoglycemic
A. indica	Meliaceae	Antimicrobial, antifungal, anthelmintic, antiviral, antipyretic, antimalarial, spermicidal, antiinflammatory, hypoglycemic
T. foenum graecum	Papilionaceae	Appetizer, demulcent, hypoglycemic

2. Materials and methods

Streptozotocin was purchased from Sisco Research Laboratories Pvt. Ltd., Mumbai, India; Gliclazide was purchased from Nu-Life Laboratories, India. All other chemicals and reagents used were of analytical grade and purchased from ASSES Chemicals, Jodhpur, Rajasthan. Glucose, cholesterol, triglyceride, total cholesterol, cholesterol–HDL, serum creatinine, SGPT, and SGOT kits were purchased from Logotech Delhi (India) Pvt. Ltd.

2.1. Plant material

The medicinal plants were identified and collected from local places of Jodhpur in month of August and September, authenticated by Botanical Survey of India, Jodhpur. *A.*