e-ISSN: 2320-4230, p-ISSN: 2961-6085

Journal of Drug Discovery and Therapeutics

Available Online at www.jddt.in

CODEN: - JDDTBP (Source: - American Chemical Society)

Volume 12, Issue 02; 2024, 167-174

Effect of Poly Herbal Extract of *Momordica Muricata* and *Trigonella Caerulea* Blend in Diabetes and Cardiomyopathy

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Received: 19-02-2024 / Revised: 09-03-2024 / Accepted: 10-04-2024

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Conflict of interest: No conflict of interest.

Abstract:

This study provides a thorough examination of the impact of a poly herbal extract including Momordica muricata (bitter melon) and Trigonella caerulea (fenugreek) on human well-being. Both herbs have a rich historical background of traditional use in several cultures and are acknowledged for their potential therapeutic advantages. This study emphasises the distinct therapeutic characteristics of each component and investigates the collective impact when used as a poly herbal extract. Momordica muricata and Trigonella caerulea are well-known for their therapeutic qualities and have been extensively used in many culinary and medicinal applications. The research study demonstrates the impact of a mixture on the buildup of lipids generated by diabetes, as well as the activities of ATPases in the serum and heart, levels of urea, creatinine, endogenous antioxidants, and lipid peroxidation in mice with STZ-induced diabetes. The research investigates how the distinct substances found in each plant may synergistically enhance and magnify the impacts of one another, possibly augmenting the overall health advantages.

INTRODUCTION

Diabetic cardiomyopathy and its therapeutic implications

Despite substantial progress in understanding the biology of diabetes and the existence of several therapeutic hypoglycemic medicines, the disease persists in deteriorating. Potentially, new thoroughfares might be constructed based on the development of diabetic drugs that exhibit both safety and promising potential. However, only a limited number of drugs, including metformin, vitamins C and E, and insulin, have the ability to reduce elevated blood glucose levels in diabetes. Achieving normal blood sugar levels, known as normoglycemia, is a desired outcome of any treatment used alone or in combination to treat the illness. While antioxidants are often used as adjuvants to insulin therapy, they are typically ineffectual in combating diabetes-induced hyperglycemia, as stated by Mudaliar et al. (2010). Various therapeutic interventions might be beneficial in preventing or postponing the development of diabetic cardiomyopathy and its related complications, which arise from many factors such as metabolic irregularities, heart

fibrosis, microvascular dysfunction, and insulin resistance. Studies have shown that antioxidants, insulin sensitizers, and exercise programmes may effectively decrease the likelihood of experiencing problems related to diabetes (Abuissa et al., 2005).

Hypoglycemic drugs

Sulfonylureas and biguanides are two widely used categories of oral anti-diabetic medications, however, they differ from each other in terms of their chemical composition and mode of action. Clinical studies using animal models have shown the efficacy of ciglitazone and other thiazolidinedione (TZD) analogues, sometimes known as glitazones or TZDs, as effective anti-hyperglycemic agents for NIDDM. Both pioglitazone and rosiglitazone, which are chemically identical chemicals, are already available for clinical use. Chlorpropamide, glibenclamide, and tolbutamide are three specific instances of sulfonylureas. The therapeutic efficacy of sulfonylureas for type II diabetics is believed to be due to their activities in both the pancreas and outside of it. Sulfonylureas have the ability to stimulate insulin release from beta cells in the islets of Langerhans without requiring glucose, as shown by Aspinwall et al. in 1999.

Metformin and phenformin, which are oral biguanide medicines, have been used for diabetic treatment since the 1960s. During the early 1990s, only metformin was approved for use in the United States (Stafford and Elasy, 2007). Phenformin was withdrawn off the market in many countries in the 1970s due to its association with lactic acidosis. Metformin, in contrast to sulfonylureas, specifically reduces blood glucose levels in individuals with diabetes and does not induce hypoglycemia in those without diabetes. Metformin does not have an impact on the basal insulin release from the pancreas or isolated islets of non-diabetic animals, as shown in a study by Bailey in 1992. The introduction of a-glucosidase inhibitors in the mid-1990s has led to a simplification and improved rationality in the treatment of diabetes. For over half a century, physicians have been endeavouring to discover an oral hypoglycemic drug capable of effectively regulating the abnormalities in glucose, lipid, and protein metabolism seen in individuals with diabetes. The use of current oral hypoglycemic medications, including sulfonylureas, metformin, thiazolidinediones, alpha-glucosidase inhibitors, and biguanides, has shown toxic side effects and limited positive benefits beyond their ability to lower blood glucose levels (Moss and Delawter, 1960).

Experimental work

MATERIALS AND METHODS

Experimental induction of diabetes in male Swiss albino mice

Animals

Male Swiss albino mice, aged eight weeks and weighing between 25-35 g, were acquired and kept in a controlled environment with regulated temperature and humidity. They were subjected to alternating 12-hour cycles of light and darkness and were acclimated to the conditions of the animal home. Throughout the trial period, the animals were provided with a standard pellet food (Hindustan Lever Ltd., Bangalore) and had unrestricted access to water. The experimental procedure received approval from the Institutional Animals Care and Ethical Committee.

Induction of diabetes

Prior to the tail vein injection of streptozotocin (100 mg/kg body weight) in 0.1M citrate buffer with a pH of 4.5, the mice were subjected to a 12-hour fasting period. The streptozotocin was made freshly for this single dosage administration, as

described by Rakieten et al. in 1963. Animals treated with STZ were given access to a 5% glucose solution overnight to counteract the hyperglycemia caused by the medication. The mice used as control subjects were administered an equivalent amount of sodium citrate as the animals induced with STZ at the time of induction. On the fifth day after STZ induction, blood glucose was measured from the mouse's tail vein using a comprehensive blood glucose monitor. According to Canepa et al. (1990), mice that were induced with STZ and had fasting blood glucose levels over 250 mg/dl were classified as diabetic animals.

Optimization and fixation of *Momordica muricata* and *Trigonella caerulea* blend dosage

The study evaluated the most efficient and ideal dosage of a combination of Momordica muricata and Trigonella caerulea by delivering several doses (150, 300, and 500 mg/kg) for varied durations (20, 40, and 60 days) to both a control group and a group of mice with diabetes. A group of rats were administered with STZ (100 mg/kg) to develop diabetes, and they were kept under routine conditions until the conclusion of the 60-day experimental period for toxicity tests. This section of the experiment aimed to determine the optimal dosage of a mix of Momordica muricata and Trigonella caerulea for treating organ toxicity generated by diabetes. Additionally, it sought to investigate if the blend itself caused any toxicity in normal control subjects. The animals were euthanized and the whole blood sample was obtained. (Canepa et al., 1990).

Experimental design

The normal and STZ-diabetic mice (fasting blood glucose 250 mg/dl) were divided in to four groups, each group consists of six animals. The animals were grouped as follows:

Group-I: Normal control mice received saline orally

Group-II: STZ-induced diabetic mice

Group-III: STZ-induced mice treated with poly herbal extract of *Momordica muricata and Trigonella caerulea* (250 mg/kg/mice/day-orally)

Group-IV: Normal mice treated with poly herbal extract of *Momordica muricata* and *Trigonella caerulea* (500 mg/kg/mice/day-orally)

Throughout the trial duration, the subjects' body weight and blood glucose levels were consistently observed and recorded. After the eight-week study period, the mice were anaesthetized and killed via cervical decapitation. Plasma and serum for biochemical assessments were collected with and without the addition of ethylenediamine-tetra-acetic acid (EDTA). The heart and kidney tissues were extracted and rinsed with cold saline solution before being used for further experimental procedures. (Canepa et al., 1990).

Evaluation of biological activity

Effects of poly herbal extract of *Momordica muricata and Trigonella caerulea* against diabetes induced lipid accumulation in STZ-diabetic mice.

The total amount of lipids, which includes cholesterol, triglycerides (TGL), and phospholipids, in the hearts of the different groups being studied. The STZ-diabetic mice exhibited substantially elevated levels of total cardiac lipids, cholesterol, triglycerides (TGL), and phospholipids ($p < 0.05$). The presence of abnormal lipid accumulation in the heart of diabetic individuals is indicated by the significant increase or reduction in these cardiac lipids seen in STZ-diabetic mice. The accumulation of lipids in the heart muscle is decreased in STZ-diabetic mice treated with

a combination of poly herbal extract from Momordica muricata and Trigonella caerulea. No discernible disparities were seen when comparing the control animals to those administered with a pure poly herbal extract of Momordica muricata and Trigonella caerulea. The reference is from Canepa et al. (1990).

Table 1: Cardiac total lipids, total cholesterol, triglycerides and phospholipids in the control, STZ-induced diabetic, and poly herbal extract of *Momordica muricata and Trigonella caerulea* treated animals

Groups	Total lipids	Total Cholesterol	Triglycerides	Phospholipids
Normal control mice (Group-I)	20 ± 1.03	2.11 ± 0.10	13.48 ± 0.87	14.52 ±0.66
STZ-Diabetic mice (Group-II)	38 ± 5.6[a]	3.98 ± 0.23[a]	28.89 ±1.73[a]	24.75 ± 1.29[a]
STZ-Diabetic mice + PHEMM-TC 250 mg/kg bw (Group-III)	26 ± 8.30[b]	2.80 ± 0.15[b]	20.56 ±1.35[b]	18.29 ± 1.08[b]
STZ-Diabetic mice + PHEMM-TC 500 mg/kg bw (Group-IV)	22 ± 6.11 [NS]	2.20 ± 8.24[NS]	12.32 ± 2.3[NS]	13.35 ±0.98[NS]

Mean standard deviation (n = 6 mice/group). a = significantly different from Group I at the 0.05 level; b = significantly different from Group II at the 0.05 level; NS = not significant. Superoxide dismutase (SOD) levels are reported in Units/mg protein; catalase (CAT) levels are reported in micrograms of hydrogen peroxide (H2O2) consumed (per minute) per milligramme of protein; glutathione (GSH) levels are reported in micrograms of glutathione (per minute) per milligramme of protein.

Effects of poly herbal extract of *Momordica muricata and Trigonella caerulea* and STZ on the activities of serum and cardiac ATPases.

The study investigated the effects of a polyherbal extract including Momordica muricata and Trigonella caerulea, as well as STZ, on the activity of ATPase in both serum and cardiac tissues. Group II animals with STZ-induced diabetes exhibited significantly reduced activity of Na+/K+ ATPase and Ca2+ ATPase enzymes compared to the normal control Group I animals ($p<0.05$). The activities are significantly improved with polyherbal extract treatment of Momordica muricata and Trigonella caerulea as compared to STZ-diabetic mice. Animals in Group IV, when administered a poly herbal extract of Momordica muricata and Trigonella caerulea, did not exhibit any significant differences compared to the normal control animals in Group I (Canepa et al, 1990).

Table 2: Membrane bound Na^+/K^+-ATPase and Ca^{2+}-ATPase in the normal control,diabetic control and poly herbal extract of *Momordica muricata and Trigonella caerulea* **treated animals**

Groups	Serum Na^+/K^+ ATPase	Cardiac Na^+/K^+ ATPase	Cardiac Ca^{2+} ATPase
Normal control mice (Group-I)	0.626 ± 0.006	4.21 ± 0.65	1.93 ± 0.25
STZ-Diabetic mice (Group-II)	0.438 ± 0.024[a]	2.89 ± 0.32[a]	0.87 ± 0.10[a]
STZ-Diabetic mice + PHEMM-TC 250 mg/kg bw (Group-III)	0.560 ± 0.014[b]	3.84 ± 0.51[b]	1.68 ± 0.21[b]
STZ-Diabetic mice + PHEMM-TC 500 mg/kg bw (Group-IV)	0.609 ± 0.010[NS]	4.28 ± 0.60[NS]	1.90 ± 0.26[NS]

Mean standard deviation (n = 6 mice/group). a = significantly different from Group I at the 0.05 level; b = significantly different from Group II at the 0.05 level; NS = not significant. Superoxide dismutase (SOD) levels are reported in Units/mg protein; catalase (CAT) levels are reported in micrograms of hydrogen peroxide (H2O2) consumed (per minute) per milligramme of protein; glutathione (GSH) levels are reported in micrograms of glutathione (per minute) per milligramme of protein.

Effect of poly herbal extract of *Momordica muricata and Trigonella caerulea* on STZ-diabetes induced urea and creatinine levels

Diabetic mice have considerably elevated levels of urea and creatinine in comparison to normal control animals ($p < 0.05$). Group IV mice, who were administered a poly herbal extract including Momordica muricata and Trigonella caerulea, had significantly reduced levels of this marker compared to group III diabetic animals. The polyherbal extract consists of Momordica muricata and Trigonella caerulea. There were no noticeable changes in these parameters in the mice in Group II (Canepa et al, 1990).

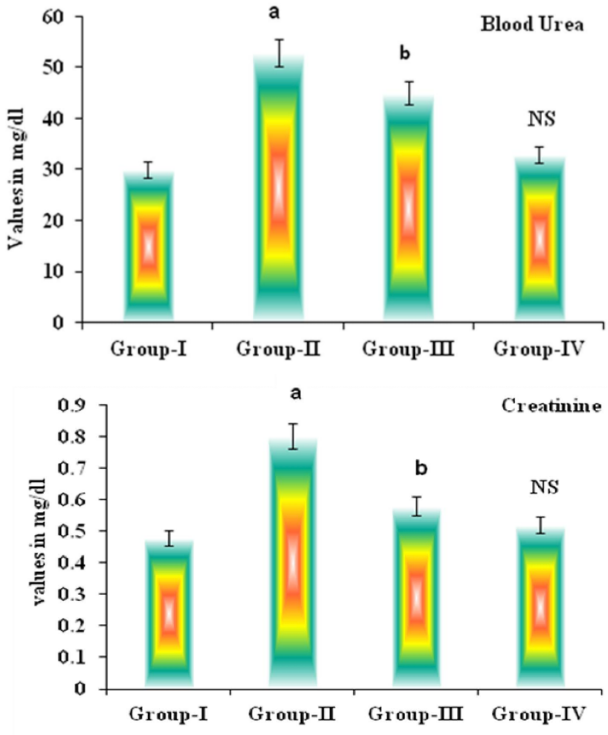

Figure 1: Blood Urea and Creatinine levels in the control, STZ-induced diabetic, andpoly herbal extract of *Momordica muricata and Trigonella caerulea* treated animals

Effect of poly herbal extract of *Momordica muricata* and *Trigonella caerulea* on MDA, nitric oxide and endogenous anti-oxidant levels in experimental groups

Levels of MDA, nitric oxide, and endogenous antioxidants were measured in mice treated with a poly herbal extract of Momordica muricata and Trigonella caerulea. The study included both normal and diabetic control groups. Mice in the STZ-induced diabetes group II had significantly elevated levels of MDA and NO compared to the normal control group. When comparing the effects of a polyherbal extract of Momordica muricata and Trigonella caerulea on mice treated in group III to mice with diabetes caused by STZ in group II, the levels of MDA and NO were restored to normal in group III. Group IV mice, who were administered just a poly herbal extract of Momordica muricata and Trigonella caerulea, did not exhibit any noteworthy changes. The table provides information on the levels of intracellular antioxidants, such as catalase, glutathione peroxidase, and superoxide dismutase. The concentrations of glutathione $(GSH), superoxide dismutase (SOD), and catalase were significantly reduced in the mouse groups induced with STZ, in comparison to the normal control mouse groups. Group-IV animals administered with a poly herbal extract including Momordica muricata and Trigonella caerulea exhibited significantly elevated levels in comparison to group II diabetic mice. Mice in group II that were not administered the drug had no discernible alterations. The reference is from Canepa et al. (1990).

Table 3: MDA, NO and endogenous anti-oxidant levels in the control, STZ-induceddiabetic, and poly herbal extract of *Momordica muricata and Trigonella caerulea* treated animals

Groups	MDA	NO	GSH	SOD (U/mg)	CAT
Normal control mice (Group-I)	74.04 ± 4.98	4.20± 0.20	35.53 ± 1.87	27.33 ± 1.19	20.83 ± 1.29
STZ-Diabetic mice (Group-II)	167.9 ±11.85[a]	8.36 ± 0.61[a]	8.36 ± 0.61[a]	11.89 ± 0.43[a]	5.73 ± 0.40[a]
STZ-Diabetic mice + PHEMM-TC 250 mg/kg bw (Group-III)	94.78 ± 6.45[b]	6.02 ± 0.52[b]	28.75 ± 1.68[b]	22.54 ± 0.99[b]	16.40± 0.96[b]
STZ-Diabetic mice + PHEMM-TC 500 mg/kg bw (Group-IV)	76.89 ±5.06[NS]	4.85 ±0.54[NS]	34.48 ± 1.72 NS	26.10 ±0.85[NS]	9.36± 1.11 NS

Mean standard deviation (n = 6 mice/group). a = significantly different from Group I at the 0.05 level; b = significantly different from Group II at the 0.05 level; NS = not significant. Superoxide dismutase (SOD) levels are reported in Units/mg protein; catalase (CAT) levels are reported in micrograms of hydrogen peroxide (H2O2) consumed (per minute) per milligramme of protein; glutathione (GSH) levels are reported in micrograms of glutathione (per minute) per milligramme of protein.

Effects of poly herbal extract of *Momordica muricata and Trigonella caerulea* and STZ-diabetes induced lipid peroxidation

The graphical representation depicts the lipid peroxidation in both blood and cardiac tissue induced by streptozotocin (STZ) and a poly herbal extract derived from Momordica muricata and Trigonella caerulea. The concentration of TBARS directly indicated the level of lipid peroxidation. Elevated levels of TBARS were detected in the serum and cardiac tissue of Group II-STZ diabetic mice in comparison to the normal control. Diabetic mice administered with a poly herbal extract of Momordica muricata and Trigonella caerulea (group-III) exhibited

reduced levels of TBARS in comparison to diabetic animals administered with STZ (group-II). No significant changes were seen when comparing Group-I animals to those administered with a poly herbal extract of Momordica muricata and Trigonella caerulea (Group-IV). (Canepa et al., 1990).

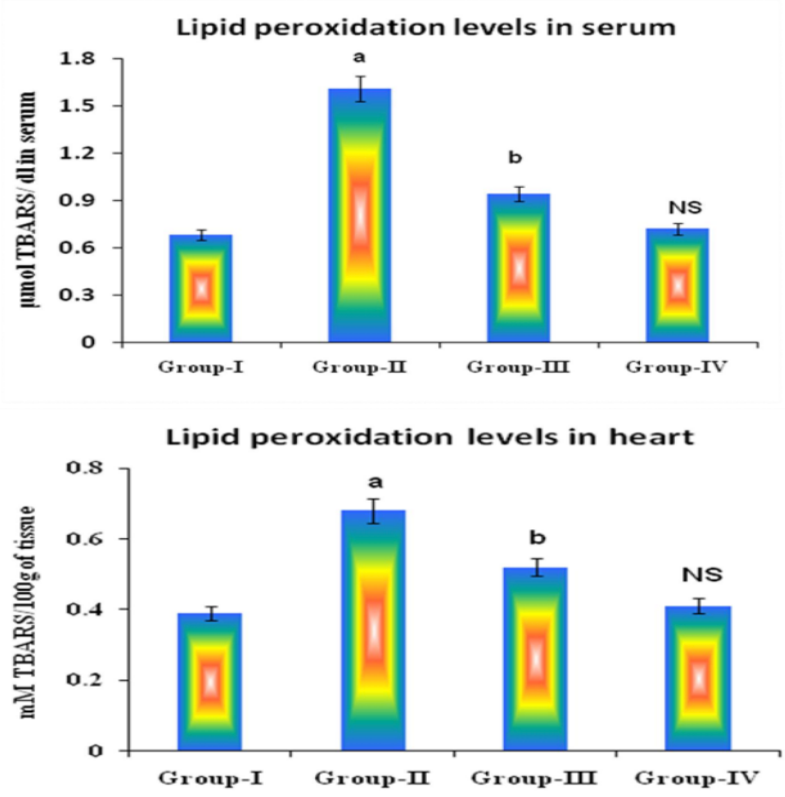

Figure 2: Lipid peroxidation levels in serum and heart tissue in the control, STZ-induced diabetic, and poly herbal extract of *Momordica muricata and Trigonella caerulea* treated animals

Mean standard deviation (n = 6 mice/group). a = significantly different from Group I at the 0.05 level; b = significantly different from Group II at the 0.05 level; NS = not significant. Serum TBARS concentrations are reported in nmol/dl, whereas tissue concentrations are reported in millimoles/100 milligrammes.

Conclusion

The combination of poly herbal extract from Momordica muricata and Trigonella caerulea shows potential as a natural medicine that offers a wide range of health advantages. The study highlights the need for more research to confirm its effectiveness, clarify the best doses, and comprehend its mechanisms of action in different health scenarios. Through ongoing research, this poly herbal extract has the potential to become a helpful supplemental method for enhancing human health and well-being.

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